How the brain controls hand actions: TMS, fMRI and behavioural studies

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Abstract

This thesis focused on testing the predictions made in Milner and Goodale's model and reports finding from experiments investigating how inputs from both the dorsal and the ventral streams are required when we perform hand actions with objects (Chapter 2) and tools (Chapter 3 & 4) using different paradigms such as real and pantomimed grasping and techniques such as transcranial magnetic stimulation, motion-tracking of hand movements and cutting-edge fMRI multivoxel pattern analysis. The primary aim was to gain a new insight on the role of the dorsal and the ventral visual streams in real grasping and pantomiming and to understand what specific aspects of objects and movements associated with them are represented within the two streams. The first experiment (Chapter 2) examined the causal role of the anterior intraparietal and the lateral occipital in object's real and pantomimed grasping using TMS. The results showed that real object grasping and pantomime actions without the objects in hand require the left dorsal stream but that information from the ventral stream is additionally required for pantomiming. The experiments in Chapter 3 and 4 investigated how tools and tool related actions are represented within the dorsal and the ventral stream (Chapter 3) and whether different action end-goals affected early grasping kinematics (Chapter 4). Using MVPA we showed that both dorsal and ventral stream regions represent information about functional and structural manipulation knowledge of tools. Moreover, we showed that both streams represent tool identity, which seems in line with our behavioural findings that tool identity affects grasping kinematics. The current work provided a detailed understanding of how the dorsal and the ventral streams interact in tool processing and propose a more sophisticated view of the distributed representations across the two streams. These findings open up a number of research avenues as well as help understanding how actions are disrupted in brain-damaged patients and advance the development of neural prosthetics.

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Author's Declaration

I declare that the work contained in this thesis has not been submitted for any other award and that it is all my own work. I also confirm that this work fully acknowledges opinions, ideas and contributions from the work of others.

Any ethical clearance for the research presented in this thesis has been approved. Approval has been sought and granted by the School of Psychology Ethics Committee at the University of East Anglia.

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Chapter 1

1. General introduction

1.1 Why study vision and action in psychology?

Vision is one of the main sources of information in our daily interactions with the environment. Every day we are able to process countless visual information in order to make decisions on how to interact and perform actions within our surroundings. Performing movements with our bodies and in particular with our hands, is a meaningful way of interacting with the environment and with people and objects within it. For example, we use hand gestures to communicate with others, to manipulate and move objects around us and also to create music and art.

Nearly all aspects of everyday life require a visually-guided object-directed behaviour (e.g., reaching to grasp an object). For example, when I need to write a note, I need to find a pen on my desk. I look around the room and when I find it, my eyes focus on the pen and the axons coming from the retina of each eye meet at the optic chiasms. Here, information from both the left and the right hemifield is divided and through the lateral geniculate nucleus projected to the contralateral occipital cortex, where visual information is first elaborated (Polyak, 1957). The information is then passed to higher and more specific visual areas for further elaboration. The visual cortex is hierarchically organised into different regions, called V1, V2, V3, V4 and V5/MT+ (Van Essen & Maunsell, 1983). These regions are organised in an orderly manner, so that low-level visual information passes through these regions and become more and more complex and detailed representations through successive stages (Van Essen & Maunsell, 1983). Each region extracts increasingly complex features of the target stimulus, such as lines, orientation, colour, texture, etc. (Livingstone & Hubel, 1988). Following some other intermediary stages of processing, from the visual cortex, information is then projected along two separate, but interacting streams. A ventral stream that extends from the visual cortex to the inferotemporal cortex and is responsible for the extraction of visual perceptual features such as shape, texture, which then lead to object recognition (Goodale

& Milner, 1992, 2013; Milner & Goodale, 1995, 2006, 2008) and a dorsal stream that extends from the visual cortex to the posterior parietal cortex. Is it here, that relevant information for movement planning and execution are processed (Goodale & Milner, 1992, 2013; Milner & Goodale, 1995, 2006, 2008; figure 1.1). Moreover, parietal regions are interconnected with regions in the frontal lobe, such as the primary motor cortex, the supplementary motor area and the dorsal and ventral premotor cortex, and it is in the frontal lobe that intention and decisions to act with objects are coded (e.g., Andersen & Buneo, 2002; Cisek & Kalaska, 2010).

Going back to my example, once I identified the pen, I need to pick it up to be able to use it. A fundamental characteristic of all grasping movements is that grasping points need to be established so that a stable grip can be performed (Napier, 1956). When grasping a small objects, such as a pen, a common way is to use a two-digit precision grip with the index finger and the thumb (Napier, 1956). Although objects can be grasped in a variety of ways (for example: precision grip, whole hand grip, opposition of the thumb and one/two fingers), functional and physical constraints of the objects and the hand limit the number of appropriate grasp types (e.g., although I can grasp a hammer with a precision grip, a whole hand grasp would allow a more stable grasp). Specifically, physical constraints are related to the object's intrinsic (e.g., size, shape and texture) and extrinsic (e.g., location, orientation) characteristics, as well as the postural properties of the hand, while functional constraints depend on how the object will be grasped for the end-goal (MacKenzie & Iberall, 1994). During hand-object interactions, visual feedback provides critical information about both object's characteristics and the position of the hand (Connolly & Goodale, 1999).

In summary, vision has two main functions: the perception of objects and their relationships in our everyday environment and the control of actions directed towards these objects (e.g., visuomotor control) (Goodale & Humphrey, 1998; Milner & Goodale, 1995, 2006). However, for years in classical psychology, the perceptual and the motor systems have been studied separately and while many studies have investigated perception, less attention has been given to visuomotor control (e.g., how vision is critical to programme and control our hand actions; Goodale, 2014; Rosenbaum, 2005). Although it might be necessary to describe the perceptual and the motor systems as two separate systems, this is only an artificial division, as in fact, the two systems process different information but closely work together (Goodale, 1998; Goodale, 2014). Thus, the study of perception and action should not be separated, as vision and the motor output it controls are strictly linked (Rosenbaum, 2005).

The current work will test the predictions based on Milner and Goodale's model (Goodale, 2014; Goodale & Milner, 1992; Milner, 2017; Milner & Goodale, 1995, 2006, 2008) and will investigate specifically how the two visual streams interact using tasks that are thought to require the involvement of both the dorsal and the ventral stream, such as pantomime and tasks involving tool processing and use. In project 1, using continuous theta-burst stimulation (cTBS), I investigated the causal role of the aIPS, a key region for grasping in the dorsal stream, and the causal role of Lateral Occipital (LO) a key region in the ventral stream thought to be involved in shape processing, in real and pantomimed grasping. While in project 1 I used meaningless shapes, in project 2 and 3 I used everyday tools. Specifically, in project 2, I investigated the representations within the tools processing regions and whether these representations vary according to the task (i.e., view or pantomime) and the type of manipulation knowledge (e.g., functional: how a tool is used; or structural: how a tool is grasped for use). In project 3, using real 3D tools and a grasp-to-use and grasp-to-move task, I explored how tool identity and the action end goal modulate grasping kinematics even when structural differences (e.g., the handle) between objects are controlled for.

In the next sections, I will review the relevant literature that led Milner and Goodale to the development of their account of the distinction between the vision-for-perception and the vision-for-action systems, to then move onto evidence that shows how the two streams interact. To date, little is known about how the two streams interact and here, I will review neuropsychological, behavioural and neuroimaging studies investigating the interactions of the two streams using a variety of paradigms such as delayed and pantomimed grasping and tasks using tools.

1.2 One brain, multiple visual streams

Although we experience the visual world as a unitary phenomenon, psychologists and neuroscientists argued that vision is a highly modular process. In 1968, Trevarthen (1968), based on experiments with split-brain monkeys, proposed that "vision of space" and "vision of object identity" are mediated by anatomically distinct processes in the brain. One called "ambient" vision, mediated by the midbrain system (which comprises the tectum, the tegmentum, the substantia nigra, the cerebral peduncle and the cerebral aqueduct) and responsible for visual guidance; the other one, called "focal" vision, mediated by the geniculostriate system (which comprises axons from the neurons in the lateral geniculate nucleus to the primary visual cortex), and responsible for form recognition and identification.

One year later, Schneider (1969), using a lesion approach in hamsters, revealed that ablations of the geniculostriate system were associated with an impairment in the discrimination of patterns, whereas lesions within the superior colliculus (or optic tectum) were linked with the suppression of visually-elicited movements of the head towards objects (e.g., hamsters did not turn their head towards objects). These findings provided evidence for the different functional roles between the retinal projections to the superior colliculus, which plays a crucial role in the localisation of objects in space (Sprague, 1966; for a review see Krauzlis, Lovejoy, & Zénon, 2013) and the system that projects from the retina to the geniculostriate system, which is concerned with the identification of the stimuli. In other words, he proposed a two visual systems model in which there is a distinction between "what" (e.g., object identification) and "where" (e.g., spatial localisation).

Further evidence of the division of the visual system into two distinct pathways, came from a new series of studies of vision in the frog. In the central nervous systems of frogs (and other non-mammalian) the projections from the retina to the brain can be transected and induced to regrow in a different location. By re-wiring neural pathways in the frog, Ingle (1973) showed that visually elicited feeding and visually guided movements around obstacles are mediated by different visuomotor pathways in re-wired frogs. In fact, after unilateral ablation of the frogs' superior colliculus, Ingle (1973) observed that frogs were directing their responses towards the prey presented towards a location that was mirror symmetrical to the actual location of the prey. Similarly, instead of jumping away from the looming obstacle, the frogs were jumping towards it. However, when the same frogs were escaping a touch on their rear by jumping away from it, they always oriented their jump correctly to avoid obstacles in front of them. Histological observation of the frog's brain revealed that the axons of the optic tract, that was transected when the superior colliculus was ablated, regenerated and innervated the contralateral intact tectum, which explained mirror-symmetrical behaviour (Ingle, 1973). The author concluded that, rewired frogs were able to use their vision to guide their jump to avoid a barrier and that the remaining retinal projections were responsible for the visual guidance of barrier avoidance. These observations led him to the hypothesis that there are at least two visuomotor systems in the frog's brain that are independent: a tectal system (which includes the inferior and superior colliculi) which mediates visually elicited prey catching and a pretectal system, which mediates visually guided jumps around barriers.

However, the first great steps in demonstrating the functional modularity of vision at a cortical level, were made by Mishkin, Ungerleider and colleagues in their work with macaque monkeys (Mishkin, 1972; Mishkin, Lewis, & Ungerleider, 1982; Mishkin, Ungerleider, & Macko, 1983; Mishkin & Pribram, 1954; Mishkin & Ungerleider, 1982; Ungerleider & Mishkin, 1982; Ungerleider & Pribram, 1977). In a seminal paper, Ungerleider and Mishkin (1982), proposed that objects' features (what) and objects' location (where) information is carried out in two separate visual streams. In this model, both streams are important for visual perception with different specialisations: the dorsal pathway, that projects from the visual cortex to the posterior parietal cortex, is specialised for spatial vision and is tuned to spatial relationships between objects, whereas the ventral pathway, that projects from the visual cortex to the inferotemporal cortex, is specialised for object vision and is tuned to objects' features (see also Mishkin, 1972; Mishkin et al., 1983). Ungerleider and Mishkin's (1982) model poses a distinction between "where" and "what" at a cortical level and has its roots from studies with monkeys with a lesion in one pathway but not the other (Mishkin & Ungerleider, 1982). According to this model, both streams are important for visual perception, however, for different purposes: the dorsal "where" pathway is tuned to spatial relations between objects and mediates objects 'localisation, while the ventral "what" stream is tuned to intrinsic object features (e.g., size, shape, texture) and mediates object identification.

1.3 Two visual systems hypothesis

In 1992, Goodale and Milner (Goodale & Milner, 1992; Milner & Goodale, 1995, 2008), proposed an alternative perspective of Ungerleider and Mishkin's (1982) model known as the perception and action model (figure 1.1) which places less emphasis on the input to the two streams (e.g., visual object and its location) but instead highlights the output of the two streams (e.g., the way visual information is used, such as for guidance

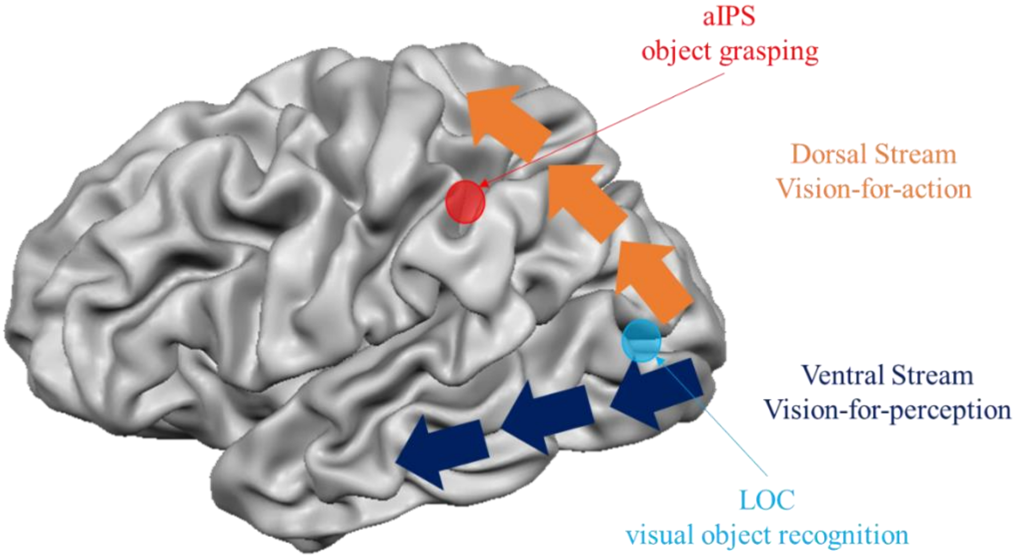


Figure 1.1 The ventral and dorsal visual streams for perception and action (adapted Milner & Goodale, 1992). The ventral stream projects from the occipital to the lateral and inferior temporal cortex (blue arrows) and is specialised for visual perception. The lateral occipital complex (LOC), in cyan, is involved in visual object recognition (Malach et al., 1995). The dorsal stream projects from the occipital to the posterior parietal cortex (in orange) and mediates the visual control of skilled hand actions. At the anterior part of the intraparietal sulcus, area aIPS, in red, is thought to be critical for grasping (Culham, 2003).

of actions). According to this view, both streams process information about the location and the intrinsic features of the objects, however within each stream the information is processed in different ways and transmitted for different purposes.

1.3.1 The ventral stream and visual object recognition

The ventral stream, from V1 to the inferotemporal cortex (ITC), processes visual inputs and transforms them into long-lasting perceptual representations (vision-for-perception) and plays a critical role to the perception and recognition of objects. For example, the ventral stream will allow me to recognise a mug that I previously saw on my desk, even if this is now in the kitchen. Patient DF, and other patients with ventral stream lesions, such as patient MC (Culham, Witt, Valyear, Dutton, & Goodale, 2008) and patient JS (Karnath, Ruter, Mandler, & Himmelbach, 2009) have been critical in gaining insights into the causal functions of the ventral and dorsal stream. The medial and lateral structures of the temporal lobe, known to be critical for memory formation, storage and retrieval of information about object features and identity (Chao & Martin, 2000; Eichenbaum, Yonelinas, & Ranganath, 2007; Patterson, Nestor, & Rogers, 2007; Squire, Stark, & Clark, 2004) are positioned just anterior to the ventral stream, which runs downward from V1 into the temporal lobe. Therefore, the ventral stream is well positioned to receive and integrate low-level visual information with long-term memory representations.

1.3.2 The dorsal stream and visuomotor control

The dorsal stream originates in the primary visual cortex and then extends to the posterior parietal cortex (PPC), which is interconnected with the ventral and dorsal premotor areas in the frontal cortex. It is thought that the dorsal stream processes visual information on a moment-to-moment basis, to transform the information into appropriate motor plans (vision-for-action) and to mediate the visual control of skilled actions online (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006, 2008). With the visual cortex situated posterior and the somatosensory cortex anterior, the PPC is largely recognized as the main associative area dedicated to the coordination between sensory and motor information (Sakata, Taira, Kusunoki, Murata, & Tanaka, 1997). The intraparietal sulcus

(IPS) divides the superior parietal lobe (SPL) from the inferior parietal lobe (IPL). Extensive research using electrophysiological data from macaque monkey have identified various division within the IPS that have been involved in the control of hand actions (e.g., Lewis & Van Essen, 2000b; Seelke et al., 2012), and together with the prefrontal areas, these circuits are critical for the planning and online control of hand actions. With the advent of neuroimaging, similar patterns of functionality have been identified the human PPC (Culham & Valyear, 2006; Culham, Cavina-Pratesi, & Singhal, 2006) which will be reviewed in section 1.7.

Moreover, the connectivity between the parietal and frontal cortices has been comprehensively mapped in a number of studies in monkeys (Andersen, Asanuma, Essick, & Siegel, 1990; Cavada & Goldman-Rakic, 1989; Gharbawie, Stepniewska, & Kaas, 2011; Goldman-Rakic, 1996; Lewis & Van Essen, 2000; Seltzer & Pandya, 1980; Wise, Boussaoud, Johnson, & Caminiti, 1997). In the macaque monkey, neural recordings from the intraparietal sulcus revealed a more specific subdivision that includes a lateral bank that is involved in eye movements (Andersen et al., 1990), a medial intraparietal area that is involved in reaching (Cohen & Andersen, 2002; Johnson, Ferraina, Bianchi, & Caminiti, 1996), and an anterior intraparietal area (AIP) that is involved in grasping (Murata, Gallese, Luppino, Kaseda, & Sakata, 2000; Sakata, Taira, Murata, & Mine, 1995). Gharbawie et al. (2011), examined the connection of the posterior parietal cortex with motor and premotor cortex in New World monkeys using electrical stimulation combined with tracer injections. They found a dorsal parietofrontal network involved in reaching connecting the posterior parietal cortex (PPC) with the dorsal premotor cortex (PMd), and a more ventral parietofrontal network interconnecting the PPC with the primary motor cortex (M1) and the ventral premotor cortex (PMv) involved in grasping.

In the next section, I will review the most relevant findings for the perception and action model derived from testing visual form agnosic patient DF. In fact, although the formulation of the perception and action model is backed by scientific evidence from different disciplines, including primate neurophysiology, neuropsychological neuroimaging and behavioural studies in humans, the centrepiece of the two visual streams hypothesis is findings derived from single neuropsychology cases, in particular patient DF, who presented visual form agnosia.

However, before moving on, I wish to clarify what the authors mean by "perception" and "action". According to the authors (Milner & Goodale, 2008), perception represents our visual experience of the surroundings, but it does not provide the information required for actions, although it does influence actions. By "action" they refer to the use of visual information in the programming and real-time control of hand actions (Milner & Goodale, 2008). Since the formulation of the model, different tasks have been used to assess how the computations require for vision-for-perception differ from the computations required in vision-for-action (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006, 2008) based on their functions (section 1.5).

1.4 Neuropsychological evidence for the perception and action model

1.4.1 From patient DF to the two visual streams hypothesis

In 1988, DF was 34 years old and whilst taking a shower in her house in northern Italy, she suddenly collapsed and lost consciousness due to carbon monoxide intoxication from a leak in her gas water boiler. As reported by Milner and colleagues (Milner et al., 1991), when DF was admitted to hospital, she was in deep coma and had dilated pupils. After two days, she re-gained consciousness and was then transferred to the neurological clinic at the Ospedale Maggiore in Novara for further examinations where she appeared to be blind. However, at clinical examination, the interior surface of her eyes was normal, and she had spare pupillary light reflex. After ten days from the event, she started to see again and she was able to name bright colours, however, she was still showing severe difficulties with ocular fixation.

DF did not show any evidence of neglect or aphasia, however she performed poorly in the visual recognition sub-task in the battery for aphasia, although her auditory and tactile recognition were good (77% correct at 1 month and 100% correct at 12 months). Five weeks after the accident, DF returned to Scotland (where she was originally from), were neuropsychological and psychological testing were carried out at St Andrew's Hospital (for a complete list see Milner et al., 1991). Magnetic resonance imagining investigations carried out close to the event revealed that she had damage ventrally in the lateral occipital region and in the parasagittal occipitoparietal region, however area V1 was largely intact (Milner et al., 1991). Based on the patient report, Milner and Goodale diagnosed patient DF with a severe visual form agnosia, and then decided to investigate her deficits further. Although DF was unable to verbally report the orientation of the slot (Milner et al., 1991) and to rotate the card she was holding to match the orientation of the target slot (Goodale et al., 1991), she oriented her wrist correctly when posting her hand or a card through the slot. This observation was interpreted as evidence that despite having a deficit in perception, DF had a well-preserved ability to coordinate her motor behaviour to the orientation of visually presented targets in front of her (Milner et al., 1991).

To extend these findings and to understand whether other features of an object could be used to drive DF's grasping actions, Goodale et al. (1991) presented pairs of blocks (such as size and shape) with same surface area (Efron, 1969) but different dimensions. DF and two healthy controls were asked to verbally judge if the blocks were alike or different. Moreover, in a separate block, they were instructed to use her index finger and thumb to indicate the width of the blocks. When DF was required to estimate the size of the blocks with her index finger and thumb, her aperture was not related to the size of the blocks (e.g., bigger hand aperture for bigger blocks and smaller for smaller blocks, as observed in healthy participants; Goodale, Jakobson, & Keillor, 1994). Thus, compared to the controls, DF's performance was very poor in both the verbal size judgements and manual estimation tasks, demonstrating that she was insensitive to differences in the size of the stimuli. Remarkably, when DF picked-up the same blocks, the maximum aperture of her fingers (which was achieved in-flight well before touching the object) was systematically related to the size of the object, just as observed in healthy controls. Taken together, these findings suggest that the neural substrates underlying vision-for-perception are distinct from those mediating vision-for-action (Goodale et al., 1991; Goodale et al., 1994; Milner et al., 1991).

Despite her severe deficits in perception (e.g., she cannot recognise a mug), DF had little difficulties in her everyday activities such as grasping a mug, eating meals, reaching out to grasp a pencil and avoiding obstacles on her path. Thus, suggesting that, although she performed poorly when she had to report perceptual features and qualities of objects, she was able to access and use those same features and qualities to guide her actions. In other words, it seems that she could still transform visual information into motor acts (e.g., visuomotor control).

The dissociation between perception and action observed in DF's behaviour is one of the most crucial pieces of evidence that led Goodale and Milner (1992) to develop the perception and action model. Based on DF's neuroimaging evidence and behaviour in visuomotor and perceptual tasks, Milner and Goodale (1992) proposed that while the projections from the visual cortex to the dorsal stream remained largely intact, the projections from the visual cortex to the ventral stream were compromised. Since these observations, other patients have been reported to present similar dissociations, such as for example patient MC (Culham et al., 2008) and patient JS (Karnath et al., 2009).However, in recent years, the evidential basis for the dissociation between perception and action in patient DF has been questioned (see section 1.8). While the lesion data from patient with brain damage is informative, the number of patients showing a particular behaviour and neural plasticity makes it challenging to be certain about the specific role played by areas in the brain. The experiment in chapter 2 in this thesis has been developed to shed the light on the contribution of the dorsal and the ventral stream in visuomotor and perceptual tasks.

1.4.2 Optic ataxia

Indeed, the original formulation of the two visual systems hypothesis was largely built upon observation of patient DF. However, it has also been shown that patients with damage to the dorsal, but not the ventral stream, present the opposite pattern of deficits and preserved functions, with impaired visuomotor performance in the absence of perceptual deficits. In particular, patients with optic ataxia, as a result of damage in their posterior parietal cortex, have been shown to present deficits like misreaching occurring for actions directed to their peripheral visual field and in the online control of reaching and grasping, but are able to perceive and recognise objects well (Milner & Goodale, 1995, 2006; Perenin & Vighetto, 1988).

Optic ataxia was first described in 1909 by Bálint who examined a patient that showed misreaching with his right hand to targets in the peripheral hemifield following bilateral brain infarcts in the parietal region (Bálint, 1909). In the original case observed by Bálint, optic ataxia was associated with other symptoms, such as oculomotor apraxia and spatial disorder of attention (Bálint, 1909), which constitute the Bálint-Holmes syndrome. However, these disorders could not account for optic ataxia, as misreaching only affected the right hand of the patient, whereas the spatial disorder of attention and oculomotor apraxia were exhibited in the left hemispace (Perenin & Vighetto, 1988). Bálint suggested that the deficits observed in his patient were linked to the fact that the hand motor area lacked access to the visual information from the visual cortex. Specifically, he proposed that the deficits in optic ataxia were visuomotor, and not attributable to impairment to sensory and motor functions.

Following Bálint's description, patients with bilateral parietal lesions have been often referred to as Bálint-Holmes syndrome and the misreaching behaviour observed in the first patient has rarely been observed. Since early work conducted by Ratcliff & Davies-jones (1972) in patients with missile wound brain injuries, it has been accepted that the most commonly damaged area in optic ataxia is the intraparietal sulcus, encompassing aspects of the superior parietal lobe (e.g., Perenin & Vighetto, 1988). Garcin (1967) was the first that described a patient with optic ataxia symptoms in isolation from other deficits. In Garcin's (1967) case and in similar later reports, optic ataxia was observed following unilateral (Auerbach & Alexander, 1981; Ferro, Bravo Marques, Castro Caldas, & Antunes, 1983; Levine, Kaufman, & Mohr, 1978; Perenin & Vighetto, 1988; Rondot, De Recondo, & Dumas, 1977) and sometimes bilateral posterior parietal cortex lesions (Boller, Cole, Kim, Mack, & Patawaran, 1975; Damasio & Benton, 1979; Denes, Caviezel, & Semenza, 1982; Perenin & Vighetto, 1988). Patients are typically impaired in reaching objects placed in the periphery in the visual hemifield contralateral to the lesion, with both the right and the left hands, however, cases in which misreaching affects only one hand in one hemifield have also been reported (Perenin & Vighetto, 1988; Rondot et al., 1977).

Based on these observations, optic ataxia has been characterised for the occurrence of misreaching to targets in the peripheral vision, while movements to targets in the central visual field seem unimpaired, thus suggesting that optic ataxia represents a visuomotor coordination deficit (Perenin & Vighetto, 1988). However, more recently, it has been observed that the vast majority of these patients show no or poor grip scaling (e.g., closing their index-finger and thumb in-flight to object size) when grasping objects in their periphery (e.g., Gréa et al., 2002; Jakobson, Archibald, Carey, & Goodale, 1991; Perenin & Vighetto, 1988; Rossetti, Pisella, & Vighetto, 2003). Interestingly, although these patients are unable to reach out to grasp an object, they have no major difficulties in reporting the location and orientation of the same object (Perenin & Vighetto, 1988).

Lesions in optic ataxia have been shown to be located within the intraparietal sulcus (IPS) and adjacent medial superior parietal lobule and upper parietal lobule, are critical for optic ataxia (Auerbach & Alexander, 1981; Buxbaum & Coslett, 1998; Perenin & Vighetto, 1988). Moreover, Karnath and Perenin (2005), using lesion subtraction methods in 10 patients with optic ataxia, identified the centre of the overlap of the lesions at the junction between the inferior parietal lobule, the superior parietal lobule (SPL) and the superior occipital cortex, and extended medially to the precuneus, in the vicinity of the parieto-occipital sulcus (POS). Subsequently, Pisella et al. (2009) reported similar results in a group of patients with optic ataxia, with lesion overlap centred on the parieto-occipital regions.

Although there is controversy (Pisella, Binkofski, Lasek, Toni, & Rossetti, 2006), visual form agnosia and optic ataxia have been argued to constitute a double dissociation between vision-for-perception and vision-for-action in support to the two visual streams hypothesis (Goodale and Milner, 1992; Milner and Goodale, 1995, 2006, 2008; Rossetti, 1998).

In this section, I have reviewed how observations from individuals with visual form agnosia and optic ataxia provide a double dissociation that support the two visual systems hypothesis proposed by Milner and Goodale (Goodale, 2014; Goodale & Milner, 1992; Milner & Goodale, 1995, 2006, 2008). In the next section, I will review evidence for the model from behavioural studies in healthy participants.

1.5 Different neural transformations for vision-for-perception and vision-for-action

According to Milner and Goodale (Goodale & Milner, 1992; Milner & Goodale 2006, 1995), the two visual streams evolved because vision-for-perception and vision-for-action require different transformations of the visual inputs. For example, to be able to grasp the cup of coffee on my desk, my brain must compute the actual size, orientation and position of the mug with respect to the hand I am going to use to pick it up. Some of these transformations reflect the metrics of the object, such as the size, while others are necessary in determining the location of the object in the space and the position of the approaching hand and arm. Critical, is also the time at which these transformations are performed. In fact, the actor and the target object are not in a static relationship with each other and, as a consequence, the position of the target with respect to the hand (i.e., egocentric) can change from moment-to-moment. Thus, it is crucial that the coordinates for action are computed at the moment the movements are performed (Goodale, 2011; Goodale & Milner, 1992; Goodale, Westwood, & Milner, 2004; Milner & Goodale, 1995, 2006, 2008).

On the other hand, Milner and Goodale (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006, 2008) suggested that vision-for-perception does not require the computation of the absolute size of the target objects, nor their location in respect to our hand (i.e., egocentric). This is because our view point over time does not remain constant in respect to the target object, and therefore the ventral stream constructs the visual representations of the surroundings and allows us to identify objects and attach meaning and significance to them, so that we can recognise them in future interactions. For these reasons for the perceptual processing of objects in the environment, the ventral stream processes the size, orientation and location of objects relative to each other (i.e., allocentric) as this allows the observer to generalise over time, thus preserving information about spatial relationships as well as objects' relative size and orientation, even if the observer changes viewpoint. Again, the time is critical, as the products of perception need to be available for a longer time than the information used to control actions, as we might need to recognize objects that we have seen minutes, hours, days or even years before. Computing perceptual representations that are scene-based allow us to maintain the constancies of size, shape, colour and location independently of the viewing condition and over time (Goodale, 2011; Goodale & Milner, 1992; Goodale et al. 2004; Milner & Goodale, 1995, 2006, 2008).

Over the last two decades, these differences in metrics, timing and frames of references of vision-for-action and vision-for-perception have been tested using different paradigms (e.g., size estimation, real grasping, pantomimed and delayed grasping).

1.5.1 Metrics and Timing

In a seminal paper Goodale et al. (1994) carried out a series of experiments to investigate differences in movement kinematics in real, delayed pantomimed and pantomimed grasping with healthy participants and patient DF. In the first experiment, healthy participants were presented with objects and were asked to reach out and grasp them with a precision grip. In one block of trials, participants were presented with an object, then their vision of the object was occluded for 2s, and participants were instructed to reach out and pick up the object as soon as it was visible again (delayed real grasping). In another block of trials, the object was on the table at the beginning of the trial, however, during the 2 s in which the object was not visible, the object was removed from the table and participants had to remember where the object was and how it looked like to pretend to pick-up from memory (delayed-pantomimed grasping). The two tasks were presented in blocked and mixed order. The main difference between the two tasks is that the delayed real grasping task is a target-driven movement, and the delayed-pantomimed grasping task is a memory-driven action as the object is no longer present when the grasping is initiated and executed and, therefore the grasping movement is pantomimed. The authors observed that pantomimed delayed movements reached lower velocity during the transport of the hand, lasted longer, followed more curvilinear trajectories and participants raised their wrist higher off the table, compared to delayed real grasping movements. Participants scaled their grip in-flight to the object size in both tasks, however, grip apertures in the delayed-pantomimed task were smaller compared to the real grasping task. Moreover, participants took proportionately less time to open their hand under the delayed pantomimed task compared to the normal grasping. These effects were observed in the blocked and in the mixed task (the only difference that was found is that movement amplitude and height of the wrist were slightly greater in the mixed than the blocked task). The authors suggested that these tasks relied on different mechanisms, a hypothesis that was then tested with patient DF. In particular, visuomotor information is computed immediately before the action started. In the real grasping trials, the programming of the action relied on the visual information available at the moment, whereas in the delayed pantomimed trials, the programme would rely on information about the object and its location stored in memory (as the object is not visible at the moment the action is initiated). To ensure the accuracy in target-directed grasping movements, information such as the size, the orientation and position of the object in relation to the observer need to be computed at the precise moment the action is initiated and updated constantly as the hand moves towards the object. Thus, the visuomotor networks controlling real grasping appear to operate in real time and do not rely on memory. On the other hand, delayed pantomimed actions might rely on stored representation of the object, provided by the ventral stream.

To test the idea that delayed-pantomimed actions and real grasping actions relied on different mechanisms, the authors tested DF under real and delayed-pantomimed grasping. The authors predicted that, if it is true that delayed-pantomimed actions depend on information stored in the perceptual system, DF's performance should be inaccurate following from her lesion in the perceptual system underlying object recognition. Here, DF and healthy controls were tested under the same conditions described in the first experiment, however, in addition to the 2 s delay, a longer delay of 30 s was included. In the real grasping task, DF's consistently scaled her grip aperture to object size, which was consistent with the authors earlier reports (Milner et al., 1991). However, when even a short delay was imposed between the viewing of the object and the initiation of the movement, DF's grip scaling was no longer evident. The authors argued that, in delayed-pantomimed grasping task, DF cannot use the stored representation of the object as she cannot perceive the object's features in the first place. Importantly, the authors reported that differences in DF's performance between real grasping and delayed-pantomimed cannot be explained by a difference related to the absence of visual feedback in the latter task (versus presence of visual feedback in the real grasping). To clarify their point, Goodale et al. (1994) reported as evidence an unpublished observation that even when the view of the target and the moving hand is prevented (e.g., open-loop), DF showed appropriate scaling of her grip aperture during real grasping.

In the third experiment, DF and healthy controls were presented with two tasks: in the first condition, they were required to reach out and grasp an object presented along their midline (real grasping), while in the second condition they viewed an object presented slightly off the midline and were then required to imagine an identical object on the midline and pretend to grasp it (immediate pantomimed grasping). DF's performance in this task was marginally better than in the delayed pantomimed grasping, however, her responses in the immediate pantomimed task were extremely variable compared to the real grasping task. As such, DF showed poor grip scaling to object size in the immediate pantomimed grasping (figure 2.1). Based on DF's poor grip scaling in the immediate pantomimed grasping task, the authors suggested that not only delayed-pantomimed actions, but also immediate pantomimed actions rely on stored perceptual information about the object (Goodale et al., 1994). Critically, DF's poor performance in delayed pantomimed grasping cannot be associated with a more general impairment in her memory. In fact, in a series of experiments, used as control, Goodale et al. (1994) reported that DF was able scale her grip aperture as accurately as healthy participants when asked to show how she would pick up an imaginary grapefruit or a tangerine (Goodale et al., 1994). However, if she had to make a manual perceptual judgement of the size of an object in front of her, her manual estimations did not correlate to the object's size (unlike healthy controls), but she was able to match the distance between her thumb and index finger to verbally specified (either inches or centimetres) measures (e.g., 5 cm, 4.5 cm, 3.5 cm) by the experimenter.

To summarise, Milner and Goodale (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006) argued that the kinematics of pantomimed and real grasping are substantially different, reflecting different neural substrates. Specifically, pantomimed actions consistently tend to last longer and reach lower peak velocities, follow more curvilinear trajectories, undershoot target location and reach smaller in-flight grip apertures. Based on evidence from patient DF, they proposed that DF's spared real grasping is mediated by the visuomotor system in the dorsal stream, which although shows evidence of reduced cortical thickness, appeared largely intact (Bridge et al., 2013), however, for offline actions, such as delayed-pantomimed grasping, the information from the ventral stream is additionally required. This argument has been supported by studies with patients with optic ataxia who showed poor grip scaling during real grasping for objects presented in their periphery, but paradoxically improved when they were pantomiming a grasping movement (Milner et al., 2001).

1.5.2 Frames of reference

In 1981, Pick and Lockman (1981) defined the notion of frame of reference as "a locus or set of loci with respect to which spatial position is defined" (Pick and Lockman, 1981, p.40). In other words, the spatial location of an object in the surroundings can be computed in two ways: (i) in relation to the spatial position of the observer (i.e. egocentric frame of reference), (ii) in relation to the spatial position of other objects in the scene (i.e., allocentric frame of reference), which is independent from the presence or the position of the observer.

For example, when I grasp the mug on my desk, my brain must compute the actual size, shape and orientation of the mug, and represent its location in relation to me (i.e. egocentric frame of reference). Moreover, as the action unfolds, the position of the object relative to the actor quickly changes and therefore the coordinates of the location of the object must be continuously updated with respect to my hand and body. For this reason, it is critical that the information required to perform online actions is computed in an egocentric frame of reference (Milner & Goodale, 1995, 2006, 2008).

On the other hand, perceptual representations of the size and shape of objects, use a scene-based frame of reference (i.e., allocentric) (Jacob & Jeannerod, 2003; Milner & Goodale, 1995, 2006, 2008). Encoding information in an allocentric frame of reference preserves information about the relative features of an object (such as size, location and orientation), however, it does not store information such as the distance from the observer.

When we interact with objects, we are never in the same exact position relative to the object, thus, the recognition of objects over time and in different settings requires an object-dependent representation, which is independent from the viewer's position. Milner and Goodale (1995, 2006, 2008) hypothesised that the ventral stream might play a crucial role in allocentric visuospatial coding and creates long-term representations of objects (Milner & Goodale 1995, 2006, 2008; Schenk, 2006), whereas the dorsal stream processes egocentric representations necessary to guide actions (Foley, Whitwell, & Goodale, 2015; Milner & Goodale, 1995, 2006, 2008).

In this view, DF's relatively spared dorsal stream enables her to grasp a target object, which suggests that she can code the spatial position of an object in an egocentric frame of reference. However, she is unable to make perceptual judgements of the relative size and shape of the same objects, which require allocentric coordinates.

Nevertheless, there is controversy around this and other claims of the model (see section 1.8).

1.6 Parietal mechanisms of hand actions

1.6.1 Neurophysiology of reaching and grasping in monkeys

The first indication of the crucial role of the posterior parietal cortex (PPC) in the visual guidance and control of grasping has its roots in early electrophysiological investigations in non-human primates, which showed "hand manipulation" neurons in Broadmann's area 7 in the inferior parietal lobule (IPL) (Hyvärinen & Poranen, 1974; Mountcastle, Lynch, Georgopoulos, Sakata, & Acuna, 1975). The authors recorded from single neurons in PPC in monkey and reported that there are neurons that fire selectively when the monkey grasped and manipulated an object, but were not activated during the transport phase of grasping nor during random movements with the hand (Hyvärinen & Poranen, 1974; Mountcastle et al., 1975).

Further electrophysiological studies revealed that neurons in the anterior intraparietal area (area AIP) on the ventral bank of the intraparietal sulcus play an important role in hand preshaping and grasping (Murata et al., 2000; Sakata et al., 1997; Taira, Mine, Georgopoulos, Murata, & Sakata, 1990). Area AIP is strongly interconnected with area F5 in the ventral premotor cortex (Rizzolatti et al., 1988), in which neurons are activated during object manipulation (e.g. pull a lever) (Sakata et al., 1995; Taira et al., 1990).

In a series of experiments, Sakata and colleagues (Sakata et al., 1997, 1995; Taira et al., 1990) have looked at visual and motor responses of neurons during hand actions and have shown that neurons within area AIP were tuned to the configuration of the hand in accordance with the objects shape. Additionally, they reported that neurons that showed a selectivity for a given object in the view condition, showed selectivity for the same object during grasping. Moreover, when the AIP is inactivated (using injections of a GABA agonist), the monkey's ability to use vision to pre-shape its contralateral hand to reach and grasp objects of different shape, size and orientation is severely impaired. Specifically, in the baseline condition, to grasp a small object placed in a groove, the monkey was using a precision grip in which it was extending the index finger and simultaneously flexing the three other fingers during the approaching phase. However, after the inactivation injection, this pattern was lost, and the monkey's fingers were often touching the flat surface with failure of inserting the index finger into the groove. The authors suggested that AIP plays a critical role in visually guided hands movements (Gallese, Murata, Kaseda, Niki, & Sakata, 1994).

As mentioned above, AIP is strongly interconnected and sends outputs to area F5 in the premotor cortex (Borra et al., 2008; Luppino, Murata, Govoni, & Matelli, 1999; Matelli & Luppino, 2001). Response properties of neurons in the parietal area AIP show similarities with those in F5, but also important differences. Like AIP, area F5 contains neurons that show selectivity for particular objects, meaning that they fire when the object is presented visually but also when an action towards it is required (Murata et al., 1997; Vassilis Raos, Umiltá, Murata, Fogassi, & Gallese, 2006; Rizzolatti et al., 1988; Rizzolatti, Fadiga, Gallese, & Fogassi, 1996). Additionally, Murata et al. (1997) have shown that objects that make neurons in F5 fire more strongly when viewed are typically of a shape that makes the same neurons fire when grasping the object.

Area F5 has been shown to have neurons specifying the kinematics of actions tuned to the goal of the action, as such two actions requiring similar movement kinematics, but with different action goals outcomes, will not activate the same F5 neurons (Rizzolatti & Luppino, 2001). Reversible inactivation of area F5, results in disruptions in hand preshaping during grasping movements (Fogassi, 2001), a similar effect to the one observed after inactivation of AIP (Gallese et al., 1994). Notably, recording from population of neurons in F5 can accurately predict the upcoming kinematic features of reaching and grasping actions (Stark & Abeles, 2007). Moreover, it has been shown that neurons in F5 show greater and earlier responses for particulars objects (e.g., plate, ring, cylinder, cone, cube) or grasping movement (e.g., side precision grip, precision grip, hook grip with the index finger or all the fingers) compared to M1 (Umilta, Brochier, Spinks, & Lemon, 2007). The authors argued that these observations are consistent with the view that neurons within F5 translate the visual information about the object features into the corresponding motor plans that are then received by M1, in which these plans are refined and sent to the "spinal machinery" that controls hands and digits muscles (Umilta et al., 2007)

It has been proposed that in the macaque the circuit between AIP and F5 constitutes the cortical mechanisms responsible for the visuomotor transformation underlying the guidance and the control of objects' grasping and manipulation (Fagg & Arbib, 1998; Jeannerod, Arbib, Rizzolatti, & Sakata, 1995; Matelli & Luppino, 2001). However, these regions do not operate alone but in parallel with others such as area F2 (e.g., Castiello & Begliomini, 2008) and parietal area V6A (Fattori et al., 2010; Fattori, Breveglieri et al., 2009). In area AIP and F5, with neurons that fire when an action is performed (called canonical neurons), Rizzolatti and collaborators (1996) observed another type of neurons, known as "mirror neurons" that fire both when the monkey executed the action and when was observing someone else performing the action (di Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992; Gallese, Fadiga, Fogassi, & Rizzolatti, 1996; Rizzolatti et al., 1996).

Mirror neurons were originally discovered in the premotor cortex of the monkey (for a review: Rizzolatti & Craighero, 2004) and subsequently around the intraparietal sulcus (Fogassi et al., 2005). While canonical neurons respond to the presentation of an object, mirror neurons respond to the execution of an action as well as to the observation of object-directed actions (Rizzolatti & Craighero, 2004; Rizzolatti, & Luppino, 2001) Thus, mirror neurons fire both when the same actions are executed and observed (Gallese et al., 1996), which led to the account that an observer is able to understand the action performed by someone else through an implicit motor simulation process (Gallese & Goldman, 1998; Rizzolatti & Craighero, 2004). In addition to action understanding, mirror neurons have been proposed to underlie a wide range of functions including observational learning (Cross, Kraemer, Hamilton, Kelley, & Grafton, 2009; Frey & Gerry, 2006; Mattar & Gribble, 2005), imitation (Buccino et al., 2004; Iacoboni et al., 1999), theory of mind (Agnew, Bhakoo, & Puri, 2007; Iacoboni, Molnar-Szakacs, Gallese, Buccino, & Mazziotta, 2005) and social cognition (Gallese, 2006; Marco Iacoboni & Dapretto, 2006; Leslie, Johnson-Frey, & Grafton, 2004). Although there is evidence that mirror neurons are present throughout the motor system in humans, including the dorsal and ventral premotor cortices and the primary motor cortex (for a review: Kilner & Lemon, 2013), the functional role and significance of mirror neurons is still not well established (Decety & Grèzes, 1999; Hauser & Wood, 2010; Hickok & Hauser, 2010; Jacob & Jeannerod, 2003; Kilner & Lemon, 2013).

Taken together, evidence from monkey neurophysiology suggests that the parietal cortex plays an important role in the control of actions and consistent results suggests that the homologue of the macaque AIP in humans is located at the junction between the intraparietal sulcus and the inferior post-central sulcus (Culham, Cavina-Pratesi, & Singhal, 2006). Moreover, electrophysiological studies indicated that area V6 in the parieto-occipital sulcus, which was thought to be specifically related to reaching and the direction of arm movements, shows response for grasping similar to area AIP (Fattori et al., 2010; Fattori, Breveglieri et al., 2009). Specifically, reaching-related neurons in macaque area V6A appear to be sensitive to reach direction (Fattori, Breveglieri, Amoroso, & Galletti, 2004), target orientation (Fattori, Pitzalis, & Galletti, 2009; Galletti, Fattori, Gamberini, & Kutz, 1999) and grasp configuration (Fattori et al., 2010). Similarly, grasping-related activations have been reported in the superior parieto-occipital cortex (SPOC; e.g., Begliomini, Caria, Grodd, & Castiello, 2007; Begliomini, Wall, Smith, & Castiello, 2007; Gallivan, McLean, Valyear, Pettypiece, & Culham, 2011), which is considered the human homolog for the monkey area V6A (Cavina-Pratesi et al., 2010; Pitzalis et al., 2013; Rossit, McAdam, Mclean, Goodale, & Culham, 2013).

1.7 Neuroimaging evidence

Human neuroimaging experiments confirmed a broad overlap between cortical areas that show activation during action observation and areas where mirror neurons have been observed in monkeys, such as ventral and dorsal premotor cortex and the inferior parietal lobule (Kilner & Lemon, 2013; Molenberghs, Cunnington, & Mattingley, 2012). Kilner and Lemon (2013) suggested that changes in BOLD signal during action observation tasks seem to be consistent with the account that the mirror neuron system exists in humans, however this is still unclear. The authors proposed that a possible way of attributing the fMRI response to mirror neurons may be to use fMRI adaptation or repetition suppression. The rationale behind fMRI adaptation is that during single-unit recording studies with non-human primates, neurons that are selective for a particular attribute, such as movement type, reduce their firing rate when the same stimulus is shown repeatedly (Dinstein, Hasson, Rubin, & Heeger, 2007). Similarly, it has been argued that the BOLD signal will also decrease with repeated presentations (Krekelberg, Boynton and van Wezel, 2006).

It is important to highlight that since the advent of modern neuroimaging techniques, progress in mapping the functional organisation of the ventral and the dorsal streams has moved forward rapidly.

One year after the accident, DF’s structural MRI scan showed that she has a damage bilaterally in the ventrolateral region of the occipital cortex, however, her visual cortex remained largely intact (Milner et al., 1991). Based on this evidence and on DF’s behaviour in visuomotor and perceptual tasks, Milner and Goodale (1992) proposed that while the projections from the visual cortex to the dorsal stream remained largely intact, the projections from the visual cortex to the ventral stream were compromised. With the advent of modern high-resolution functional neuroimaging techniques James, Culham, Humphrey, Milner and Goodale (2003) examined DF’s brain activation while she was presented with intact and scrambled images of common objects or she was instructed to reach and grasp blocks. Based on the anatomical images collected during this testing session, the authors confirmed the earlier assessment made from fMRI scans carried out one year after the incident (Milner et al., 1991). Specifically, James et al. (2003) reported a diffuse pattern of cortical brain damage with a concentration of damage in bilateral ventral lateral-occipital cortex, larger in the right than in the left hemisphere. Despite the diffuse damage, the primary visual cortex and the fusiform gyrus appeared to be spared, James et al. (2003), reported that DF has bilateral damage in her ventral stream and particularly in the lateral occipital complex (LOC), a region implicated in visual object recognition (Grill-Spector, Kourtzi, & Kanwisher, 2001; Malach et al., 1995). Crucially, the comparison of DF's ventral lesion sites with functional activation in neurologically intact participants when they are presented with intact versus scrambled images of objects (Culham et al., 2003) highlighted that the lesion was restricted to the object selective area, named lateral occipital (LO). However, DF did not show any activation in this region. Furthermore, James and colleagues (2003) reported previously undetected lesions (despite smaller than to the ones in the ventral stream) in the left posterior parietal cortex (PPC). In the goal-directed task, DF, like the healthy controls, showed activation during reaching and grasping in her dorsal stream. In particular, during grasping, DF (like healthy controls) showed activation at the junction of the post-central sulcus and the anterior intraparietal sulcus. This activation was clear in the right hemisphere (compared to bilateral activation in healthy controls), but no activation was found in the same region in the left hemisphere. Moreover, DF showed no activation in the superior parieto-occipital sulcus (SPOC), a region that has repeatedly been shown to be involved in visuomotor control, especially for reaching in peripheral vision (e.g., Cavina-Pratesi et al., 2010; Connolly, Andersen, & Goodale, 2003; Gallivan & Culham, 2015; Gallivan, McLean, & Culham, 2011; Monaco et al., 2011; Rossit, McAdam, Mclean, Goodale, & Culham, 2013). Although lesions have been observed in the parietal cortex and in particular in the left hemisphere, grasp-related activation was evident in DF's right hemisphere. The authors concluded that DF can use her dorsal stream to perform visually guided movements and that this system is able to work well to process size and orientation to guide object-directed grasping movements, although the object recognition network in the ventral stream is destroyed.

More recently Bridge et al. (2013) found regions with reduced cortical thickness in DF's ventrolateral cortex (including the LOC) and posterior IPS. Additionally, they observed reduced detection of stimuli in the right and left lower visual field. Overall, the authors confirmed that DF's early visual areas are fairly normal (in line with Milner et al., 1991). Based on their results, Bridge et al. (2013) suggested that DF's spared visuomotor control of grasping is mediated by a relatively intact visuomotor network in her dorsal, while her impaired performance in perceiving objects is the results of her ventral stream's lesions.

With respect to the functional characterisation of areas within the ventral stream important for object recognition, neuroimaging studies have identify different activation foci within the lateral and inferior temporal occipital cortex known as the lateral occipital complex (LOC; Malach et al., 1995). Areas within the LOC are selectively activated by images of objects versus scrambled images, suggesting that this area is involved in shape processing (e.g., Grill-Spector, Kushnir, Edelman, Itzchak, & Malach, 1998). Moreover, the anterior fusiform components of area LOC show size, position and orientation invariance (Grill-Spector et al., 1999; James, Humphrey, Gati, Menon, & Goodale, 2002; Valyear, Culham, Sharif, Westwood, & Goodale, 2006; Vuilleumier, Henson, Driver, & Dolan, 2002), which is expected within a brain region underlying object recognition (i.e., to achieve recognition despite variation in the size, location or position of the object and the position of the observer). Several areas within the ventral stream have been reported to be activated selectively for particular categories, such as objects, tools, faces, scenes, and body parts (e.g., Bracci, Cavina-Pratesi, Ietswaart, Caramazza, & Peelen, 2012; Lingnau & Downing, 2015; Peelen et al., 2013). fMRI studies revealed that viewing pictures of tools, performing visual task on pictures of tools, reading names of tools or planning tool-related-gesture or actions preferentially activated the lateral occipitotemporal cortex (LOTC) (e.g., Gallivan, McLean, Valyear, & Culham, 2013; Johnson-Frey, 2004; Orban & Caruana, 2014). Additionally, fMRI studies identified a region within the lateral occipitotemporal cortex (LOTC), called the extrastriate body area (EBA) that selectively responded to images of human bodies and body parts versus images of faces, animals, objects or scenes (Downing, Jiang, Shuman, & Kanwisher, 2001;

Downing & Peelen, 2011). Moreover, Bracci, Ietswaart, Peelen and Cavina-Pratesi (2010), identified multiple subregions of LOTC that coded for specific body parts, including a left-lateralised hand-selective area, which closely overlap with a region that is preferentially activate for tools versus objects (Bracci et al., 2012; for a description of studies see chapter 3). Although the ventral stream lies distant from the motor regions in the frontal and parietal cortex, fMRI studies have shown that activity within LOTC increases during the preparation and execution of unseen movements with the arm (Astafiev, Stanley, Shulman, & Corbetta, 2004) and the hand (Kühn, Keizer, Rombouts, & Hommel, 2011). Thus, it has been hypothesised that hand and tools representations within the LOTC are integrated (Lingnau & Downing, 2015) and interact with regions in the parietal cortex implicated in tool manipulation knowledge (Bracci et al., 2012; Lingnau & Downing, 2015).

In the dorsal stream, fMRI studies have repeatedly shown that the anterior intraparietal sulcus (aIPS) is strongly activated by visually guided grasping (Binkofski et al., 1998; Culham et al., 2003; Frey, Vinton, Norlund, & Grafton, 2005; Grèzes, Tucker, Armony, Ellis, & Passingham, 2003) and by the mere presentation of graspable objects, even when no hand actions are required (Grèzes et al., 2003; Peuskens et al., 2004; Shikata et al., 2001, 2003). Using fMRI, Culham et al. (2003) showed that contrasting brain activation for grasping versus reaching revealed left lateralised activation at the junction between the intraparietal sulcus (IPS) and the post-central sulcus, in the aIPS for actions performed with the right hand. On the other hand, while no aIPS activation was found for images of intact versus scrambled images of familiar objects, this contrast showed bilateral activation in the lateral occipital cortex (LOC). In line with the perception and action model (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006), the authors concluded that, although object-directed action and perceptual processing of objects both require the processing of objects' properties (such as size and shape), these features are differently computed in different pathways. Moreover, they argued that these findings are in line with DF's performance in real grasping tasks. Moreover, similar to non-human primates, the aIPS has been shown to be activated when participants were performing visually-guided grasping to a target object, object manipulation with no vision available and the mere view of 3D graspable objects, such as tools (Chao & Martin, 2000; Creem-Regehr & Lee, 2005; Culham & Valyear, 2006; Culham et al., 2003; Vingerhoets, 2014). In contrast, the mere view of objects that are not graspable does not activate the aIPS (Culham et al., 2003). Additionally, a similar circuit to the one observed between AIP and F5 in monkeys, has been identified in humans linking the aIPS with the ventral premotor cortex (PMv), which is involved in selecting the appropriate grip type (Ehrsson et al., 2000).

Moreover, although reaching and grasping can be studied separately, in our everyday interactions they often occur together. Different lines of research have identified two sub-networks in the dorso-dorsal dorsal stream: one between aIPS and PMv relevant for grasping and another between the superior posterior occipital cortex (SPOC) to middle IPS and the dorsal premotor cortex relevant for reaching (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010; Rizzolatti & Matelli, 2003, see section 1.10.3).

1.8 Critics to the two visual systems hypothesis

The two visual streams hypothesis proposed by Milner and Goodale (1992; 1995) almost 20 years ago and subsequently refined (Milner & Goodale, 2006, 2008) has been inspiring to stimulate novel research in vision science and has served well in organizing a large body of evidence from the fields of neuropsychology, animal and human neurophysiology, neuroimaging and psychophysics. Milner and Goodale's paper "*Separate visual pathways for perception and action*" has been cited 5725 times (information retrieved from Google Scholar, August 2018), however, over the last decade, the division of labour between the ventral and the dorsal stream originally proposed by Milner and Goodale (1992, 1995) has received critiques (Franz & Gegenfurtner, 2008; Rizzolatti & Matelli, 2003; Schenk, 2006; Schenk, 2012a,b; Schenk, Franz, & Bruno, 2011; Schenk & McIntosh, 2010; Smeets & Brenner, 2006).

Before proceeding, I would like to clarify that, in addition to the evidence reviewed below, one of the aspects that has proven to be a controversial evidence for the two visual systems hypothesis is the interpretation of motor and perceptual responses to visual illusion paradigms. However, the literature on visual illusions is long, extensive, and well beyond the purpose of this thesis, and therefore it will not be reviewed here (for a review, see for example: Bruno, 2001; Bruno & Franz, 2009; Carey, 2001; Milner & Goodale, 1995, 2006, 2008).

I have already discussed how the most compelling evidence for the key assertions of Milner and Goodale's model (1992) is the reported dissociation between perception and action in patients with lesions to the ventral or the dorsal stream respectively (Goodale & Milner, 1992; Goodale et al., 1991; Milner et al., 1991). However, behavioural evidence for the double dissociation between action and perception in these patients is incomplete. In fact, patients with visual form agnosia and optic ataxia have not been tested under matching condition (Pisella et al., 2006; Rossetti et al., 2003; Rossit et al., 2017). In particular, patients with optic ataxia generally show impaired visuomotor performance in tasks performed under peripheral vision, in contrast to near-normal performance in central or free-vision (e.g. Cavina-Pratesi et al., 2010, Pisella et al., 2006), while DF's performance has been tested mainly in central or free vision (althoug see Hesse, Ball, & Schenk, 2012, 2014; Rossit et al., 2017).

Investigation of perception in optic ataxia patients has shown the existence of perceptual deficits in peripheral vision (Michel & Henaff, 2004; Perenin & Vighetto, 1988; Pisella et al., 2009; Rossetti et al., 2005). On the other hand, patients with visual form agnosia (mainly DF), have been mostly tested in central vision. More recently, Hesse, Ball and Schenk (2012) investigated DF's grip scaling performance in central and peripheral vision and reported that DF scaled her grip to object size in free vision, however, when targets were presented in her periphery, she was unable to scale her grip to object size, showing an impairment similar to optic ataxia patients. The authors hypothesised that DF (i) due to her damage in the dorsal stream (as reviewed in 1.7), has optic ataxia in addition to visual form agnosia or (ii) the visuomotor deficits observed in DF are related to her destroyed ventral stream. In a second study, Hesse, Ball, & Schenk, (2014), showed that DF was impaired in pointing in the periphery with both hands and in both visual fields.

Recently, Rossit et al. (2017) tested DF's and a group of healthy controls' reaching abilities in central and peripheral vision. The authors observed that, while in the free-vision condition, DF was as accurate as the control group, she was severely impaired when reaching to targets in the periphery. As such, she presented a bias toward the fixation, undershot the target position and her error rate increased with the increase of the eccentricity of the target. Based on evidence that patients with optic ataxia are impaired in quickly correcting reaching movements online under free vision (Pisella et al., 2000), in two additional experiment, Rossit et al. (2017) examined DF's (and healthy controls) reaching corrections under a fixation-controlled condition and under free vision. The authors reported that DF was unable to make fast corrections to the target jump to the left or to the right, which is thought to be a core function of the dorsal stream (Pisella et al., 2000). Specifically, DF was showing much slower correction times compared to controls in both the fixation-controlled and free vision condition. The authors concluded that DF might not be a good example of a patient with a lesion restricted to her ventral stream (due to her lesion in the dorsal stream, as shown by James et al. (2003)), and instead she could be characterised as a patient with both visual form agnosia and optic ataxia following a combined dorsal and ventral stream lesion (Hesse et al., 2012; Rossit et al., 2017). As such, the previously observed dissociations between perception and action in DF might need to be further investigated as the originally proposed hypothesis of her preserved dorsal stream guiding her hand action, despite her destroyed ventral stream, has now been challenged.

Another criticism to the two visual system hypothesis, has been put forward by Schenk (2006), who challenged the interpretation of the perception and action dissociation observed in DF, by proposing that the dissociation is not between perception and action but instead between allocentric and egocentric coding.

Schenk (2006) tested DF's and a group of healthy controls' ability to use egocentric or allocentric spatial processing in different perceptual and motor tasks (figure 1.2).

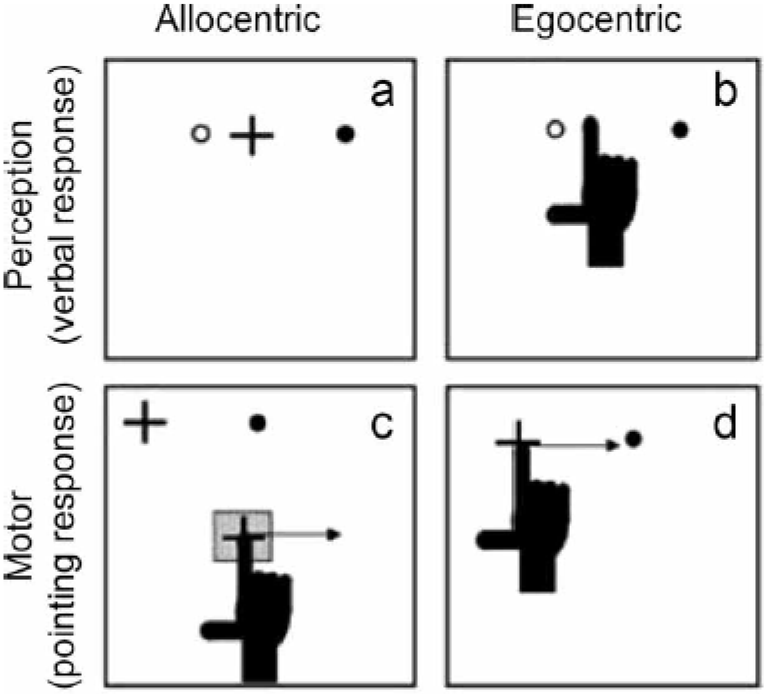


Figure 1.2 The tasks used by Schenk (2006). (a) Allocentric perception task: DF was instructed to make a verbal judgement as to which of two stimuli was closer to a target cross located between them. (b) Egocentric perception task: DF was instructed to make a judgement as to which of two stimuli was closer to a target cross located between them, but this time her index finger was located at the reference point. (c) Allocentric motor task: DF was instructed to make a motor response (pointing) from an arbitrary start point to match the distance of the target stimulus from the reference point. (d) Egocentric motor task: DF was instructed to make a direct pointing response from a start location to the target stimulus. From "An Allocentric Rather than Perceptual Deficit in Patient D.F.", by Schenk, 2006, Nature Neuroscience, 9, pp. 1369–1370. Copyright 2006 by the Nature Publishing Group. Adapted with permission.

DF's performance in the allocentric perceptual task, was significantly impaired when compared to controls. As such, her judgements were less accurate than controls. In contrast, her performance in the egocentric motor task, was similar to the controls. Taken together these results are in line with the two visual streams account (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006) as pointed out by Schenk (2006). However, DF's performance in the perceptual egocentric task appeared to be as accurate as controls, while her performance in the motor allocentric condition was significantly less accurate than controls. Schenk (2006) argued that these results did not fit the pattern of results predicted by Milner & Goodale account (1992; 1995; 2006). Instead, Schenk (2006) proposed that is not the task (perceptual versus action) determining DF's performance, but the frame of reference (allocentric versus egocentric).

In response to Schenk's (2006) criticism, Milner and Goodale (2008) argued that it was not surprisingly that DF did poorly in the allocentric perceptual task (figure 1.2a) and that her performance improved in the egocentric perceptual task and that these results could be explained by the model. Milner and Goodale (2008) also pointed out that, although DF did not perform significantly worse than controls in the egocentric perceptual task, the amplitude of her responses was more variable than controls. Thus, they suggested that in the egocentric perceptual task, DF might have used a different strategy in which she imagined making pointing movement to the stimuli to help her judge which one was closer, and therefore she might have implemented a non-perceptual strategy to complete the task (Milner & Goodale, 2008). Regarding DF's poor performance in the allocentric motor task, Milner and Goodale (2008) argued that the task was not actually testing vision for action. Instead, what DF was required to do was to produce what she perceived using a non-verbal manual estimation approach, similarly to when she is required to estimate the size of objects with her finger, pantomime or to complete anti-pointing tasks, and which was also similar in essence to the verbal report used in the allocentric perceptual task. Therefore it wasn't surprisingly that DF's performance was poor in both the allocentric tasks, as they were testing spatial perception (Milner & Goodale, 2008).

More recently, in another series of experiments Schenk (2012a) investigated whether DF uses tactile feedback to compensate for her deficit in size perception (figure 1.3). As reviewed in 1.4.1, Goodale et al. (1994) showed that DF is unable to pantomime grasping movements, although she can reach out and grasp an object. This observation prompted the suggestion that her ability to accurately perform grasping tasks relies on the availability of a contact with the object (i.e., haptic feedback; DF performed well on the standard grasping task (figure 1.3a), however in the grasping without haptic feedback (figure 1.3b), she was unable to scale her grip to object size (as previously observed by Goodale et al., 1991). In the grasping task in which haptic feedback was provided in 50% of trials (figure 1.3 c and d), DF's grip scaling performance was less accurate than healthy controls, however this difference was not significant, while in the grasping with dissociated position (figure 1.3e) DF’s grip scaling was significantly less accurate compared to healthy controls. Based on these evidence, Schenk (2012a) argued that DF’s ability to scale her grip to object size in the standard grasping condition does not reflect intact visuomotor control but is instead related to the availability of haptic feedback. Schenk (2012a) hypothesised that in the grasping task, DF is able to use different sensory information (e.g., egocentric cues and haptic feedback), which are not available in other tasks, such as for example the manual size estimation or grasping without haptic feedback. In other words, in the grasping task, DF relies on haptic feedback to compensate for her deficit in the perception of size and that her grip scaling relies on the integration of visual and haptic feedback. Schenk (2012a) concluded that haptic feedback plays a critical role in DF’s grasping performance which highlights the multimodal nature of the control of grasping. In fact, Schenk (2012a) highlights that the information within the dorsal stream about the target object is not enough to successfully control grasping. He suggested that other information such as haptic feedback or visual information from the ventral stream is additionally required to produce accurate grasping.

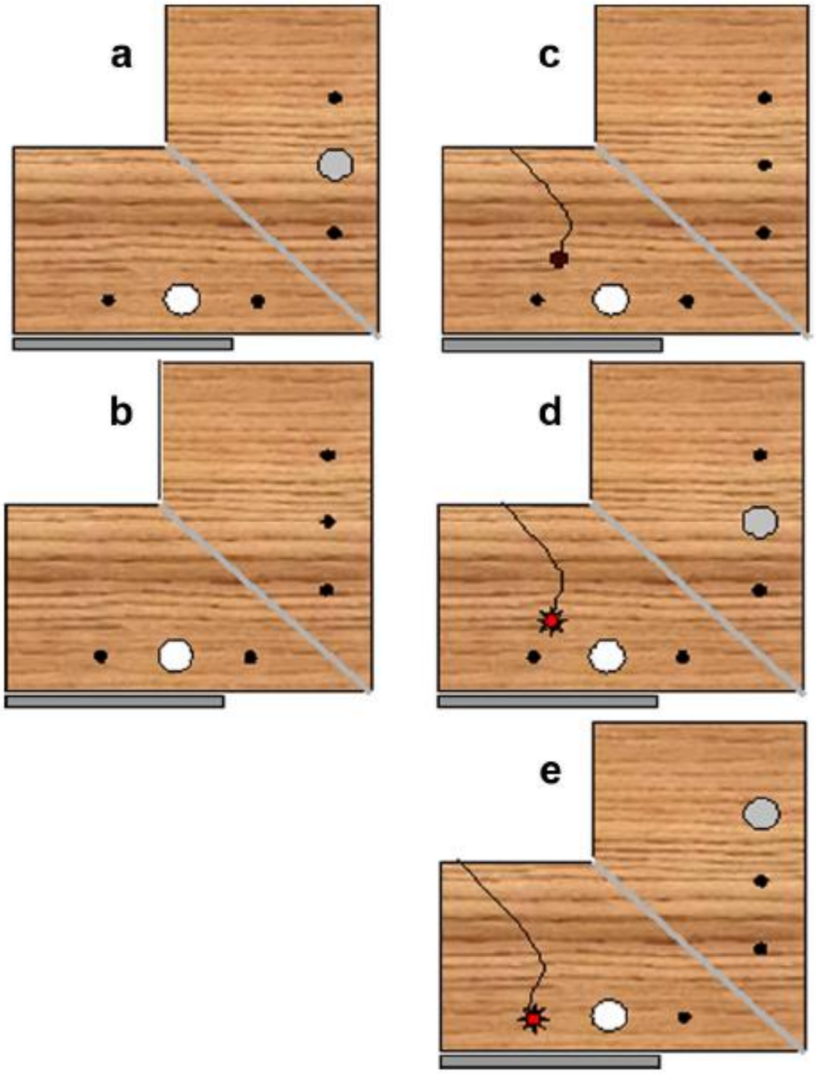


Figure 1.3 Set-up of the different grasping tasks. (a) Standard grasping task in which the visible cylinder (white circle) and the grasped cylinder (grey circle) were in matching positions. (b) Grasping without grasping feedback. Task was similar to standard grasping; however, no object was to be grasped behind the mirror. (c and d) Haptic feedback in 50% of all trials. The red dot represents the LED. When the LED was switched off, no haptic feedback was provided (c), while when the LED was switched on haptic feedback was provide (d). (e) Grasping with dissociated position. The perceived cylinder (white circle) was placed in the middle position, while the grasped cylinder (grey circle) was placed in the far condition. The LED indicated the position of the target cylinder behind the mirror, which provided haptic feedback. From "No Dissociation between Perception and Action in Patient DF When Haptic Feedback is Withdrawn", by Schenk, 2012, Journal of Neuroscience, 32(6), 2013-2017. Adapted with permission.

Milner, Ganel and Goodale (2012) offered an alternative and more straightforward explanation. According to their account, a grasping task in which the target object is visible, but not available to grasp is actually a pantomime task, in which participants have to pretend to grasp the object. They argued that the visuomotor systems in the dorsal stream are properly engaged only when the grasping movement is made directly towards the target and the hand touches the object at the end of the movement, otherwise, the task shift from real grasping to pantomimed grasping, which requires the ventral stream to be additionally engaged. In other words, when haptic feedback was removed or the location of the visible and grasped object was dissociated in Schenk's study, the task shifted from real, to pantomimed grasping. Therefore, is not surprising that DF was impaired (Milner et al., 2012). The authors concluded that DF does not use haptic feedback information in order to scale her grip, but she needs some sort of tactile contact at the end of the grasping movement to keep her dorsal stream engaged.

To further test this idea, in a series of experiments, Whitwell, Milner, Cavina-Pratesi, Barat & Goodale (2014), examined DF's and a group of healthy controls' performance using the same mirror set-up implemented by Schenk (2012a) using both cylinders and Efron blocks (Efron, 1969). In this experiments, there was always an object behind the mirror to grasp, however, whilst the width of that object never changed, the width of the object viewed in the mirror varied from trial to trial. Here, DF always experience tactile feedback at the end of the movements even if the feedback was completely uninformative to whether or not her grasp was tuned to the size of the object in the mirror. The authors reported that DF continued to scale her grip aperture in-flight to object size in the grasping tasks, and her performance was not significantly different from the performance observed in the control group. The authors concluded that, even when the size of the cylinder behind the mirror was uninformative, the tactile contact by itself was enough to keep DF's visuomotor systems in her dorsal stream engaged. This result seems to contradict Schenk's (2012a,b) hypothesis that DF needs to have access to veridical haptic feedback in order to scale her grip aperture. Whitwell, Milner et al. (2014), argued that, without any haptic feedback (i.e. hand closing to thin air) at the end of the grasp, the movement would become a pantomimed act and therefore without haptic feedback, the visuomotor system is not properly engaged, and participants are carrying out a pantomimed grasp (Whitwell, Milner et al., 2014). Whitwell, Milner et al. (2014) pointed out that this hypothesis was further supported by the fact that control participants in Schenk (2012a) showed a similar performance between the no haptic feedback and the size estimation tasks. Additionally, they proposed that the dorsal visuomotor system is not engaged solely by the task of reaching to grasp a visual stimulus, but the hand has to encounter a tangible endpoint for the visuomotor system to be engaged. This hypothesis was based on the differences in scaling accuracy observed between the no-haptic feedback task in Schenk (2012a) and the non-veridical haptic feedback task in Whitwell, Milner et al. (2014).

I would like to highlight that, although the model focuses on the division of labour between the dorsal and the ventral stream, Milner and Goodale never stated that the two visual streams do not interact with each other. In fact, in the final section of the first edition of their book (Milner & Goodale, 1995), they clearly stated that the two streams cooperate to program and coordinate actions, hence they never excluded the possibility that the two streams are interconnected. So far, I have been focusing on the division of labour between the dorsal and the ventral stream, however, over the years, it has become clearer that the two visual streams must interact closely in our everyday life in the production of adaptive behaviour (Goodale, 2014).

1.9 Interactions between the dorsal and the ventral visual streams

In their proposal of the perception and action model, Milner & Goodale (1995; 2006) predicted, that a particular category of objects, tools, would require the dorsal and ventral pathways to cooperate. Additionally, they speculated that the ventral stream, implicated in the recognition of tools, would be involved in the selection of where and how tools should be grasped according to the intended use of the object and its function. Finally, the information reaches the dorsal stream which is responsible for the transformation of the sensory information critical to implement and control the subsequent action. In other words, when grasping our mugs of coffee on our desk, each object in the scene is analysed and the target object is identified by the ventral stream, while the dorsal stream is responsible for selecting the particular motor acts necessary to grasp the mug and to control the movement online (Goodale & Humphrey, 1998).

The collaboration between the two streams is critical for tool use as it depends not only on physical properties of the object (such as size, orientation and shape), but also on the stored knowledge of the specific function associated with it. In fact, familiar tools (e.g., hammer, fork, knife) are bound to action plans that are beyond the mere surface of the objects, but that are instead defined by previous experience, and that could only be unlocked after successful recognition. When grasping familiar tools, how the hand is shaped to grasp to use them depends on both the physical aspect (i.e., size, shape, orientation) and on the stored knowledge of their function and use. Once the actions associated with a specific tool are known, the recognition of the identity of the tool, represents an efficient way to retrieve the learned motor plans associated with it. Thus, familiar tool use is likely to involve the cooperation between the dorsal and the ventral visual streams. In fact, familiar tool use extends beyond the physical properties of the objects and the timeframe by which the dorsal stream operates, and appears to rely, instead on the stored representations and successful recognition, which are mediated by the ventral stream.

The idea was supported by functional neuroimaging investigations in healthy participants showing that although the dorsal pathway is sufficient for programming complex movements, when the movements involve actions with tools, the ventral network is co-activated (Decety et al., 1997).

Additional strong evidence for the involvement of the ventral stream in tool use comes from testing the ability of DF in grasping and using familiar tools (Carey, Harvey, & Milner, 1996). When DF was requested to grasp and use familiar tools, DF was able to shape and orient her hand with respect to the tool metrical properties (e.g., size and orientation). However, she often failed to grasp the object in a way that reflected her knowledge of function and use. Moreover, when the tools were presented with the handle facing away, while controls typically rotated their hand to end up in a final posture that was suitable for use (Rosenbaum & Jorgensen, 1992; Rosenbaum, Van Heugten, & Caldwell, 1996), DF did not. Specifically, when the objects were presented with an unusual orientation (i.e., with the handle pointed away from her), DF often grasped the objects inappropriately and needed to touch them in an exploratory fashion to identify the identity before demonstrating their use. The authors concluded that DF's initial grasp was always guided by visual information about the size and orientation of the object, but often not guided by the functional knowledge of the object. Thus, DF was unable to use functional information to guide her grasps (Carey et al., 1996).

The behaviour observed in healthy controls (rotating their hand to grasp the tools in a way that was suitable for its use) by Carey et al. (1996), is consistent with Rosenbaum and colleagues' (Rosenbaum & Jorgensen, 1992; Rosenbaum, Van Heugten, & Caldwell, 1996) proposal that people are more likely to reliably adopt relatively awkward grasping postures if this will enable a more comfortable posture for the completion of the end-goal (also called end-state comfort effect, which will be further discussed in section 10.1.1).

This tendency to grasp tool handles in a way that is appropriate for functional use was further investigated by Creem & Proffitt (2001). They have shown that when participants were asked to grasp tools, they tended to grasp them by the handle in a way that is appropriate for tool use, however, when they were performing a concurrent semantic task (i.e., say the second word of pairs of words previously learned in response to the first word), they rarely picked up the tools appropriately. The authors argued that when planning a functional grasp with tools, the semantic system is involved, which presumably involves ventral stream areas. Thus, when the semantic task was performed at the same time of the grasping, the tool functional knowledge was not incorporated in the grasping. The authors speculated that this happened because the resources from the semantic system were not fully available. In contrast, a spatial imagery task (i.e., imagine a block letter and classify the corners) did not impair grasping performance. The authors concluded that the visuomotor system can reach and grasp an object effectively. However, to functionally grasp an object based on its identity, information from the semantic system, is additionally needed. These results illustrate a necessary interaction between the dorsal and the ventral stream and are consistent with those of functional grasping in patient DF (Carey et al., 1996).

1.10 Neural basis of tool use

1.10.1 Neurophysiology of tool use in monkeys

Although macaque monkeys rarely use tools in the wild (Tomasello & Call, 1997), neuroscientists across the world have been training monkeys in the lab to use tools (e.g., Iriki & Sakura, 2008; Ishibashi, Hihara, & Iriki, 2000), which has allowed researchers to make new discoveries regarding the neural basis of tool use in monkeys.

In 1996, Iriki et al. (1996), recorded neural activity within the anterior bank of the IPS before and after macaque monkeys were trained to use a rake to retrieve food that was placed further away. Before the training, the neurons of interest showed a bimodal response to both visual and tactile stimuli. They observed that the visual receptive field (i.e., the part of the space in which a stimulus would make the neurons fire) were linked to the tactile receptive fields of particular body parts, independently of where the monkeys were fixating. After the monkeys were trained to use the rake, they observed that the visual receptive fields of many of these bimodal neurons within the IPS changed to include the area of the space around the tool. To give an example, neurons with a visual receptive field tied to the hand before the training showed sensitivity to visual stimuli in the space around the tool after the training, which means that the receptive fields expanded to the tool use space to include both the hand and the tool. However, this visual receptive fields expansion was strictly linked on the monkey actively using the rake. In fact, after approximately 5 minutes of rest without using the tool, the visual receptive fields would only include the area of space coded prior to the training, even if the monkey was passively holding the tool. The results suggests that a tool can actually become incorporated into the body schema and that neuronal changes induced by tool use depend on the goal state of the monkey (Iriki et al., 1996). The theory put forward by Iriki et al. (1996; Ishibashi et al., 2002a, 2000; Maravita & Iriki, 2004) to account for changes in the receptive field properties of the IPS is linked to the concept of the body schema (Head & Holmes, 1911). This refers to a representation of the position of our body and its parts in space that is continually being updated (Head & Holmes, 1911). In their original notion of body schema, Head and Holmes (1911) proposed that this representation may incorporate objects when these are relevant for motor control. Notion that has been elegantly demonstrated almost a century later (e.g., Iriki et al., 1996; Maravita & Iriki, 2004).

Expansion of the reach space encoding effects similar to the one observed in monkeys after tool use training, have been observed in humans using tools (Berti & Frassinetti, 2000; Gallivan et al., 2011; Maravita & Iriki, 2004; Maravita, Spence, Kennett, & Driver, 2002). However, tool use in humans is more skilled compared to other primates (Frey, 2007; Johnson-Frey, 2003, 2004), thus only an expanded space is not sufficient to the neural mechanisms underlying more complex tool use (Arbib, Bonaiuto, Jacobs, & Frey, 2009). In fact, while other species uses only simple tools, such as a rake for reaching or a stone for pounding, humans are also able to create complex tools, such as hammers, axes, spoons (Johnson-Frey, 2004). Moreover, humans are the only species that refine these artifacts and the skills associated with their usage and actively transmit the use to future generations (Tomasello, 1999). Thus, while neural mechanisms underlying tool use in monkeys represent the foundation to understand the neural mechanisms underlying tool use in humans, the skilled tool use abilities in humans must rely at least on newly evolved brain networks (Frey, 2007; Peeters et al., 2009).

1.10.2 Neural basis of tool use in humans

It has been shown that viewing images of tools activate not only ventral stream areas implicated in tool identification, but also dorsal stream areas implicated in the visuomotor control of actions (e.g., Lewis, 2006). In the human brain, different regions have been identified to carry out different aspects of tool recognition and use. Areas in the occipitotemporal cortex typically activated by tools include the fusiform gyrus (FG) (Chao, Haxby, & Martin, 1999; Garcea & Mahon, 2014; Mahon et al., 2007; Whatmough, Chertkow, Murtha, & Hanratty, 2002), the lateral occipitotemporal cortex (LOTC) (Bracci et al., 2012; Perini, Caramazza, & Peelen, 2014) and the middle temporal gyrus (MTG) (Boronat et al., 2005; Chao et al., 1999; Emmorey et al., 2004; Kellenbach, Brett, & Patterson, 2003; Macdonald & Culham, 2015; Valyear & Culham, 2009). It has been shown that regions within the occipitotemporal cortex represent the visual surface and texture properties of objects (e.g., Cant & Goodale, 2011; Cant & Goodale, 2007; Miceli et al., 2001; Simmons et al., 2007; Stasenko, Garcea, Dombovy, & Mahon, 2014). The left middle temporal gyrus, which has been shown to be sensitive to mechanical motion of manipulable objects (e.g., Beauchamp, Lee, Haxby, & Martin, 2002), is thought to process action relevant semantic information related to manipulable objects (e.g., Mahon et al., 2007; Martin, 2007; Peelen & Caramazza, 2012). Areas typically activated by tools in the frontoparietal network include the intraparietal sulcus (IPS), the inferior parietal lobule (IPL) and the superior parietal lobule (SPL) (Boronat et al., 2005; Buxbaum & Saffran, 2002; Chao & Martin, 2000; Hermsdorfer, Terlinden, Muhlau, Goldenberg, & Wohlschlager, 2007; Macdonald & Culham, 2015; Mruczek et al., 2013), the ventral (PMv) and dorsal (PMd) premotor cortex (Chao & Martin, 2000; Creem-Regehr & Lee, 2005; Johnson-Frey, Newman-Norlund, & Grafton, 2005; Kellenbach et al., 2003). With respect to the PMd and PMv, it has been shown that these regions are involved in action planning and sequencing (e.g., Chao & Martin, 2000; Grafton, Fadiga, Arbib, & Rizzolatti, 1997).

Although processes mediated by the posterior parietal cortex have been typically associated with visually-guided actions (e.g., Goodale et al., 1994; Goodale & Milner, 1992), more recently it has been shown that visuomotor posterior parietal cortex information interact with conceptual decisions about tools (Almeida, Mahon, Nakayama, & Caramazza, 2008; Almeida, Mahon, & Caramazza, 2010). With the advent of neuroimaging, it has been shown that the human posterior parietal cortex was selectively activated by simply viewing pictures of tools, even when no overt action was required. To my knowledge, the first study to show that the parietal cortex was selectively activated by simply viewing graspable objects in the human brain was conducted by Chao and Martin (2000). They compared viewing and silent naming pictures of familiar tools with viewing pictures of animals and showed that graspable objects elicited higher activation in both left ventral premotor and left posterior parietal cortex compared to pictures of animals. As the authors pointed out, their results were consistent with Binkofski et al. (1999) observation that grasping objects activated the intraparietal sulcus within the parietal cortex. The authors suggested that the observed parietal activity represented stored manipulation knowledge of tool use function and use (Chao & Martin, 2000).

However, as animals are usually not graspable, the activation observed may be related to the fact that tools afford grasping, whereas animals do not (Valyear, Cavina-Pratesi, Stiglick, & Culham, 2007). To explore this, Valyear et al. (2007) presented images of graspable object (e.g., tomato), non-graspable objects (e.g., bridge), tools (e.g., tongs) and scrambled images while participants were performing a silent naming task in the scanner. The difference between graspable objects and tools was that, graspable-objects could be grasped, but had less clearly defined actions associated with them compared to tools. The authors replicated Chao and Martin (2000) findings and additionally showed that activity within the tool selective area in the intraparietal sulcus was selective for tools versus graspable objects and non-graspable objects and no differences were evident between graspable and non-graspable objects. Moreover, they aligned data from a previous study investigating grasping versus reaching movement with real objects (e.g., 3D blocks; Culham et al., 2003) and they observed that the activity associated with tool naming and object grasping were reliably distinct, with activity associated with tool naming located more posterior to that associated with object grasping. The authors postulated that parietal responses to viewing tools do not reflect processing of affordance for grasping and also do not overlap with activation for grasping objects. Valyear et al. (2007) suggested that tool related activity in the parietal cortex does not reflect only the graspable property of the stimuli, but that the activity relates to action representations which are linked to knowledge of use and prior experience (Valyear et al., 2007). According to the authors, these results seems to fit well with the hypothesis of the existence of two streams in the posterior parietal cortex for grasping and tool use (Binkofski & Buxbaum, 2013, section 1.10.3). However, they pointed out that while Binkofski and Buxbaum (2013) hypothesised a distinction between medial and lateral areas within the posterior parietal cortex, they identified a separation between posterior and anterior aspects of the intraparietal sulcus.

There is also another possibility which needs to be taken into account which is that most tools are elongated (Almeida et al., 2014; Chen, Snow, Culham, & Goodale, 2017), while animal, faces, objects and other stimuli are not (Almeida et al., 2008; Almeida et al., 2014; Chen et al., 2017). According to Almeida et al. (2014), object elongation may facilitate the visuomotor description of an object and be useful in selecting a specific grasp. The authors argued that most everyday tools (e.g., a knife, a spoon, a hammer) have an elongated shape which have peculiar characteristics, such as the handle, that may facilitate the preparation of a particular grasp. In a series of experiments using priming and images of elongated or blob-like animals and tools, they explored different psychophysical manipulations known to bias the processing toward the dorsal to test whether elongation triggers processing by the dorsal stream. They showed that elongated shaped stimuli, regardless of their semantic category (e.g., animals or tools), when processed by the dorsal stream, elicit visuomotor grasp-related information that facilitated categorisation responses to elongated targets. The authors suggested that elongated stimuli may reduce ambiguity during grasp preparation as provide information about hand shaping and orientation to support action planning.

Recently, Chen et al. (2017) explored the extent to which activity in different areas in the dorsal and ventral stream is modulated by tools versus elongation and the connectivity between these areas using fMRI. Participants were presented with pictures of elongated tools (e.g., hammer), stubby tools (e.g., ping-pong racket), elongated non-tools (e.g., bottle) and stubby non-tools (e.g., plate) while in the scanner and were instructed to passively view the stimuli. The authors found that the middle temporal gyrus (MTG) and the superior parietal lobe (SPL) bilaterally were more activated for elongated (versus stubby) tools (versus non-tools), while the anterior intraparietal sulcus (aIPS) was more activated for tools versus non-tools, but not for elongated versus stubby images. On the other hand, the left middle and posterior IPS and the left premotor cortex were more activated for elongated images (whether tools or non-tools) versus stubby images. Based on their results the authors suggested that “toolness” and shape activated different areas in the brain usually associated with tools. Moreover, the authors investigated connectivity between tool-selective areas and showed that “toolness” but not elongation modulated the connectivity between the left aIPS and the lateral occipitotemporal cortex (LOTC). Additionally, elongated tools (versus stubby tools) increased the reciprocal modulation of the connections between left MTG and left aIPS. Overall, the authors concluded that elongation is a particularly relevant property of shape processed by the dorsal stream and that the connections between the left MTG and the left aIPS may play a critical role in identifying the function and the selection of tool-appropriated actions. Disentangling if the activity in the dorsal stream may be modulated by tools or elongation is a critical issue. In fact, most tools are elongated and therefore the effects of tools and elongation may be confounded. Further evidence that regions in the dorsal stream are sensitive to elongation comes from the observation that neurons in caudal IPS in monkeys fire preferentially for elongated versus flat stimuli (Sakata et al., 1998).

1.10.3 Two parallel streams for actions with tools in the posterior parietal cortex

Several groups have suggested that the role of the posterior parietal cortex in action execution extends beyond sensorimotor control (Buxbaum & Kalénine, 2010; Creem-Regehr, 2009; Culham & Valyear, 2006; Daprati & Sirigu, 2006; Frey, 2007; Jeannerod & Jacob, 2005; Rizzolatti & Matelli, 2003). Specifically, they suggested that the dorsal visual stream is subdivided into two distinct sub-pathways, namely the dorso-dorsal stream and the ventro-dorsal stream, which are separated by the intraparietal sulcus (Binkofski & Buxbaum, 2013; Galletti, Fattori, Gamberini, & Kutz, 2004; Jeannerod & Jacob, 2005; Kravitz, Saleem, Baker, & Mishkin, 2011; Tanné-Gariépy, Rouiller, & Boussaoud, 2002).

The idea of the existence of two parallel parietal streams in the brain for action stems from the observation of the existence of two parallel distinct parieto-frontal pathways in the macaque monkey (Rizzolatti & Matelli, 2003). In particular, the dorso-dorsal pathway projecting from visual area V6 over the superior parietal lobule (SPL) towards the dorsal premotor cortex is thought to be involved in the online sensorimotor control of arm movements. On the other hand, the ventral-dorsal pathway leading from the middle temporal and medial superior temporal areas (MT/MST) to the ventral premotor cortex, via the inferior parietal lobule (IPL) contains representations of learned skilled movements such as tool use. Areas within the IPL have been shown to be well connected with the ventral visual stream (Harries & Perrett, 1991) and to areas in the superior temporal sulcus (STS). These connections are not present in the dorso-dorsal pathway (Rizzolatti & Matelli, 2003). Neurons in the STS are important for high-level multimodal integration of visual form and motion properties (Barraclough, Xiao, Baker, Oram, & Perrett, 2005;

Oram & Perrett, 1996; Oram, Perrett, & Hietanen, 1993), object processing (Baker, Keysers, Jellema, Wicker, & Perrett, 2001; Hietanen & Perrett, 1996), selectively discharge when observing others' actions (e.g., grasping) (Barraclough, Keith, Xiao, Oram, & Perrett, 2009; Perrett et al., 1989; Perrett, Mistlin, Harries, Chitty, & Goodale, 1990) and show sensitivity to the gaze direction of the actors (Perrett et al., 1985). Thus, it is thought that these responses observed in STS may implicate a role for STS in encoding intentionality of others actions (Jellema, Maassen, & Perrett, 2004; Jellema & Perrett, 2006).

Hihara et al. (2006) observed changes in physiological properties of the intraparietal neural circuit and mapped new connections between the STS and the anterior intraparietal sulcus when monkeys were trained to use tools. However, the same changes were not observed in naïve monkeys. These findings led the authors to speculate that newly acquired tool use behaviour may require an added level of cognitive and contextual flexibility (Hihara et al., 2006). In addition, it has been observed that neurons within the STS show selectivity for responses to movements when an object is held with the hand (Hietanen & Perrett, 1996) and receive inputs form the middle and medial superior temporal cortex, which are motion specialised areas (Maunsell, 1987). Thus, in the monkey, the IPL, in the ventro-dorsal pathway, has access to high level visual form and motion properties, as well as object and action processing that occurs in the temporal cortex, which would contribute to the guidance of movements towards tools (Orban, Van Essen, & Vanduffel, 2004).

In the human brain, the IPL appears expanded compared to the monkey brain (Orban et al., 2004), and it is thought to be the precursor of some additional functions that evolved in humans, such as tool use (Hihara et al., 2006). However, humans are skilled tools users compared to other primates (Frey, 2007; Johnson-Frey, 2003) and explaining the high-level transformations involved in more complex tool use with expanded space in the IPL is not sufficient (Arbib et al., 2009). Thus, it is thought that skilled tool use in humans must rely in part on newly evolved brain areas (Frey, 2007). The emphasis of the recent discussions is that the posterior parietal cortex is divided in two separate parallel streams devoted to process information to guide the online control of actions versus planning and use tools (Binkofski & Buxbaum, 2013; figure 1.4).

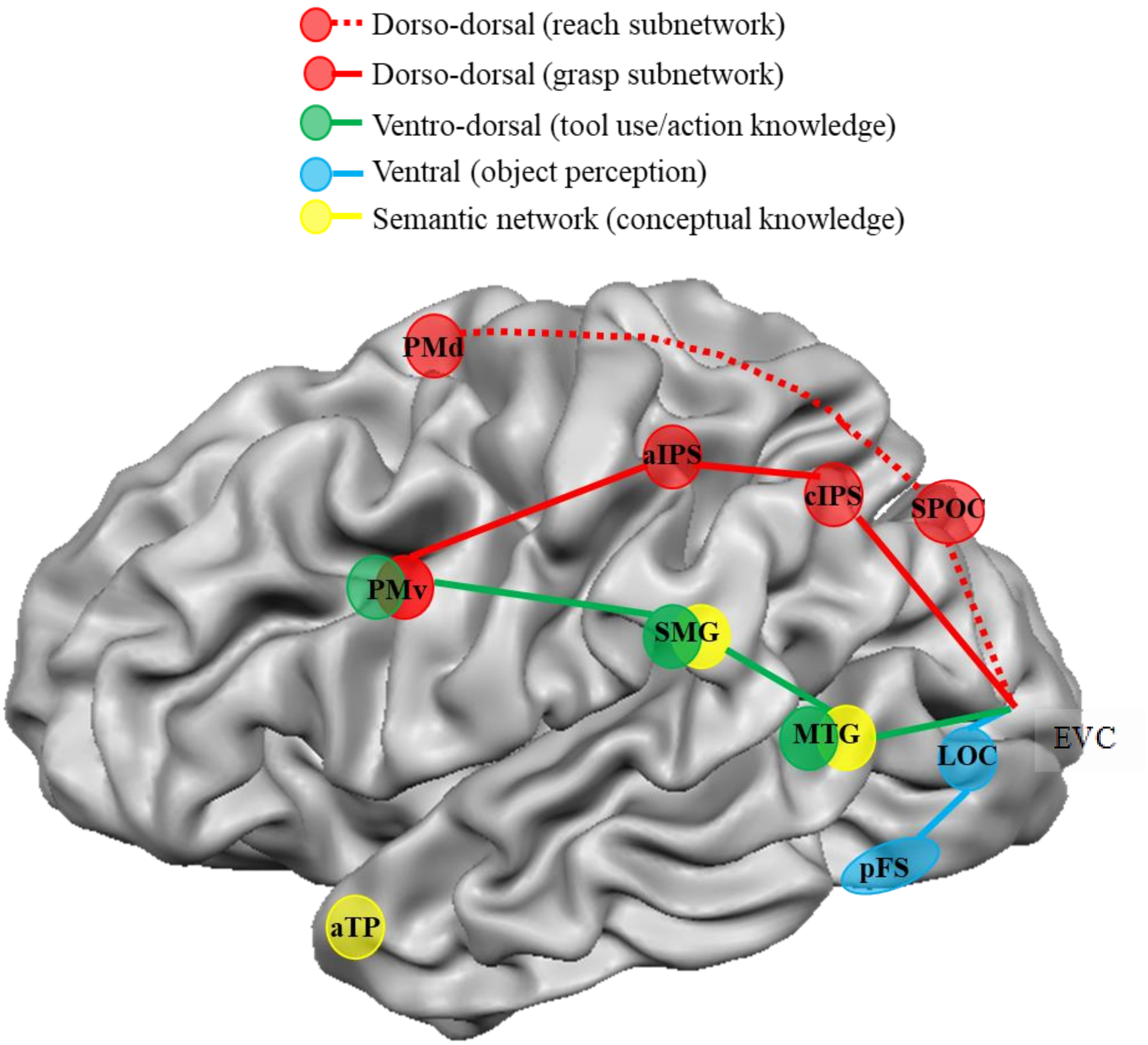


Figure 1.4 Theorised tool processing networks in the human brain (adapted from Buxbaum & Kalénine, 2010; Binkofski & Buxbaum, 2013; Lewis, 2006). Left hemisphere of the human brain is shown in lateral view. Colours and connections are used to highlight the hypothesised role of each region in hand actions (red: dorso-dorsal network including reach and grasp subnetworks), action knowledge (green: ventro-dorsal network), conceptual knowledge (yellow: semantic network) and object perception (blue: ventral stream network). Abbreviations: EVC = early visual cortex; LOC = lateral occipital cortex; pFS = posterior fusiform cortex; MTG = middle temporal gyrus; aTP = anterior temporal pole; SMG = supramarginal gyrus; PMv = ventral premotor cortex; PMd = dorsal premotor cortex; cIPS = caudal intraparietal sulcus; SPOC = superior parietal occipital cortex; aIPS = anterior intraparietal sulcus.

The dorso-dorsal stream, responsible for the sensorimotor transformation and the online control of prehensile actions, is operating in real time within egocentric coordinates and tuned to objects metrics directly accessible form information available on the retina (Binkofski & Buxbaum, 2013) and corresponds with the dorsal stream traditionally described by Milner & Goodale (1995, 2006). The main processing module of this stream is the superior parietal cortex with key projections from areas along the medial surface of the parietooccipital cortex (Gamberini et al., 2009).

On the other hand, the ventro-dorsal stream is specialised for processing sensorimotor information for learned tool use and is responsible for action planning and conceptual knowledge of actions and objects. The main processing module is the inferior parietal cortex, with key connections with MT/MST, which then projects to the ventral premotor cortex (Buxbaum & Kalénine, 2010). Moreover, recent evidence suggested that the regions within the posterior parietal cortex contribute to the processing of the structure and shape of objects (e.g., Freud et al., 2017; Van Dromme, Premereur, Verhoef, Vanduffel, & Janssen, 2016). In particular the left supramarginal gyrus (SMG), located in the inferior parietal lobule and part of the ventro-dorsal stream, is thought to process object-associated functional manipulation knowledge (i.e., how to move our hands to use a tool functionally such as using a rotation movement to use a screw-driver), while the aIPS in the dorso-dorsal stream is thought to support structural manipulation knowledge (i.e., how tools are grasped when picked up such as using a whole-hand power grasp to pick-up a screwdriver; e.g., Brandi, Wohlschlager, Sorg, & Hermsdorfer, 2014; Chen, Garcea, & Mahon, 2016; Konen, Mruczek, Montoya, & Kastner, 2013; Valyear et al., 2007). Specifically, the dorso-dorsal network represents structural manipulation knowledge about objects such as how they are grasped when picked-up (e.g., use a whole-hand power grip to pick up a screwdriver), while the ventro-dorsal network represents functional manipulation knowledge about objects such as how to move our hands to use a tool functionally (e.g., rotation movement to use a screwdriver).

Evidence from neuropsychology, supports the idea that online visuomotor control and learned tool use are supported by separate systems within the human parietal cortex. Lesions to the dorso-dorsal stream lead to optic ataxia (Binkofski & Buxbaum, 2013). I mentioned optic ataxia in the context of the two visual streams, where I highlighted that it follows a damage to the dorsal stream and is characterised by problems with reaching (e.g., Rossetti et al., 2005) and grasping (Tunik, Frey, & Grafton, 2005) that are most flagrant in visual periphery (see section 1.4.2). Thus, it is thought that in optic ataxia, impairments in reaching and grasping are associated with damage to bilateral superior parietal lobe and the dorso-dorsal stream (Goldenberg, 2009). On the other hand, lesions to the ventro-dorsal stream lead to ideomotor apraxia (e.g., Buxbaum, 2001). In the 19th century, Liepmann was the first to identify and explain ideomotor apraxia as a selective impairment in performing learned skilled actions, in the absence of any sensory or motor deficits, or related to general deficits in attention, cognition or comprehension (Liepmann, 1977, 1988). Patients with ideomotor apraxia can recognise tools and understand what they are supposed to do with the tools (i.e., a toothbrush if for brushing teeth), however, they have severe problems when they have to carry out real movements with tools (Poizner et al., 1998). Moreover, when these patients were asked to pantomime tool use actions (e.g., without the tool in their hand), errors were more profound; the performance of some patients actually improves when they hold the tool in their hand and demonstrate how to use it (Goldenberg & Hagmann, 1998; Hermsdörfer, Hentze, & Goldenberg, 2006; Buxbaum, Giovannetti, & Libon, 2000; Wada et al., 1999). It is thought that the motor impairment observed in these patients results from their inability to mentally evoke actions or to use stored motor representations to form mental images of the actions (Jeannerod & Decety, 1995). Liepmann also reported that ideomotor apraxia is usually observed after left inferior parietal lesions, which has been subsequently confirmed by other authors (e.g., Buxbaum, 2017; Goldenberg & Spatt, 2009; Goldenberg, 2009; Haaland, Harrington, & Knight, 2000; Johnson-Frey, 2004; Martin, 2016; Negri et al., 2007).

1.10.4 Structural versus functional manipulation knowledge of tool use

In the paragraph above, I highlighted how different behaviours link with grasping and how using or demonstrating tool use might be linked to different lesion foci in the parietal system. Moreover, also depending on a person's goals and intentions, grasping itself might depend on distinct pathways in the parietal cortex.

To my knowledge, the first study that distinguished and evaluated the components of grasping and tool use was conducted by Sirigu et al. (1995) in ideomotor apraxic patient LL. Patient LL suffered from a severe hypotensive episode during a surgery. Neuroimaging investigations (PET and SPECT) conducted after the episode, revealed evidence of bilateral occipitoparietal hypometabolism. Behaviourally, she was impaired in pantomiming and using familiar tools, and therefore in performing her everyday activities such as using a fork and a knife to eat and locking a door (Sirigu et al., 1995). The authors asked four independent judges to rate LL's performance, correctness of hand posture and movement trajectories separately, when using 20 common objects (e.g., key, screwdriver, spoon). For the hand posture and reaching trajectories, the judges were instructed to base their evaluation on a set of well-defined expectations. For example, in the case of the spoon, for hand posture, the handle of the spoon was expected to be held "between the thumb, index and middle finger with the palm of the hand turned slightly upward and towards the subject's body" (Sirigu et al., 1995, p.44), while for movement trajectory, the spoon "had to be moved in a back and forth manner between the table and the subject's mouth" (Sirigu et al., 1995, p. 44). Thus, while the specifications for hand posture was evaluated on the basis of functional grasping with the goal of using the tool, the evaluation of movement trajectory was strictly linked to global movements of the body, their spatial localisation and timing to determine if the finality of the action and the path of the tool in space were consistent. Results showed that LL was profoundly impaired at shaping her hand for grasp-to-use a tool, however, her movement trajectories were unimpaired. In addition, the authors looked at LL's trajectories and movement smoothness, as well as her grip scaling. LL's in-flight grip scaling was highly correlated with the size of the grasped portion of each tool, her wrist orientation in flight was matched with the orientation of the tool and overall she showed smooth and well directed grasping (Sirigu et al., 1995). Thus, LL, just like DF (Carey et al., 1996), was able to shape her hand according to physical properties of tools; however, she was severely impaired when she had to execute the grasp-to-use component of the movement with those same tools.

In a later study, Sirigu, Daprati, Buxbaum, Giraux, & Pradat-Diehl (2003) tested grasping-to-use and grasping-to-move in a group of five patients with left IPL lesions and healthy controls. Participants were required to either reach out and grasp an object in front of them with their right hand (grasp-to-move), pantomime how they would handle the same object in order to functionally use it and to reach out for the object and actually use it (grasp-to-use). They used a specialised glove with multiple sensors to record the real time information about finger joints to characterise the detailed kinematics. Sirigu et al. (2003) observed that in healthy participants, two principal components accounted for the variance observed in grasp-to-move. However, in healthy participants in the grasp-to-use task, they observed an additional component that accounted for the variance, that was not present in grasp-to-move and pantomime. The authors speculated that this factor may underlie more fine motor adjustments, necessary in tool use, and therefore be use-specific (Sirigu et al., 2003). Analysis of grasping in the patient group revealed that performance in the grasp-to-move condition was similar to that of the control group, while the third use-specific component observed in healthy participants was absent in the grasp-to-use condition in patients. Taken together, the results show that patients, in contrast with the controls, adopted an undifferentiated posture across all object (Sirigu et al., 2003), similarly to patient DF (Carey et al., 1996). These findings confirm the dissociation observed in patient LL, and indicate a selective impairment in the production of grasping based on objects' function and intention of use, while preserving hand shaping in grasp-to-move (Sirigu et al., 2003).

Consistent with this, Buxbaum, Sirigu, Schwartz, & Klatzky (2003) presented participants with pictures of different manipulable objects and hand postures (clench, pinch, palm and poke), real objects (e.g., pencil, clothespin, key, doorbell, etc,) and novel objects (e.g., a blue 3D rectangular block positioned upon a white base). The authors showed that when real objects were presented most apraxic patients were impaired in both recognition and production, however, when novel objects were presented, nearly all apraxic patients performed similar to the control group in recognising the hand postures appropriate for interacting with the object. Buxbaum et al. (2003) argued that the latter observation suggests relative integrity to respond to the structure of the objects, which is mediated by their intact dorsal stream processes. On the other hand, impaired responses to familiar objects deficit in pantomimes, are linked to damage to the representations underlying knowledge of the appropriate hand posture for functional object use and pantomime, which are attributable to damages to structures in the inferior parietal lobe, more closely aligned to the ventral stream and responsible for the stored representations (Buxbaum, 2001).

Randerath, Li, Goldenberg and Hermsdörfer (2009) subsequently confirmed this observation and showed that when the handle was facing away from the body, participants, including apraxic patients, did not show a consistent behaviour in which they rotated their hand in half of the trials in the grasp-to-move task (i.e., participants chose an awkward grasping position in half of the trials). However, in the grasp-to-use task, non apraxic patients and controls rotated their hand nearly in all trials, only apraxic patients produced significantly more non-functional grasping movement when the tools were presented with the handle facing away. They concluded that grasping behaviour is influenced by the end-goal of the task and the position of the handle and that the selection of grip type is determined by several factors (e.g., functional knowledge, structural characteristics, end-goal and experience) and that patients with apraxia may fail to access this information (Randerath et al., 2009).

Evidence reviewed above showed that grasping based on knowledge of tool function and use can dissociate from grasping based on structure, however, also the reverse pattern is possible. For example, Jeannerod et al. (1994) described patient AT, with bilateral damage to the posterior-parietal cortex, disrupting her medial superior parietal lobe (SPL). She was unable to scale her grip to the size of plastic cylinders, however, when the cylinders were replaced with real manipulable objects (e.g., lipstick), her grip scaling significantly improved. Moreover, she was able to match her finger to the size of the cylinders and to imagine the size of familiar objects and reproduce the corresponding imagined size with her grip. The dissociation observed led the authors to suggest that visual information about object size are mediated by different neural pathways according to whether information is used to guide visuomotor control (i.e., dorsal stream) or perceptual analysis (i.e., ventral stream) (Goodale & Milner, 1992). The author discussed their results within the framework of a dual representation of objects: one representation relates to the object as a goal for an action, in which objects attributed are presented as affordance and trigger specific actions (Gibson, 1979) and is mediated by the dorsal stream (also called pragmatic system); while the other representation relates to the process of recognition, by which objects can be named, categorised and memorised, which implies a semantic representation and is mediated by the ventral stream (also called sematic system). Based on this, the authors attributed AT's deficit as a consequence of damage to the dorsal stream, whereas her ventral stream was intact. In fact, the hand shaping deficit observed with cylinders was less marked with familiar objects, for which she could retrieve information to determine the size of the objects from previous knowledge and interactions with the objects, stored in her semantic system. The authors suggested that impairments in grasping due to a disruption of the dorsal visual pathway, may have been compensated using object-centred information from the ventral stream in the case of familiar objects (Jeannerod et al., 1994).

However, the hypothesis suggested by the authors did not take into account the findings from patients with lesion to their inferior parietal lobe (IPL) as reviewed above. In fact, these patients show selective impairment in shaping their hand for functional based grasping (e.g., grasp-to-use) but not for structural based grasping (e.g., grasp-to-move). Therefore, an account of the involvement of the ventral stream in grasp-to-use, should consider the IPL. Milner and Goodale (1995), made it clear that their model did not deal well with the human IPL, and initially speculated that the human IPL may transform information derived from both streams, but mainly from the ventral stream. Several research groups have shown that the left IPL is more strongly activated during explicit retrieval of manipulation versus functional knowledge of tool use (Boronat et al., 2005; Canessa et al., 2008; Kellenbach et al., 2003). Moreover, the IPL is increasingly being thought to be involved in integrating information about stored object knowledge information from the ventral stream and visuomotor information coming from the dorsal stream to create a specific action plan (Almeida, Fintzi, & Mahon, 2013; Binkofski & Buxbaum, 2013; Frey, 2007; Grafton, 2010; Randerath, Goldenberg, Spijkers, Li, & Hermsdörfer, 2010).

Almeida et al. (2013) used fMRI and images of tools and animals to explore how manipulation knowledge is accessed in the brain. They exploited an asymmetry in how different cellular channels within the visual system (i.e., parvocellular and koniocellular) projects to the dorsal and the ventral streams. The authors manipulated the chromatic profiles of line-drawings images of animal and tool stimuli so that they were biased toward being processed by either the parvocellular or the kaniocellular pathways and instructed participants to passively view the images. The authors found that parvocellular-biased stimuli drive tool-preferences selectively in the inferior parietal regions, while kaniocellular-biased stimuli drive tool-preferences in posterior and posterior/superior parietal regions. Additionally, they performed connectivity analysis between the inferior and superior parietal lobes with the ventral stream and MT/V5 and showed that inferior parietal region exhibits functional connectivity to the ventral stream, while the posterior/superior parietal lobe exhibits functional connectivity to MT/V5 but not to the ventral stream. The authors concluded that the inferior parietal lobule receives inputs from the ventral stream structures that are known to support object identification and that play and integrative function that may be important for selecting the appropriate grip for a given object (based on information extracted from the dorsal stream) and for reaching toward an object in a way that anticipates the functional manipulation (based on information extracted from the ventral stream). In other words, a screwdriver may be grasped in a more efficient and biomechanical way when we are grasping it to move it only (based on manipulation knowledge), while if we are grasping a screwdriver to use it we grasp it in a specific way associated with its functional knowledge.

Recently, Garcea, Chen, Vargas, Narayan and Mahon (2018) used fMRI to explore the functional connectivity between ventral stream regions and regions in the left parietal cortex in a pantomime task and in a picture-matching task. In the pantomiming experiment, participants were instructed to pantomime object use when the images of the objects were presented while in the picture-matching task they were instructed to simply view the images and hit a button if any of the images was repeated. The authors found that there were strong increases in functional connectivity during tool pantomiming (compared to tool picture matching) between ventral stream regions and the left inferior parietal lobule, primary and premotor cortex. On the other hand, tool picture matching elicited increased functional connectivity among regions in the temporal lobe and the left lateral occipital cortex. The authors concluded that pantomime object use engaged a network integrating ventral and lateral occipitotemporal areas with frontal and parietal structures, while the picture matching task led to higher connectivity between ventral and lateral occipitotemporal areas, demonstrating a task-specific modulation of functional interactions between regions in the tool network (Garcea et al., 2018)

To summarise, these findings suggest that in the human brain there are at least three separate, but interacting streams, involved in tool processing and use: while the ventral occipitotemporal stream mediates object recognition, the dorsal occipito-parietal stream mediates visually guided action. Moreover, it has been hypothesised that the dorsal stream is additionally sub-divided into a dorso-dorsal stream and a ventro-dorsal stream. The frontoparietal dorso-dorsal stream (with a reach and grasp subnetworks), characterised as the grasp-to-move system, is tuned to hand preshaping and processes structural manipulation characteristics of objects for the purpose of prehensile actions. On the other hand, the temporoparietal ventro-dorsal stream, characterised as the use system is concerned with the long-term storage of familiar tool-associated actions and mediates functional manipulation knowledge (Binkofski & Buxbaum, 2013). However, how tools and manipulation knowledge are represented within each stream is not clear yet. In chapter 3 of the current thesis, I present a novel experiment that provides new insights on how tools and tools manipulation knowledge are represented within each stream during view and pantomiming. My findings provide a more sophisticated view of the distributed representations of tool processing across the dorsal and ventral streams.

1.10.5 The concept of affordances

The fact that viewing pictures of tools activates regions within the parietal cortex (see sections 1.7 and 1.10.2) is in line with the concept of affordances articulated by Gibson (1979). Gibson (1979) used the term affordances to refer to the fact that the visual perception of our surroundings is not just passive perception of the objects in it. Instead it involved the direct perception of the potential for action that the observer can carry out with them. For example, if we consider object manipulation, a person seeing a mug would not only perceive the colour and the shape but will directly perceive the graspability (e.g., handle) of the mug. The affordances of any object depend not only on the object alone, but on the possibilities of the observer. For example, while a mug affords grasping for humans, it may afford a biting action for dogs.

Behaviourally, evidence has shown that viewing pictures of tools can automatically potentiate motor actions associated with the use of the tool, even if no overt action is performed (Tucker & Ellis, 1998). In an elegant experiment, Tucker and Ellis (1998) showed pictures of familiar graspable objects with handles (e.g., pan) and asked participants to decide whether or not the objects were inverted or upright. Critically, the handles of the tools were either facing left or right and button-responses were made with either the left or the right hand. The authors observed that when handles were facing right, right hand responses were facilitated (i.e., faster reaction times), while left-facing handles, facilitated responses with the left hand even though the orientation was irrelevant to the task. Taken together these results indicate that the orientation of the handle automatically gives rise to the activation of corresponding motor plans for grasping (Tucker & Ellis, 1998).

The theory of affordances, as integral to the visual perception of objects, has received support from electrophysiological recording in monkeys. As reviewed in section 1.10.1 grasp related neurons often respond to the visual presentation of object even when no overt movement is required (Murata et al., 1997, 2000; Rizzolatti et al., 1988; Taira et al., 1990). Similarly, human neuroimaging studies have identified regions in the parietal cortex that show preferential activation for picture of graspable tools versus non graspable-objects (Chao & Martin, 2000; Valyear et al., 2007). As reviewed in section 1.10.2, Valyear et al. (2007) showed that activity within the tool selective area in the intraparietal sulcus was selective for tools versus graspable objects and non-graspable objects.

Moreover, objects may elicit multiple representations of affordances based on the situation in which these are perceived. For example, a wood log may afford a sit-down action if I am tired, but it can also serve to step on it to reach something I am not able to reach. Similarly, tools are manipulable objects that elicit multiple affordances, such as those related to manipulation knowledge (e.g., using precision grip to grasp a tea-spoon) and those related to functional manipulation knowledge (e.g., using a rotation movement to stir my coffee with a spoon) (Creem-Regehr & Lee, 2005). Bub, Masson and Cree (2008) examined whether viewing objects elicits manual gestures associated with their function (e.g., using the object) and/or their shape (e.g., pick up an object). Participants were trained to make specific responses using a Grasparatus, which had different elements that afforded open grasp, close grasp, poke and trigger for functional gestures and horizontal grasp, vertical grasp, vertical pinch and horizontal pinch for manipulation gestures. Participants completed a colour-gesture training before starting the experiment to learn to associate each gesture to a colour and were then cued either by images or words of objects. The authors found that for both manipulation and functional gesture types, reaction times were longer for incongruent trials for both objects and words, indicating that both objects and words elicited functional and manipulation knowledge gestures. Additionally, the authors presented words and non-words followed by a hand gesture cue. Participants were instructed to respond with a gesture in response to the hand and then to classify whether the letter string presented was a word or a non-word. They showed that functional gestures were more readily evoked by objects names compared to manipulation gestures. The authors suggested that these two different gesture types may interact during object processing and that if a given object have distinct functional and manipulation gesture associated with it, it is possible that using the object according to its function my require the suppression of a potentially conflicting manipulation gesture associated with its shape (Bub et al., 2008).

More recently, Borghi, Flumini, Natraj and Wheaton (2012) showed that affordance activation is modulated by the context and that other objects in the scene as well as hand cues related to manipulation or functional grasps influence reaction times and that functional knowledge may be more accessible than manipulation knowledge (as shown by slower reaction times for trials in which a manipulation grip was presented).

Further evidence of the existence of multiple affordances comes from literature on “conflict objects” and “non-conflict-objects” (Jax & Buxbaum, 2010). The authors explored whether there is a direct competition between functional- and manipulation-based responses within the same familiar objects. According to the authors “conflict objects" are objects that elicit contrasting affordances for manipulations associated with object manipulation based on its structure and based on its function. For example, a calculator affords a manipulative clench grasping response and a functional poke response. On the other hand, "non-conflicting objects" are associated with one dominant action based on both manipulation and functional knowledge. For example, a drinking glass affords the same clench grasp. Participants performed two tasks: in the grasp task they were instructed to reach for the object and position their hand on the object as they would then pass it to another person, while in the use task they were instructed to reach for the object and position their hand on the object as they would then use it. Half of the participants performed the use task first while the other half performed the grasp task first. The authors found two forms of interference involving "conflict objects". Specifically, they found a short-term grasp-use interference in which reaction times to initiate the use movements to objects associated with different functional and manipulation grasps were longer compared to objects with the same grasp-to-pass actions and occurred regardless of whether or not the object was recently grasped to be passed. Additionally, they found a long-term use-on-grasp interference which occurred when participants produced grasp responses and resulted from the experience gained from previous trials. Specifically, differences in initiation of grasp responses for conflict and non-conflict objects were only observed when the objects had been recently used. The authors suggested that even if the tasks were identical and using the same identical objects, previous use experience interfered with the participant's ability to grasp "conflict objects". The authors concluded that the intention to act on an object seems to trigger a competition between functional and manipulation responses during the selection of the action and that only functional responses require activation of long-term conceptual representations and therefore manipulation responses can be activated more quickly than functional responses.

Another distinction relevant for affordance representation and selection is the one between stable and variable affordances (Borghi & Riggio, 2009; Thill, Caligiore, Borghi, Ziemke, & Baldassarre, 2013), also called micro-affordances (Ellis & Tucker, 2000; Vainio, Ellis, & Tucker, 2007). Micro-affordance refers to the fact that it is thought that affordances are composed by a number of aspects (Ellis & Tucker, 2000) that are specific action components rather than to the whole action. For example, observing an object with a given size and orientation may activate a grip component and a wrist orientation component. In this view, stable affordances relate to features of the object that tend to be constant across different presentations and context (e.g., the size and shape of a mug), while variable affordances relate to features that can vary between interactions (e.g., the mug can be found in different locations). Binkofski and Buxbaum (2013) proposed that the distinction between stable and variable affordances may be related to the difference between functional and manipulative affordances as well as the dorso-dorsal grasp system and the ventro-dorsal use system in the parietal cortex.

The existence of multiple affordances (and multiple components of affordances) raises the problem of how affordances are selected to produce actions. At a behavioural level, the compatibility effect paradigm has been used to explore this. For example, Tucker and Ellis (2001) asked participants to classify an object as either natural or artefact using a power or precision grip on a customised joystick. The authors presented objects that were either small or large and therefore tended to afford a precision or a power grip. They showed that even though the size of the object was not relevant to the categorisation task, the affordances elicited by the object interfered with the selection of the categorisation (for a description of the task see chapter 4).

Moreover, it is thought that attentional processes play a role in the selection of affordances (Tucker & Ellis, 1998). Tipper, Paul and Hayes (2006) used the same compatibility effect used by Tucker and Ellis (1998), but presented handles that could be different for colours, shape, direction and orientation ("passive state: handle in horizontal orientation or "active state": handle rotated 45°). They showed that affordances are not automatically elicited but are instead strongly modulated by the task and the related attentional processes. For instance, participants responded faster when the handle was in the active state in the shape discrimination task but not in the colour discrimination task. Moreover, when the handles were presented in active and passive state, but the door in the background was removed, there was no action affordance effect as shown by no difference between reaction times between the passive and active state. The authors concluded that active objects, with which the current action is implied, produced larger affordance effects compared to object in passive state (e.g., with which no action is implied).

To summarise, affordances might be based not only on structural object properties but also on learned functional properties, which seems compatible with the account of a dorso-dorsal stream for grasping and a ventro-dorsal stream for use within the parietal cortex. Projects 2 and 3 of this thesis aim to investigate this further.

1.11 Current projects

The overall aim of my thesis was to further understand the role of the areas identified in the literature review above within the dorsal and ventral visual streams for perceiving and grasping both meaningless objects (i.e., rectangular blocks) and objects associated with specific hand-actions and functions (i.e., tools) implementing tasks that are thought to depend on processing from both streams and/or their interaction.

In project 1 (Chapter 2), I investigated the causal role of the dorsal and ventral visual streams in different types of grasping: real and pantomimed. To do this, I used fMRI-guided continuous Theta-Burst Stimulation (cTBS) to create a virtual lesion to aIPS (a key region in the dorsal stream though to be involved in hand preshaping), LO (a key region in the ventral stream thought to be involved in shape recognition) or the vertex (control region). To localise these brain regions, I used a novel technique in which I combined high resolution individual MRI scans and activations from the NeuroSynth platform (http://neurosynth.org/). I implemented a paradigm similar to the one Goodale et al. (1994) originally used with patient DF. Milner and Goodale hypothesised that real actions (i.e., immediate and target-directed) depend on dorsal processing, while indirect actions (i.e., pantomimed or memory-guided actions) additionally require ventral visual stream processing. Based on their model, I hypothesised that cTBS-to-aIPS would impair hand preshaping in both real and pantomimed grasping tasks, while cTBS-to-LO would impair grip scaling in the pantomimed grasping task, only.

In Project 2 (Chapter 3), I investigated the representations within the tool processing regions and whether these representations vary according to the task (i.e., view or pantomime) and the type of manipulation knowledge (i.e., functional or structural manipulation knowledge). To decode brain activity in response to viewing pictures of tools and pantomimes of tool use, I used fMRI and multi voxels pattern analysis (MVPA). MVPA is a multivariate technique that uses classification algorithms to differentiate spatial voxel pattern of activity within a given area. Given that univariate fMRI analysis has previously revealed the existence of different networks in the human brain for viewing tools and pantomiming tool actions (e.g., Lewis, 2006), I used MVPA as it provides additional insight into what information different regions within the "tool processing" network code and whether they contain information about tool identity and manipulation (such as power and precision grip) and functional (such as rotation and squeeze movements) properties for perceiving and pantomiming tool use. To test our hypothesis participants were presented with either pictures of different tools (view task) or pantomimed tool use cued by tool names (pantomime task) while in the scanner. Based on previous studies, I would expect that decoding accuracy within the inferotemporal cortex would be higher in the view task, while decoding within frontal and parietal regions would be higher for the pantomime task. Moreover, I would expect higher decoding accuracy for structural manipulation knowledge in regions within the dorso-dorsal stream. On the other hand, I would expect higher decoding accuracy for functional manipulation knowledge in regions within the ventro-dorsal stream.

In project 3 (Chapter 4), I explored how tool identity and action end-goal modulates grasping kinematics even when structural differences between objects are controlled for. Based on the differences demonstrated in patients with optic ataxia and ideomotor apraxia in tasks in which they have to grasp an object based on its structural properties (i.e., manipulation knowledge) or based on its functional knowledge, I implemented a grasp-to-move and a grasp-to-use task. My interest focused on whether grasping kinematics towards the same tool are influenced by the end-goal of the subsequent action and whether tool identity is processed in both grasp-to-use (GTU) and grasp-to-move (GTM) or not. Based on the account that there is a dorso-dorsal grasp system and a ventro-dorsal use system in the parietal cortex, I hypothesised that GTU and GTM would show different grasp kinematics. Moreover, I hypothesised that for the GTU task, the identity of the tool should play a critical role in action planning and thus should affect grasp kinematics. In contrast, for the GTM task, tool identity should not play such an important role, and therefore I did not expect differences in grasping kinematics between tools.

Chapter 2

2. An fMRI-guided TMS study to investigate the causal role of LO and aIPS in real and pantomimed movements

2.1 Introduction

In 1992, Milner and Goodale (1992) proposed an influential model in which two cortical visual streams, respectively the dorsal and the ventral visual streams, separately subserve vision-for-action and vision-for-perception (Goodale & Milner, 1992; Goodale, 2014; Milner & Goodale, 1995, 2006, 2008). According to the model, the dorsal stream, projecting from V1 to the posterior parietal cortex, processes visual information online to allow us to reach and grasp objects in front of us. Whereas the ventral stream, projecting from V1 to the temporal cortex, transforms visual information into durable perceptual representations, allowing us to recognise the object. However, Milner and Goodale also proposed that not all actions are subserved by the dorsal visual stream (Goodale & Milner, 1992; Goodale, 2014; Milner, 2017; Milner & Goodale, 1995, 2006, 2008). In particular they suggested that while real actions (or immediate target-directed) depend on dorsal processing, indirect actions (such as pantomimed or memory-guided actions) may be additionally mediated by the ventral visual stream (Goodale et al., 1994; Goodale et al., 1991; Milner, 2017). Although this account may not have been made clear in the initial formulation of the perception and action model (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006), in 2008, Milner and Goodale published a paper in which they clarified their hypothesis, also taking into account more recent studies.

The perception and action model (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006, 2008) was based on evidence from a single-case study of a patient who suffered from visual form agnosia after bilateral damage to structures in her ventral stream. In particular, Goodale and others (1994) found that patient DF, could pre-shape her hand in-flight to match the size of objects in front of her (immediate real grasping) in a similar way to control participants. However, her performance when she was asked to pantomime grasping movements beside the target object was considerably worse compared to her performance in real grasping (experiment 3 in Goodale et al., 1994). In fact, in the pantomime grasping task, DF’s anticipatory hand preshaping was highly variable and correlated poorly with object size demonstrating weak grip scaling when compared to her performance in the real grasping (Goodale et al., 1994) as shown in figure 2.1. Similarly, when she was instructed to perform memory-guided grasping, all evidence of grip scaling had disappeared.

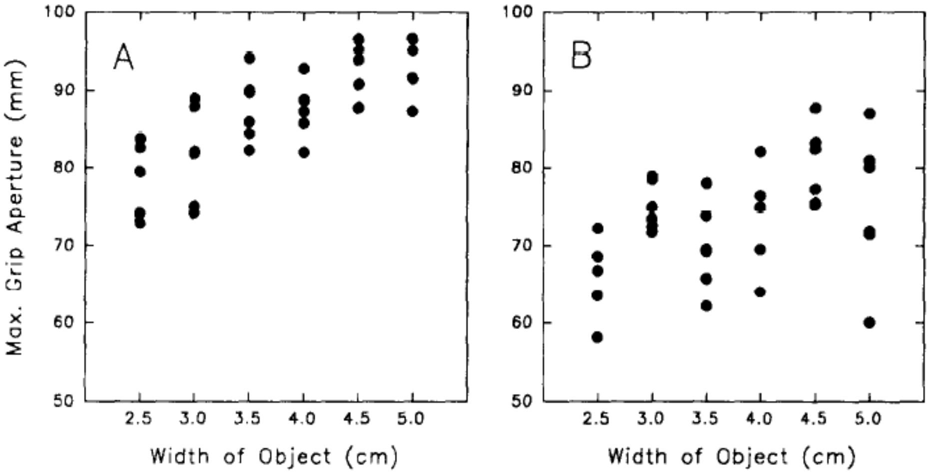


Figure 2.1 Data from patient DF showing the range of maximum grip aperture scores for individual trials directed to the various target objects used in experiment 3 in Goodale et al., 1994 during real (A) and pantomimed (B) grasping responses. From “Differences in the visual control of pantomimed and natural grasping movements”, by Goodale, Jakobson and Keilor, 1994, Neuropsychologia, 10, pp. 1159-1178. Adapted with permission.

In sharp contrast with DF, Milner and colleagues (2001) found that optic ataxic patient IG with bilateral dorsal stream lesions, was profoundly impaired in real grasping, but paradoxically her grasping performance improved when she was required to perform delayed real grasping and delayed pantomimed grasping movements (Milner et al., 2001). These observations support the idea that real and pantomimed actions might involve different brain networks, specifically that pantomimed grasping may rely on ventral stream structures that are damaged in patients with visual form agnosia.

While evidence from neuropsychology has been crucially informative to understand which regions in the brain may be causally involved in visuomotor tasks (e.g., Goodale et al., 1994; Goodale & Milner, 1992; Milner & Goodale, 2008, 2006), it is important to highlight that the number of patients showing a specific behaviour is usually small and lesions are very different from case to case. Moreover, post-lesion neuronal reorganisation makes it challenging to link the role of a specific brain network to the observed behaviour (e.g., Rorden & Karnath, 2004). To tease apart the contribution of the aIPS and LO within the dorsal and the ventral stream in hand preshaping during real and pantomimed grasping, I used an offline TMS protocol to recreate a virtual lesion in the brain. I decided to use an offline TMS protocol as it allows to create virtual lesions that last after the stimulation and therefore it allows to recreate a behaviour that is similar to patients with brain damage.

Several studies in the last 25 years have investigated the differences between real and pantomime actions in healthy participants using behavioural (e.g., Cavina-Pratesi, Kuhn, Ietswaart, & Milner, 2011; Copley-Mills, Connolly, & Cavina-Pratesi, 2016; Goodale et al., 1994) and neuroimaging methods (Kroliczak, Cavina-Pratesi, Goodman, & Culham, 2007). For example, when Goodale et al. (1994), tested DF's age/gender matched controls and observed that participants' real actions were not identical to the pantomimed ones. The authors reported that for pantomimed actions the in-flight distance between the index finger and thumb (maximum grip aperture, MGA) was smaller overall and was less precise to object size compared to real actions. In addition, pantomimed actions took longer to be completed, reached lower peak velocities and presented higher trajectories of the wrist during the reaching phase. In line with this, Zahariev & MacKenzie (2007), reported that MGA was smaller when participants had to pantomime to grasp virtual objects (i.e., no physical object present, only the reflection of the object on the workspace) versus grasping real objects. The authors speculated that because during pantomiming there is no feedback on terminal accuracy which increases uncertainty, adjustment and corrective movements might not be performed (Zahariev & MacKenzie, 2007). Similarly, Copley-Mills et al. (2016) reported smaller MGAs in pantomimed compared to real grasping actions. Taken together, these results further suggest that different networks in the healthy brain are involved in the control of real and pantomimed grasping. However, it remains unclear which regions within the dorsal and the ventral stream causally contribute to different forms of grasping.

Studies implementing functional MRI have been informative in identifying a posterior parietal network in the brain activated during target-directed grasping actions (Culham, Cavina-Pratesi, & Singhal, 2006; Davare, Kraskov, Rothwell, & Lemon, 2011; Filimon, 2010; Konen, Mruczek, Montoya, & Kastner, 2013; Vingerhoets, 2014). In particular, the anterior intraparietal sulcus (aIPS), located at the junction between the post-central sulcus and the intraparietal sulcus, has been identified for its role in hand-objects interactions both in humans (Binkofski et al., 1998; Culham et al., 2003; Frey, Vinton, Norlund, & Grafton, 2005) and monkeys (Murata et al., 2000; Sakata et al., 1995). Binkofski et al. (1998) have shown that patients with lesions of the cortex lining the anterior part of the intraparietal sulcus (either left or right) were impaired in shaping their hand to object size during grasping whereas patients with posterior parietal cortex (PPC) lesion, sparing area aIPS, do not show the same behaviour. They observed that patients with anterior intraparietal lesions reached out to the target with normal wrist velocity with either hands, but movement time was longer for actions performed on the contralesional side. Moreover, patients were not shaping their hand to the object size when grasping with the contralesional hand. In contrast, in the group with PPC lesions, without aIPS damage, the kinematics parameters were not different from control participants (Binkofski et al., 1998).

Evidence from electrophysiological recordings in non-human primates, indicates that the neurons located within the anterior-lateral bank of the intraparietal sulcus (area AIP), preferentially fire for hand shaping during object-directed grasping versus object fixation (Murata et al., 2000; Sakata et al., 1995). The involvement of area AIP in hand shaping for grasping has been further confirmed through pharmacological inactivation of the area, which led to an impairment in hand pre-shaping during object-directed grasping actions (Gallese et al., 1994). In humans, area aIPS is proposed to be the putative homologue of the macaque area AIP (e.g., Grefkes & Fink, 2005), and in parallel with monkey data, neuroimaging studies in humans have shown stronger activations in the aIPS for hand shaping compared to reaching (Culham et al., 2003). Furthermore, in neuroimaging studies with humans, higher activations in the aIPS have been observed during real versus pantomimed grasping (Kroliczak, Cavina-Pratesi, Goodman, &

Culham, 2007) and real immediate grasping versus delayed grasping (Fiehler et al., 2011; Himmelbach et al., 2009; Singhal, Monaco, Kaufman, & Culham, 2013).

All the above results fit with the two visual streams hypothesis, suggesting that the processing of visual information about the object for online grasping depends on processing carried out in the dorsal visual stream. However, it remains unclear whether visual stream regions play a critical role in more perceptual tasks (e.g., pantomimed grasping, delayed-grasping, delayed-pantomimed, object recognition). A likely candidate is the lateral occipital complex (LOC) (Malach et al., 1995) in the ventral stream. The LOC includes two spatially segregated subdivisions, a dorsal-caudal subdivision called the lateral occipital (LO) located on the lateral surface of the occipital-temporal junction, and a ventral-anterior subdivision located in the fusiform gyrus (pFs/LOa) extending also into the occipitotemporal sulcus (Grill-Spector et al., 2001). LOC is typically activated by the presentation of intact versus scrambled images of objects (Malach et al., 1995) and is thought to play a critical role in object recognition by integrating objects' visual features into coherent representations of the objects (Grill-Spector et al., 2001). As noted earlier in this thesis, following lesions in her ventral stream, patient DF, showed an impairment in pantomimed grasping and in grasping following a delay (Goodale et al., 1994), however, her performance improve when she performed real grasping. DF's lesions do not include all of LOC: area LO is damaged bilaterally in patient DF (James et al., 2003), while areas on the ventral occipitotemporal surface, such as primary visual cortex, the lingual gyrus and the face selective cortex in the fusiform gyrus, are spared (James et al., 2003; Steeves et al., 2004). Recently, a similar behaviour to DF has been shown in patient MC, who has a much more extensive bilateral lesion in the ventral stream (compared to DF), including LO (Culham et al., 2008). However, because of the extension of the lesions in both patient DF and MC, it is difficult to conclude that area LO specifically is critical for the dissociation observed between real and pantomimed grasping.

It is becoming increasingly apparent that DF's bilateral lesions are not restricted to the ventral stream, but that she has bilateral damage in more posterior parieto-occipital regions of her dorsal stream (Bridge et al., 2013; James et al., 2003) in the vicinity of the superior parieto-occipital sulcus. This region is activated during arm movement

(Connolly, Andersen, & Goodale, 2003) and is the possible homologue of the macaque parietal reach region (Snyder, Batista, & Andersen, 1997). Whilst in healthy participants grasping-related activation in the aIPS is largely bilateral, with stronger response in the contralateral hemisphere to the hand being used (Culham et al., 2001), patient DF does not show activation in the left aIPS (James et al., 2003).

Recently, it has also been hypothesised that in addition to visual form agnosia, DF has optic ataxia (Hesse et al., 2012, 2014; Rossit et al., 2017; for a description of the tasks see section 1.8). Therefore, whether DF's deficits in pantomimed grasping are related to her ventral and/or dorsal stream lesions remains unclear and a new TMS experiment will help understanding the causal involvement of aIPS and LO in real and pantomimed grasping.

In an fMRI study of real and pantomimed grasping (versus real and pantomimed reaching), Kroliczak et al. (2007) reported that bilaterally aIPS was more activated during real grasping versus real reaching, but that it did not appear to be more activated during pantomimed grasping versus pantomimed reaching. The authors suggested that making contact with the object is critical for aIPS activation and that, in contrast, pantomimed actions, are not sufficient to engage the aIPS (Kroliczak et al., 2007; but cf. Shikata et al., 2003; Simon et al., 2002). Based on previous fMRI studies, the authors hypothesised that LO should be equally activated during real grasping and real reaching (Culham et al., 2003), whereas on the basis DF's behavioural performance (Goodale et al., 1994) and neuroimaging evidence (James et al., 2003), LO should present higher activation in during pantomimed grasping versus pantomimed reaching (Kroliczak et al., 2007). However, surprisingly, the authors reported no increased activation in LO for pantomimed grasping (versus real grasping). Instead, they reported similar levels of activation in LO bilaterally across all conditions. The authors did not exclude that information about objects' features processed in LO may be retrieved for pantomimed grasping and suggested that it might be the case that the extraction of the information does not require more oxygen to reach the area, and therefore does not lead to an increase in BOLD signal (Kroliczak et al., 2007). Kroliczak et al. (2007), identified another area, which overlapped with both the right middle temporal gyrus (MTG) and superior temporal sulcus (STS), that showed increased activation during pantomimed actions compared to real actions (Kroliczack et al., 2007). Therefore, based on this study, whether LO is critical for pantomimed grasping remains questionable.

More recently, Singhal et al. (2013) using fMRI, compared activations during real (immediate) grasping versus delayed/memory-guided grasping and reported that bilaterally IPS was more activated for delayed grasping versus delayed reaching while participants were looking at the object and while performing the action, but not during the delay, confirming its critical role in action execution. Interestingly, area LO was not only activated during visual stimulus presentation but was re-activated during action execution (after the delay) when there were no visual stimuli present. The authors argue that during delayed grasping perceptual structures that are involved in object recognition are recruited to provide information about objects' features to guide the dorsal stream in performing grasping actions (Singhal et al., 2013).

Evidence from functional MRI is informative about the relationship between task-behaviour and brain activity, however, fMRI by itself cannot provide information about the causal involvement of a brain region on an observed behaviour (Weber & Thompson-Schill, 2010). Thus, studies implementing Transcranial Magnetic Stimulation (TMS) to generate transient virtual lesions may help to attribute causality between brain anatomy and function (Pascual-Leone, Bartres-Faz, & Keenan, 1999; Paus, 2005; Sack, 2006; Walsh & Rushworth, 1998). With TMS it is possible to create brief, localised and transient virtual lesions that can disrupt cognitive functions and it is possible to make inferences about the healthy brain functions (Walsh & Cowey, 2000; Walsh & Rushworth, 1998).

TMS was originally developed to investigate the physiology of the motor system (Barker, Jalinous, & Freeston, 1985), however, it is now used in several areas of cognitive neuroscience, including attention (e.g., Szczepanski & Kastner, 2013) memory (e.g., Pobric, Jefferies, & Lambon Ralph, 2010), decision making (e.g., Hartwigsen et al., 2010), language (e.g., Sakai, Noguchi, Takeuchi, & Watanabe, 2002), visual processing (e.g., Pitcher, Goldhaber, Duchaine, Walsh, & Kanwisher, 2012) and action planning (e.g., Pobric et al., 2010).

TMS has been used to delineate the perceptual dissociation between the dorsal and the ventral stream. For example, Ellison and Cowey (2006) found that while TMS to right PPC increased reaction times in the spatial discrimination task (but not in the shape or colour task) TMS to right LO increased reaction times in both spatial and shape discrimination tasks.

In a series of studies, Tunik and colleagues (Cohen, Cross, Tunik, Grafton, & Culham, 2009; Rice, Tunik, & Grafton, 2006; Rice, Tunik, Cross, & Grafton, 2007; Tunik, Rice, Hamilton, & Grafton, 2007; Tunik, Frey, & Grafton, 2005) have shown that online TMS to aIPS, but not other parietal regions, impairs the control of grasping with the contralateral hand (for a more in depth review, see chapter 1). Specifically, Tunik et al. (2005) have shown that in the context of visual perturbation of a target object, TMS-induced effects were present for adapting the grip aperture and the forearm orientation, leading the authors to conclude that left aIPS is involved in the configuration of grasping and in the rapid goal-dependent updating of grasping actions (Tunik et al., 2005). No effects of TMS were observed when TMS was delivered to left caudal IPS, left parietal occipital cortex and left primary motor cortex.

In a follow-up study, Rice et al. (2006) implemented a similar paradigm to the one used by Tunik et al. (2005) and delivered TMS over the left aIPS, medial IPS, left caudal IPS or no TMS at all. They delivered TMS at different times: during the viewing period (i.e. planning phase) or at button release (i.e., execution phase) while participants were performing grasping actions with their right hand. In the no-perturbation task, they observed that maximum grip aperture was reached earlier and presented faster peak velocities when TMS was applied to left aIPS (but not on the control sites) during the execution phase compared to when no TMS was applied. Moreover, in the perturbation task, increased maximum grip apertures and peak velocities were observed when TMS was delivered over left aIPS (but not control regions) during the correction phase versus no-TMS. This study provides evidence that left aIPS plays a causal role in programming and correcting hand preshaping during grasping (Rice et al., 2006).

Similar results were obtained by Glover et al. (2005), who observed that TMS (versus no TMS) delivered at movement onset, increased grip aperture in the first half of the movement when a correction from small to large was required. In contrast, when TMS was delivered halfway through the movement (versus no TMS), an increase in maximum grip aperture was observed in the second half of the movement only. The authors suggested that the timing of the disruption was linked to the initiation of the adjustment and concluded that the left aIPS plays a critical role in initiating the online adjustment of hand grip when a change in target size is required (Glover et al., 2005).

Subsequently, Rice et al. (2007) investigated whether the contribution of aIPS to grasping control is lateralised or not. Here, they used double-pulse online TMS at different time frames (e.g., the first TMS pulse at onset of the movement followed by the second 100 ms later) to the left or the right aIPS or no TMS. The authors showed that, TMS to the right aIPS, versus no-TMS, resulted in shorter acceleration phase for grasping with the left hand, while TMS to the left aIPS, versus no TMS, resulted in shorter acceleration phase for grasping with the right hand. Rice et al. (2007), concluded that left aIPS mediates grasping with the right hand only, and that right aIPS mediates grasping with the left hand only. Notably, in these studies, no significant effects of TMS on grip scaling were found. Based on results from monkey showing that inactivation of AIP altered hand configuration (Gallese et al., 1994) the same would have been expected in humans.

Davare, Andres, Clerget, Thonnard, & Olivier (2007) examined how repetitive TMS affected participants' grip-to-lift performance of an object. The author observed that double-pulse TMS applied at different delays between 0 and 200 ms after movement onset over aIPS bilaterally (versus the supramarginal gyrus) increased the variability and mean location of the points where the fingers contacted the target. They concluded that bilateral inactivation to aIPS caused a larger dispersion of the fingertip final position on the object surface. The difference in the findings observed by Rice at al. (2007) and Davare et al. (2007) may be explained by the difference in the timing at which the TMS pulses were delivered, the task employed and how the hand shaping was measured (e.g., hand preshaping versus final hand shape).

Additionally, Gutteling, Park, Kenemans and Neggers (2013) found that TMS to left aIPS selectively modulated the participant's sensitivity to the orientation during action preparation, but no effects were found on grasping kinematics during the execution of grasping or pointing itself. These findings seem at odds with the results reported in the studies reviewed above, however, as the authors pointed out, no previous studies reported effects on kinematics using single-pulse TMS at the go-cue, as is the case here. Thus, the authors speculated that it may be the case that aIPS was stimulated too early in the grasping preparation. The author concluded that the left aIPS is involved in the perceptual modulation preceding the manual action.

More recently Le, Vesia, Yan, Niemeier, and Crawford (2014) used TMS to probe the contribution of aIPS and caudal IPS in each hemisphere while participants were grasping an object whose orientation might or not change (e.g., size perturbation task). The authors found TMS-induced effects on grip aperture (i.e., wider grip apertures) around the time of maximum grip aperture, only when they stimulated the right aIPS at the time of movement onset and object-size perturbation. No effects were found when TMS was delivered to left aIPS or the caudal IPS. The authors concluded that while unimanual precision grasping is associated with the hemisphere contralateral to the grasping hand, the right aIPS is causally involved in bimanual grasping. Specifically, right aIPS is involved in bimanual grasping movements during object perturbation, but not in the transport of the hand (Le et al., 2014), and that this is consistent with previous observations (Tunik et al., 2005; Rice et al., 2006).

To my knowledge, to date, only one study implemented TMS to ventral and dorsal stream areas during grasping movements. Cohen et al. (2009) investigated the causal role of left aIPS and left LO in the online control of the movement and specifically in real (immediate) grasping and delayed grasping implementing MRI-guided online TMS. Two pulses of TMS were delivered (first pulse at movement onset followed by the second pulse 100ms later) over either aIPS, LO or no TMS (control condition). They reported that TMS to aIPS and LO led to different effects on timing and velocity kinematics measures associated with hand preshaping. Specifically, TMS to aIPS led to a shorter time to peak velocities of grip aperture for both real and delayed grasping (compared to no TMS condition). On the other hand, TMS to LO led to an increase in the peak velocity of the grip aperture compared to the no TMS condition in both real and delayed grasping. The authors suggested that aIPS is involved in the online comparison between the target size and grip aperture. However, during delayed grasping, additional processing is required from area LO to guide the dorsal stream. The authors suggested that it is likely that the representation of the size of the target in the dorsal stream has decayed and, thus a perceptual memory representation from the ventral stream is instead required (Cohen et al., 2009). Thus, fMRI (Singhal et al., 2013) and TMS (Cohen et al., 2009) evidence suggest that LO, a specific area within the ventral stream, is crucial in recalling information to control actions following a delay.

Inspired by these studies, we investigated whether aIPS and/or LO are causally involved in the control of real and pantomimed grasping actions. Evidence from fMRI supports the view that aIPS is involved in the online control of real and pantomimed grasping (versus real and pantomimed reaching), however, whether LO plays a critical role is still unclear. Thus, a new experiment with TMS offers the possibility to investigate the causal role of aIPS and LO in the control of real and pantomimed grasping.

Instead of using online TMS as the studies reviewed above, we applied an offline TMS protocol, named continuous Theta Burst Stimulation (cTBS), to left aIPS, left LO or the vertex (control condition). Previous TMS studies investigating the role of aIPS in the control of online movements (Cohen et al., 2009; Rice, Tunik, & Grafton, 2006; Rice et al., 2007) have observed that the effects of online TMS were transient in nature and specifically they were strongest immediately after the stimulation. Critically, they delivered one pulse of stimulation at the onset of the movement followed by the second one 100 ms later and they observed TMS induced effects on timing and velocity kinematics variables that were measured within approximately 350 ms from the stimulation (Cohen et al., 2009). Thus, we chose to implement an offline cTBS protocol, which is administered before the participant is presented with the task and allowed us to decrease the cortical excitability in a small area in the brain (approximately 0.5-1 cm, Sliwinska, Vitello, & Devlin, 2014) for up to 60 minutes (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005; see section 2.2.6). We decided to use an offline, rather than an online, TMS protocol, to be able to recreate a lesion that lasted for several minutes and that was therefore comparable to lesions in patients with brain damage. This approach gave us the possibility to explore the effects of a virtual lesion on variables throughout the task and not just on the variables measured near the time of delivery of to the stimulation as in previous TMS studies (e.g., Cohen et al., 2009). Using offline cTBS we aim at recreating virtual lesions in the healthy brain that are similar to lesions observed in patients with brain damage, without the confound of lesions that extend to other regions nearby or neural plasticity reorganisation. Moreover, cTBS allow us to test the same participants on the same tasks and to manipulate the specific region to which TMS is applied. This would help to shed the light on the nature of the double dissociation observed in patients with optic ataxia and visual form agnosia, which have not been tested under the same conditions so far (Pisella et al., 2006; Rossetti et al., 2003)

Additionally, previous studies had several limitations: small sample size ($N \leq 10$ in Cohen et al., 2009; Rice et al., 2006; Rice et al., 2007); instead of using the vertex as a control site, implemented a no-TMS condition (Cohen et al., 2009; Le et al., 2014; Rice et al., 2006; Rice et al., 2007; Tunik et al., 2005); and to my knowledge, only Cohen et al. (2009) applied TMS to both LO and aIPS and found an effect on timing and velocity kinematics of grasping. Thus, the involvement of the dorsal and the ventral stream in hand preshaping remains to be tested with TMS. Moreover, previous TMS studies used MRI-guided TMS (Cohen et al., 2009; Davare et al., 2007; Le et al., 2014; Rice et al., 2006; Rice et al., 2007), which has been shown to be less powerful than fMRI-guided TMS (Sack et al., 2009). Here, to localise the regions, we used a novel technique in which we combined high-resolution MRI and individual anatomical landmarks with population-based fMRI activations. To localise the target regions, we extracted population-based fMRI activations from the NeuroSynth database of fMRI studies (http://neurosynth.org/) which we superimposed on each participant's high-resolution MRI (see section 2.2.5).

In our study, real and pantomimed grasping tasks were performed in open loop (without online visual feedback of the hand and target during the movement), so that participants had to rely on visual feedforward programming. Based on the perception and action model (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006, 2008), we hypothesized that cTBS to left aIPS would interfere with the participants' ability to preshape their hand aperture in the real and pantomimed grasping tasks, whereas cTBS to left LO would interfere with their scaling in the pantomimed grasping task only.

2.2 Methods

2.2.1 Participants

Sixteen naïve participants (6 males; mean age = 25.1 years old, S.D. = ±2.4 years old; mean education = 18.2 years, S.D. = ±1.9) took part in the study. In total 19 participants were recruited from the University of East Anglia (Norwich, UK), but data from three participants were excluded from the analysis (one participant was discarded due to equipment error and the other two participants did not show significant grip scaling to object's size in any condition).

All participants were healthy, had normal or corrected-to-normal vision, were right-handed (Oldfield, 1971) and were all screened for adverse reactions to TMS by means of the TMS safety screening questionnaire (Rossi et al., 2009). Participants were excluded if they had history of neurological, psychiatric or motor disorders, if they had metal in their bodies (e.g., shrapnel, surgical clips), or implanted devices (e.g., cardiac pacemakers), where taking neuroactive medications (e.g., antidepressant) or drugs, had history of seizure in their family, or held a heavy goods vehicle or bus driving licence. Each participant was required to visit the lab 4 times (1 "taster" session and 3 experimental sessions) and to undergo MRI scanning at the Norfolk and Norwich University Hospital Radiology Department. Each visit lasted approximately 1 hour. To minimise the risk of any potential hazard due to the assumption of alcohol or sleep deprivation in the 24 hours prior to the experiment, the TMS safety questionnaire was administered to each participant before each TMS session.

The UEA Ethics Committee at the School of Psychology approved the study (reference 14-15-24) and participants gave informed consent in accordance with the principles of the Declaration of Helsinki (1964). All participants were reimbursed for their time.

2.2.2 Materials and Apparatus

Participants were seated in front of a grey table ($1m^2$) with their chin stabilised on a chin-rest to minimise head movements and were instructed to place their thumb and index finger on the start button positioned in front of them and aligned with their midsagittal plane. They were asked to maintain their gaze on a green fixation light-emitting diode (LED) attached to a lock line in front of them (9 cm above the table they were sitting at) at a distance of 52 cm from the participants' nose bridge. The fixation LED was positioned 12 cm on the left of the participants' midline, so that the objects appeared in the peripheral lower right visual field at ~ 13° eccentricity with respect to the fixation LED. Visual feedback was controlled using liquid crystals shutter glasses (Plato System; Translucent Technologies, Toronto, Ontario, Canada).

Six Efron white wooden objects (Efron, 1969) with constant surface area (25 cm^2, thickness = 1cm) were presented in a pseudo-randomized order (no object was presented twice in succession) with the following dimensions (height x width): 5.0 cm x 5.0 cm; 4.0 cm x 6.25 cm; 2.5 cm x 10.0 cm; 3.0 cm x 8.3 cm; 4.15 cm x 6.0 cm; 3.5 cm x 7.15 cm). Three of these objects (the 5.0, 4.0 and 2.5 cm heights) were used for later analysis and therefore presented a larger number of times. The other three objects served as foils on randomly catch trials, included to reduce practice effects (Rossit et al., 2013).

Three lightweight markers (4 mm diameter) were attached with adhesive tape to the participant's right nail tip of thumb and index finger and wrist. Six high-resolution infrared sensitive cameras (Qualisys AB, Gothenburg, Sweden) were used to record the x, y, and z positions of the markers at a frequency of 179Hz. A custom designed program written in Matlab (The MathWorks, USA) and the Psychophysics Toolbox extension (Brainard, 1997) was used to control the object presentation, goggles, fixation, and recordings. Eye movements were recorded by means of a video camera (Panasonic HD HVC-210) during the task (Chen, Sperandio, & Goodale, 2015) and visually inspected by the experimenter to ensure fixation. Only two experimental trials (out of a total of 1728) were excluded due to participants' not fixating. The use of a high-resolution eye-tracker was not possible because the participants were wearing the PLATO goggles to control viewing times.

2.2.3 Procedure

At the beginning of each session, the motion tracker markers were attached to the participants' right hand and the participants were explained the tasks and asked to complete a practice session (12 trials, 6 of real and 6 of pantomimed grasping). At the end of the practice, participants were invited to take a seat on the Brainsight TMS chair where the co-registration of their head and their MRI scan took place (see section 2.2.5). Before the stimulation, participants were invited to relax and reminded to let the experimenter know if they felt any discomfort during the stimulation (see section 2.2.6). At the end of the stimulation participants were invited to sit at the grey table to perform the grasping task reminded the instructions of the task.

Participants began each trial with the shutter goggles in opaque configuration and the right index finger and thumb touching one another and depressing the start button placed 15 cm in front of them. Then, the experimenter triggered the PLATO goggles to change to transparent configuration, and the participant was given 2s to fixate on the illuminated LED. At the end of the fixation period, the goggles changed to opaque configuration (preventing the participant from viewing the workspace), and the experimenter placed an object on the table. After a ready signal from the experimenter, the PLATO goggles changed to transparent configuration and an auditory tone (frequency 500 Hz; duration 0.25 ms) cued the participant to perform either a real or a pantomimed grasping according to block order (figure 2.2).

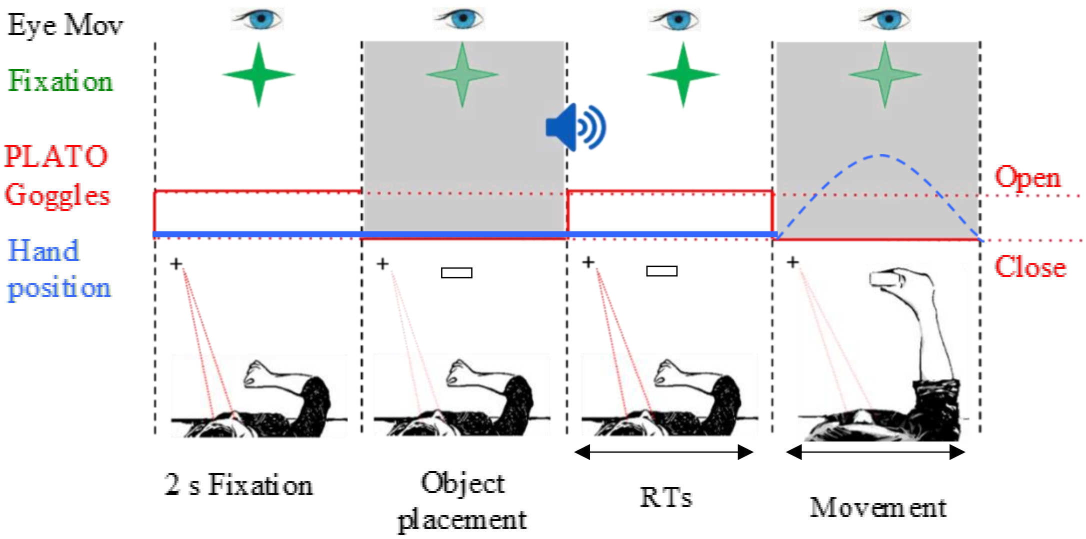


Figure 2.2 Trial timing. At the beginning of each trial the goggles opened to give time to the participant to adjust his/her eyes to the fixation, then the goggles closed to allow time for the experimenter to place the object (2s). During this time the participant was instructed to keep his/her eyes still. Simultaneously with the opening of goggles a sound played to cue the participant to reach out and grasp the object. As soon as the participant released his/her hand from the start button the goggles closed again so that no vision of their hand or the object was available during the movement.

In separate real and pantomime grasping blocks, participants were instructed, upon hearing the beep, either to reach out and pick up the object (real grasp, figure 2.3a), or to imagine that an identical object to the one in front of them was positioned on the right and to pantomime a grasping movement to that imagined object and pretend to pick it up as it was physically present (pantomime grasp, figure 2.3b; Goodale et al., 1994; Cavina-Pratesi et al., 2011). Participants were instructed to repeatedly pretend to pick up an imaginary object to the right repeatedly as we were interested in movements conducted with the right hand towards the right side after stimulation of the left hemisphere. Participants were asked to keep fixation for the whole duration of the trial and to pick-up the object by its width with the right index finger and thumb at a quick but natural pace upon hearing the auditory cue. Each block consisted of 42 trials, in which each experimental object was presented 12 times, the remaining 6 trials were included as catch trials to add more variability (which were not included in the analysis). Moreover, the viewing time of the hand and the object were the same across the two tasks, so that participants' performance was comparable across the tasks.

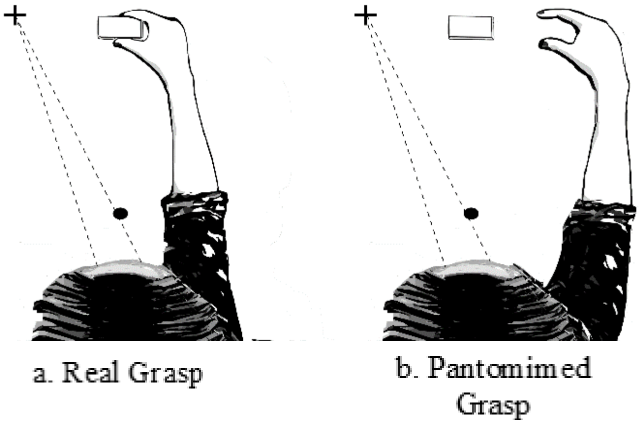


Figure 2.3 Schematic representation of a participant performing real (a) and pantomime (b) grasping tasks. The black dot represents the start position and the cross the fixation. Participants started each trial with their right hand on the start position and were asked to maintain fixation on LED for the whole duration of the trial.

2.2.4 MRI acquisition

A full-brain T1 weighted image was acquired for each participant with a GE Discovery 750w 3T MR scanner and a 32-channel coil at the Norfolk and Norwich University Hospital using a three-dimensional BRAVO sequence (repetition time, TR = 7.3 ms; time to echo, TE = 2.8 ms; flip angle = 12°; field of view, FOV = 230 mm; slice thickness = 0.9 mm; matrix = 256 x 256; https://cni.stanford.edu/wiki/MR_Prtocols).

The participant's MRI scans were transformed into standardised MNI space using the FSL software (FMRIB, Oxford; Smith et al., 2004; Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012). The brain of each participant was extracted from the skull using the brain extraction tool (BET; Smith, 2002) and normalized against a standard brain template in MNI space using the FMRIB's Linear Registration Tool (FLIRT; Jenkinson & Smith, 2001; Jenkinson, Bannister, Brady, & Smith, 2002).

2.2.5 Localisation of stimulation sites

To localise brain regions, we used fMRI activations extracted from the NeuroSynth database of previous fMRI studies and we confirmed the location of the activation, using anatomical landmarks in each participant's brain individually. In particular, we used the NeuroSynth database (Yarkoni et al., 2011), a large-scale automated synthesis of human's functional neuroimaging data. Using the data available in this database at the time of data collection, we identified the activation for aIPS using the keyword "anterior intraparietal" (70 studies; Appendix A) and LO using the keyword "lateral occipital" (180 studies; Appendix B). We used the reverse inference activation maps, which corresponds to the likelihood of a specific term being mentioned in a study given the presence of a reported activation. This implies that studies that used a specific keyword frequently, are much more likely to report activation in a specific region. NeuroSynth's reverse inference activations maps were superimposed onto the MNI brain of each individual participant for each site (figures 2.4a for aIPS and 2.4c for LO). Each ROI (3x3x3 mm voxels) was defined using MRIcron (Rorden & Brett, 2000) by selecting the peak of activation closest to the anatomical landmarks in each individual (figures 2.4b for aIPS and 2.4d for LO) and then imported back to FSL. Table 2.1 shows the mean coordinates for left LO and left aIPS.

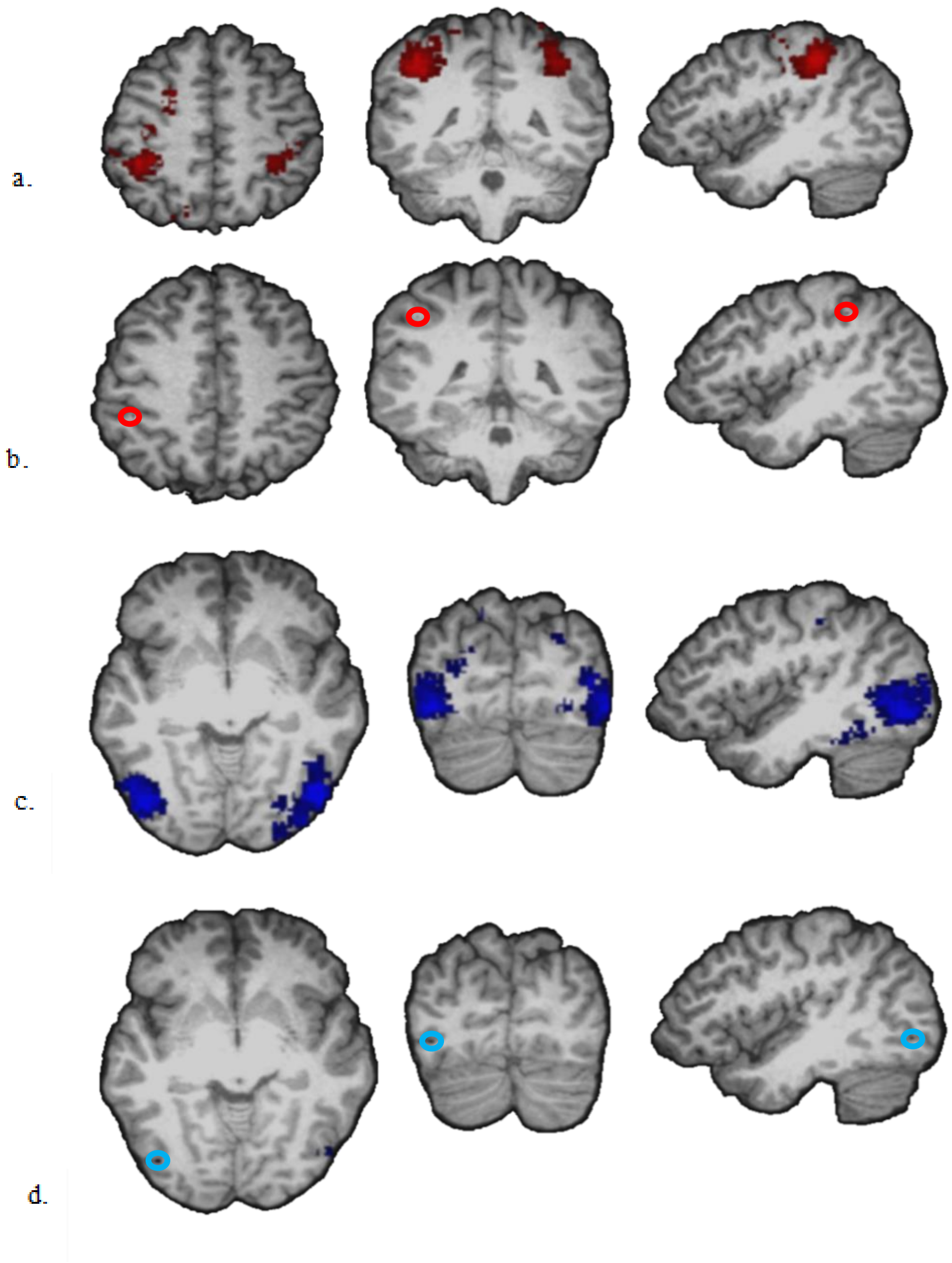


Figure 2.4 a) aIPS NeuroSynth reverse activation superimposed on a participants' MNI brain and b) the peak of the activation for aIPS ROI. c) LO NeuroSynth reverse activation superimposed on a participants' MNI brain and d) the peak of the activation for LO ROI.

The transformation was then reverse applied to each ROI using FSL to transform the coordinates in native space (Feredoes, Heinen, Weiskopf, Ruff, & Driver, 2011; Smittenaar, FitzGerald, Romei, Wright, & Dolan, 2013). We then visually confirmed based on anatomical landmarks (Feredoes et al., 2011; Smittenaar et al., 2013) that the coordinates in native space corresponded to aIPS and LO. In particular, aIPS site was located at the junction of the anterior portion of the intraparietal sulcus (IPS) and post-central sulcus in the left hemisphere (e.g., Culham et al., 2003; Rice et al., 2006; Cavina-Pratesi, Goodale, & Culham, 2007; Cohen et al., 2009; Rossit et al., 2013) and LO was located on the lateral bank of the fusiform gyrus near the lateral occipital sulcus (e.g., Grill-Spector et al., 2001) (figure 2.5). By combining population-based fMRI and anatomical landmarks with high resolution individual MRI scans, we were able to localise regions in a consistent manner across participants. Additionally, each ROI was visually checked by another researcher and was adjusted until 100% agreement was obtained.

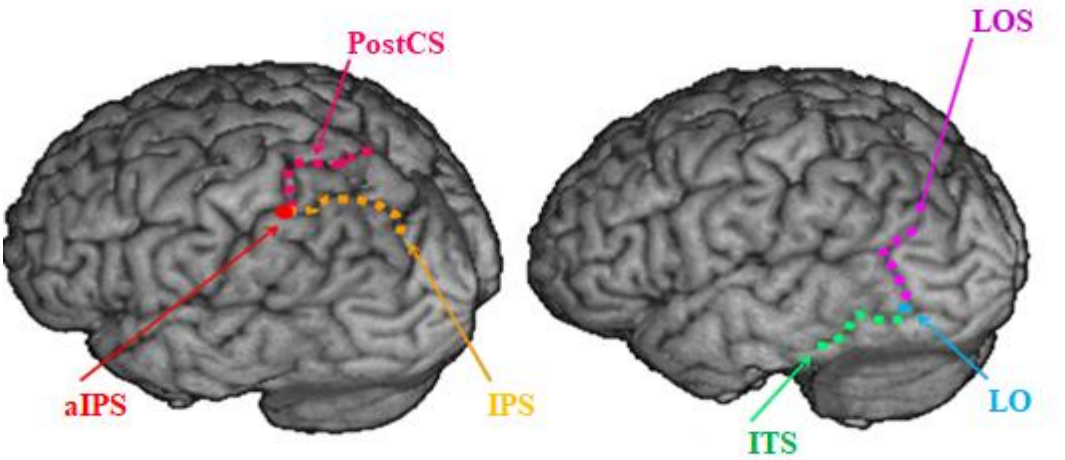


Figure 2.5 Localization of brain regions for stimulation on a three-dimensional rendering of one participant’s structural MRI in MNI space. Cortical sites are indicated with a red (aIPS) and a blue (LO) dot which represents the 95% confidence interval around the mean of the x, y, z MNI coordinates. The aIPS was located at the junction between the intraparietal sulcus (IPS) and the post-central sulcus (PostCS), while LO was located near the later occipital sulcus (LOS) and the inferior temporal sulcus (ITS; Malach et al., 1995).

Moreover, to test if our coordinates were similar to previous fMRI and TMS studies, we selected 20 published studies for aIPS and 22 for LO (Appendix C) and computed the x, y, z mean coordinates of aIPS and LO across the studies [when coordinates where reported in Talairach space, we used GingerALE (http://brainmap.org/software.html) to convert them into MNI space]. We then computed the 95% confidence intervals of the mean for the x, y, z coordinates extracted from published studies and found that for both regions, the mean of our population, was within the 95% confidence intervals of previous studies (table 2.1).

Table 2.1 Mean (and standard deviation, SD) MNI coordinates and 95% CI from previous studies for left LO and left aIPS (a) and mean (and standard deviation, SD) MNI coordinates of our sample (b). See Appendix C for a complete list of studies.

a.

	Left LO			Left aIPS		
	Mean (SD)	95% CI lower limit	95% CI upper limit	Mean (SD)	95% CI lower limit	95% CI upper limit
x	-45.68 (4.7)	-47.68	-43.75	-39.10 (5.4)	-41.56	-36.64
y	-72.29 (7.2)	-75.49	-69.07	-40.02 (4.7)	-42.15	-37.87
z	-3.78 (5.5)	-6.21	-1.34	47.58 (6.4)	44.68	50.47

b.

	Left LO	Left aIPS
	Mean (SD)	Mean (SD)
x	-43.69 (1.9)	-41.19 (4.5)
y	-74.31 (4.5)	-41.88 (2.8)
z	-4.75 (2.0)	45.13 (1.2)

2.2.6 Theta-Burst Stimulation (TBS)

Before the MRI acquisition (approximately 1 month before), potential participants were invited to the laboratory to take part in a TMS "taster" session in which they completed TMS and MRI screening questionnaires, had a chance to ask question about the technique and to try the TMS. So that each participant could familiarise with the TMS, after the participant completed the TMS safety checklist, the researcher explained the effects of the TMS over the hand motor area (e.g., visible muscle twitching in the hand simultaneously with the stimulation) and asked him/her if they were happy to try the stimulation. To locate the hand motor areas in the left hemisphere, we selected a region located 5-6 cm laterally and 1-2 cm anterior from the vertex (e.g., Buccino, Sato, Cattaneo, Rodà, & Riggio, 2009). Then the researcher asked the participant to pinch the index finger and thumb together and, using single pulse TMS with low intensity (e.g., 30% stimulator output) delivered TMS. The output of the stimulator was then increased (10% at a time) until a twitch in the hand of the participant was observed. The active motor threshold (ATM) is defined as the lowest setting at which > 5 out of 10 or stimulations result in any observable movement of the index finger (e.g., Westin, Bassi, Lisanby & Luber, 2015). However, determining the ATM was not the purpose of the session, nor relevant for the study, thus, we assessed the ATM as the minimum intensity at which at least 3 out of 5 consecutive stimuli elicited a visible movement of any fingers in their right hand. Moreover, as stimulation over occipital areas could lead to discomfort due to muscle twitching in the neck, we delivered 10 s of cTBS to the occipital cortex during the “taster” session. All participants involved in taster session experienced muscle twitching, but they reported it not to be painful and were happy to carry on with the experiment. One participant who took part in the “taster” session decided not to continue with the experiment due to personal circumstances, unrelated to the study.

Three cortical sites were chosen for stimulation: the most anterior part of the intraparietal sulcus (aIPS; Culham et al., 2003) in the left hemisphere, the lateral occipital complex (LO) in the left hemisphere and the vertex (Okamoto et al., 2004; Jung, Bungert, Bowtell, & Jackson, 2016; Cheke, Bonnici, Clayton, & Simons, 2017). We decided to use the vertex as a control site as it is assumed to play no active role in grasping (e.g., Dafotakis, Sparing, Eickhoff, Fink, & Nowak, 2008; Taubert et al., 2010). The advantage of vertex stimulation (versus sham stimulation in which the coil is placed away from the scalp) is that produces the same scalp sensation and the same sound as TMS to target regions (Jung et al., 2016). Earplugs were provided during the stimulation to dampen the noise associated with the stimulation. During the experiment, cTBS was delivered using a 70 mm figure-of-eight coil and a Magstim Super Rapid Plus Transcranial Magnetic Stimulator (Magstim Company Ltd.). The stimulation was performed using a continuous cTBS pattern (Huang et al., 2005) in which three pulses of stimulation were given at 50

Hz, repeated every 200 ms for a total of 600 pulses delivered in 40 s. The stimulus intensity was set at 40% of the stimulator output (Hayashi et al., 2013; Sharot et al., 2012; van Kemenade, Muggleton, Walsh, & Saygin, 2012). In this experiment we used fixed intensity of cTBS (defined as a percentage of the stimulator output). We decided not to tailor the intensity of the stimulation to each participant's ATM as studies suggest that different cortical regions have different excitability thresholds and we cannot assume that the cortical excitability of the motor cortex can be reliably used in the rest of the brain (Stewart, Walsh, & Rothwell, 2001). For example, studies show that there is no correlation between motor threshold and phosphenes (Antal, Nitsche, Kincses, Lampe, & Paulus, 2004; Boroojerdi et al., 2002; Oliver, Bjoertomt, Driver, Greenwood, & Rothwell, 2009), thus questioning the assumption that TMS threshold measures from different cortical regions might reflect a shared component of individual's responsiveness to TMS. In light of this evidence, using fixed stimulation output has become common practice (Cappelletti, Barth, Fregni, Spelke, & Pascual-Leone, 2007; Cattaneo, Silvanto, Pascual-Leone, & Battelli, 2009; Cohen Kadosh et al., 2007; Dormal, Andres, & Pesenti, 2008; Knops, Nuerk, Sparing, Foltys, & Willmes, 2006). Stimulation sites were located on each individual participant's MRI using Brainsight Frameless Stereotaxic software (Rogue-Research, Montreal, Quebec, Canada).

The position of the TMS coil was co-registered with the participants' head and during the stimulation, the position of the head and the coil were monitored using a Polaris Optical Tracking System (Northern Digital, Inc., Waterloo, Ontario, Canada). The coil was held tangentially to the scalp with the handle pointing backwards (Cohen et al., 2009; Le et al., 2014). To restrict movements and to help the participant keep a stable position, a chin rest and a forehead rest were used. None of the participants reported significant side effects, however, all the participants felt muscle twitching over their neck or head during LO stimulation, and three participants reported that their neck was sore the day after the stimulation. Five participants reported a mild headache in the evening after the stimulation.

After the stimulation, we waited approximately 5 minutes before starting the first task (Hayashi et al., 2013; van Kemenade, Muggleton, Walsh, & Saygin, 2012). We decided to do this based on Hubl et al.'s (2008) observations, in which they found no significant changes in the BOLD signal in the first 5 minutes after TBS over the frontal eye field compared to pre-stimulation fMRI.

According to Huang and colleagues (2005), cTBS produces consistent and rapid changes in the function of the human motor cortex that outlast the period of the stimulation for up to 60 minutes. The authors measured the peak-to-peak amplitude of MEPs in the first dorsal interosseous (FDI) muscle in 9 healthy participants after 600 pulses of cTBS. The authors found that after cTBS, MEPs were suppressed at 25 and 45 minutes and returned to baseline at 61 and 65 minutes. Although in the original paper, Huang et al. (2005), observed a significant reduction of MEP size following cTBS lasting up for nearly 60 minutes, it is worth mentioning that the duration of TBS induced effects is still controversial and varies according to the area TBS is applied to, as well as the behaviour under investigation (Huang et al., 2005; Hubl et al., 2008; Wischnewski & Schutter, 2015). To our knowledge, there are no studies investigating BOLD signal changes after TBS in aIPS and/or LO, however based on Huang et al. (2005) and Hubl et al. (2008) work, as well as Wischnewski and Schutter (2015) review which identified the effects of 600 pulses of cTBS in 40 s to last up to 60 minutes after stimulation, we ensured the duration of our experiment was not any longer than 35 minutes. This was done to allow time for participants to take short breaks during the tasks if they needed.

2.2.7 Analysis

Kinematic data were obtained by localising the x, y, z positions of markers attached to the index finger, thumb and wrist of the participants' right hand and was analysed off-line using a customised software written in Matlab (The MathWorks, USA). Raw data for each marker was filtered using a low-pass Butterworth filter (10 Hz-cut-off, 3rd order) for each trial. Each trial was visually inspected for any errors. Movement onset was defined as the time at which the velocity of the wrist marker exceeded 50 mm/s and the end of the movement was determined as the time at which the velocity of the wrist marker fell below 50 mm/s (e.g., Cohen et al., 2009).

Trials were excluded from the analysis for the following reasons: data points were missing due to occlusion of the markers (3.56 %), technical problems (4.25 %), reaction times exceeded 800 ms (Cohen et al., 2009) (1.22%), participants' errors, such as the participant was not holding down the start button when the auditory cue was played (1.65%) or failure to maintain fixation (0.01%). In addition, outliers were computed in all participants for MGA and trials were excluded from analysis if they exceeded two standard deviations from the mean MGA (6.6 %). In the real grasp condition, a total of 81.3% of all trial were included in the analysis and 81.8% were included in the pantomimed grasp condition, with a mean of approximately 11 repetitions per object size per condition (table 2.2). Given our hypothesis that cTBS-to-aIPS or cTBS-to-LO might affect grip scaling in real and pantomimed grasping, for conciseness we only analysed grip aperture related variables.

Table 2.2 Mean number of trials (and standard deviation, SD) included in the analysis for each object in each condition.

		VERTEX Participants' mean of included trials (SD)	aIPS Participants' mean of included trials (SD)	LO Participants' mean of included trials (SD)
Real grasping	Small	11.3 (0.6)	11.1 (0.6)	11.1 (1)
	Medium	11.1 (0.8)	11.4 (0.6)	11.4 (0.9)
	Large	11.2 (0.6)	11.2 (0.6)	11.1 (0.9)
Pantomimed grasping	Small	11.3 (0.7)	11.3 (1.2)	11.3 (0.6)
	Medium	10.8 (0.7)	11.5 (0.7)	11.2 (0.9)
	Large	11.19 (0.7)	11.4 (0.9)	11.3 (0.7)

Based on DF's poor performance (Goodale et al., 1994) in the pantomimed versus real grasping task, we analysed the maximum grip aperture. In addition, as maximum grip apertures linearly increases with object size (Jeannerod, 1984), we computed the maximum grip aperture as a function of object size. The best-fitting linear regressions for each participant's grip aperture data on the widths of the Efron blocks was performed separately for each cTBS condition and task. We then computed the value of the R^2 and the resultant regression coefficient (i.e., slope), which relates the average increase in MGA (mm) per incremental increase in Efron width (mm) (e.g., Keefe & Watt, 2009; Rossit et al., 2013) for each TBS site separately. The R^2 values were converted to a Fisher-transformed R^2 (e.g., Cohen, 2003; Rossit et al., 2013) to normalise the correlation coefficients (Fisher, 1921).

It is important to highlight, that slope, intercept and R^2 are indicators of grip scaling efficiency and reflect aspects of the relationship between MGA and object size (Whitwell, Milner et al., 2014). As such, the R^2 scores rely on the standard deviation of the MGA, thus removing information about the original units of the variables (Whitwell, Striemer, Nicolle, & Goodale, 2011) and reflect how tight each MGA cluster is around the slope: the greater the variability, the smaller the R^2 will be. The slope indicates the sensitivity of the grip aperture to size changes across the objects. A slope of 0 indicates no scaling of the MGA to the object, whereas a slope of 1 indicates perfect scaling, therefore higher slopes reflect greater proficiency in grasping (Smeets & Brenner, 1999). The intercept indicates the location where the line intersects an axis, and therefore higher values of the intercept corresponds to larger grip apertures (Keefe & Watt, 2009). Moreover, as virtual lesion studies (e.g. Cohen et al., 2009) reported that TMS-to-LO affects MGA velocity and the time at which it is achieved, we analysed the peak velocity of MGA and the time of the peak velocity of MGA. For a complete list of the variables, see table 2.3.

Table 2.3 List of variable analysed.

Dependent Measures	Name	Unit	Marker(s)	Description
Time to Maximum Grip Aperture	tMGA	ms	index, thumb	Time interval between MGA and movement onset
Time to Peak Velocity of grip aperure time	tPVg	ms	index, thumb	Time interval between PV of MGA and movement onset
Peak Velocity of grip aperture	PVg	mm/s	index, thumb	Maximum value for the first derivative of grip aperture
Maximum Grip Aperture	MGA	mm	index, thumb	Peak Euclidean distance between the thumb and index finger's positions
Scaling precision	R^2 Slope Intercept		index, thumb	Variables obtained from the linear regression analysis between MGA and object size

Time to maximum grip aperture (tMGA), time to peak velocity of grip aperture (tPVg), peak velocity of grip aperture (PVg) and maximum grip aperture (MGA) were entered into a 2 x 3 x 3 repeated measure analyses of variance (RM-ANOVA), with factors task (real grasp, pantomimed grasp), TBS site (vertex, aIPS, LO) and object size (small, medium, large). Scaling precision variables (i.e., R^2, slope and intercept) were entered into a 2x3 ANOVA with factors task and TBS site. All comparisons in the RM-ANOVAs were analysed using the Greenhouse-Geisser correction when sphericity was not assumed and considered significant at α-level of 0.05 (two-tailed). Post hoc pairwise contrasts used the Bonferroni correction to control for multiple comparisons. Partial eta squared (η_p^2) was calculated to determine effect size. Only significant statistics are reported.

2.3 Results

2.3.1 Maximum Grip Aperture (MGA)

Analysis of MGA (figure 2.6) revealed a main effect of task ($F_{(1, 15)} = 108.805$, $p < .001$, $\eta_p^2 = .879$) whereby participants opened their hand in-flight more widely for real (mean = 78.39 mm, $p < .001$) compared to pantomimed (mean = 63.90 mm) grasping. Moreover, we also observed a main effect of object size showing that as object size increased, MGA significantly increased ($F_{(1.3, 20)} = 833.926$, $p < .001$, $\eta_p^2 = .982$), confirming that participants were able to scale their grip to object's size for both tasks. Thus, participants were opening their hand wider for the large object (mean = 80.47 mm) compared to the medium (mean = 73.78 mm, $p < .001$) and small object (mean = 59.81 mm, $p < .001$) and less wide for the small compared to the medium ($p < .001$) and large objects. Additionally, we found a significant interaction between task and object size ($F_{(2, 30)} = 3.439$, $p = .045$, $\eta_p^2 = .187$) that was further qualified by a three-way interaction of task x object size x cTBS ($F_{(4, 60)} = 3.533$, $p = .012$, $\eta_p^2 = .191$). To determine the source of the interaction, post hoc tests were conducted comparing cTBS for each object and task separately, however these did not show any significant difference ($p > .05$ for all comparisons).

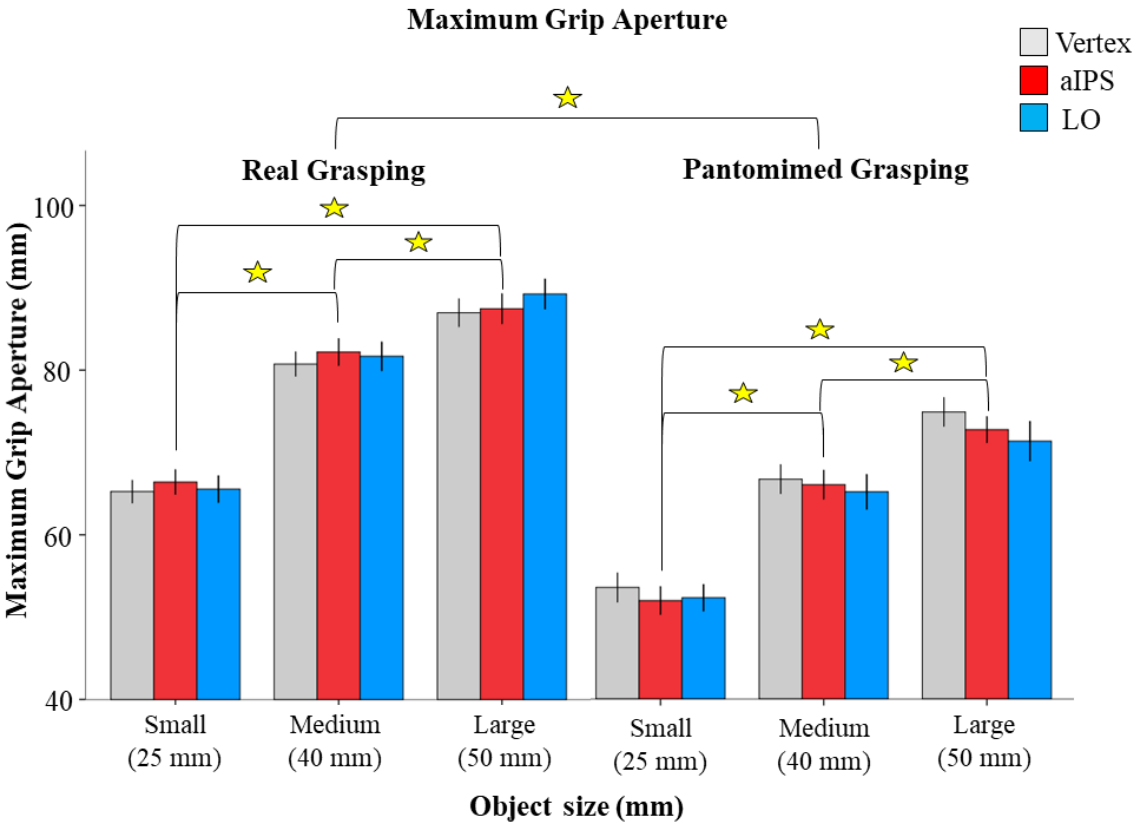


Figure 2.6 Graph depicts significant finding for the maximum grip aperture. The left graph shows data from the real grasping task and the right graph shows data from the pantomimed grasping task. Bars indicate means for each object in each cTBS condition separately, error bars represent standard error of the mean. Yellow stars denote significant differences between conditions.

2.3.2 Scaling precision

2.3.2.1 Fisher transformed R2

Analysis of the fisher transformed R^2 revealed a main effect of cTBS ($F_{(2, 30)}$ = 3.538, p = .040, η_p^2 = .193) (figure 2.7) whereby participants scaled less to object size in real and pantomimed grasping after cTBS-to-aIPS (mean = .961) compared to cTBS-to-vertex (mean = 1.115, p = .046). No difference was observed between cTBS-to-LO (mean = 1.048, p = .767) and cTBS-to-vertex (mean = 1.115), nor between cTBS-to-aIPS (mean = .961, p = .503) and cTBS-to-LO (mean = 1.048). No main effect of task ($F_{(1, 15)}$ = 1.133,

p = .304, η_p^2 = .070) or interaction between cTBS and task ($F_{(2, 30)}$ = 1.804, p = .182, η_p^2 = .347) was observed.

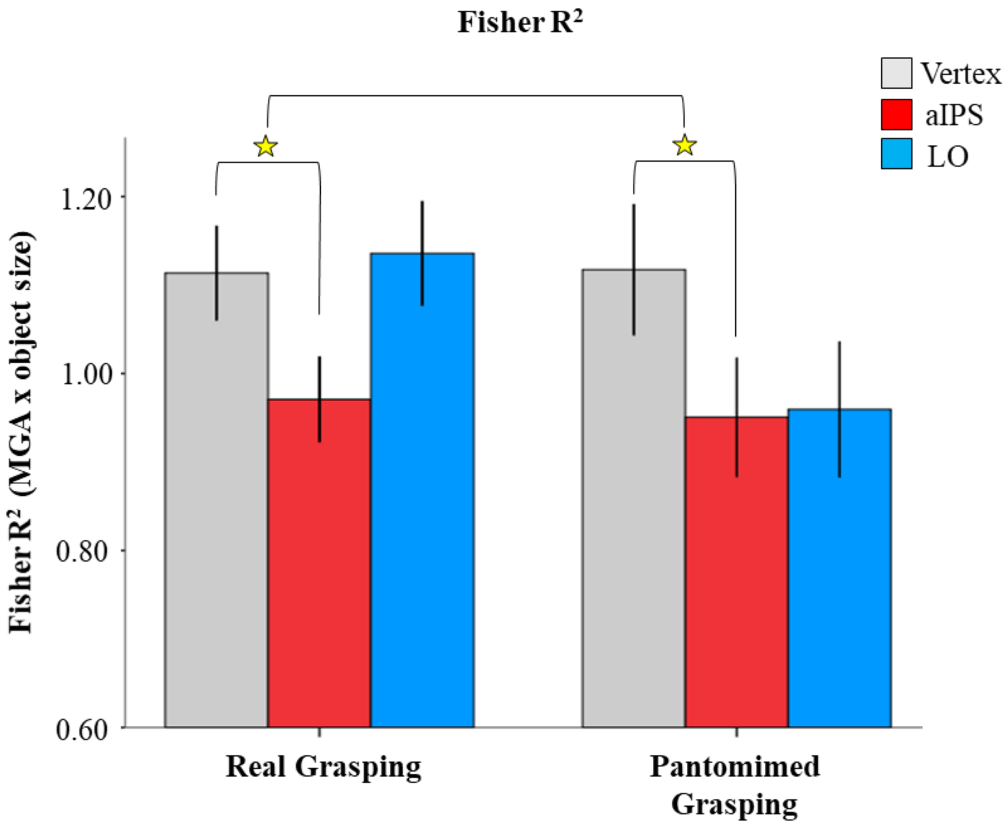


Figure 2.7 Mean R^2 under each cTBS condition in each task. Error bars denote SEM. Yellow stars denote significant differences between conditions.

2.3.2.2 Slope

Analysis of the slope of the linear regression revealed a significant interaction between task and cTBS ($F_{(2, 30)}$ = 6.425, p = .005, η_p^2 = .300). *Post hoc tests* revealed that for cTBS-to-LO, the slope was significantly less steep (mean difference = -.188, p = .005) in the pantomimed grasping task (mean = .770) compared to the real grasping task (mean = .959). This suggests that grip scaling performance was less sensitive to object size in the pantomimed compared to real grasp task for the TMS-to-LO condition (figure 2.8). No main effects of task ($F_{(1, 15)} = 3.006$, $p = .103$, $\eta_p^2 = .167$) nor cTBS ($F_{(2, 30)} = .083$, $p = .921$, $\eta_p^2 = .005$) were observed (figure 2.8).

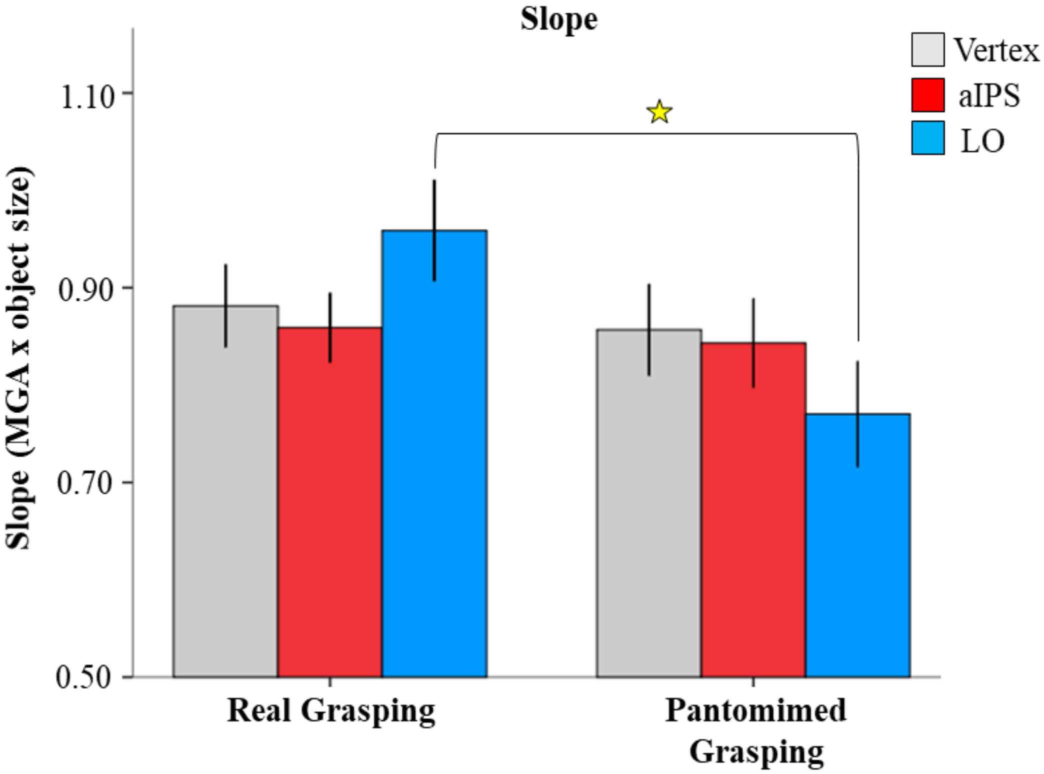


Figure 2.8 Mean slopes under each cTBS condition in each task. Error bars denote SEM. Yellow star denotes significant differences between conditions.

2.3.2.3 Intercept

Analysis of the intercept of the linear regression revealed a significant main effect of task ($F_{(1,\ 15)} = 37.664$, $p < .001$, $\eta_p^2 = .715$; figure 2.9). The intercept of the linear regression was higher for real (mean = 43.914, $p < .001$) versus pantomimed grasping (mean = 32.359), which is not surprising as participants tend to open their hand wider in real versus pantomimed grasping. No main effects of cTBS ($F_{(2,\ 30)} = .072$, $p = .930$, $\eta_p^2 = .005$), nor an interaction between task and cTBS ($F_{(2,\ 30)} = 3.175$, $p = .056$, $\eta_p^2 = .175$) were observed.

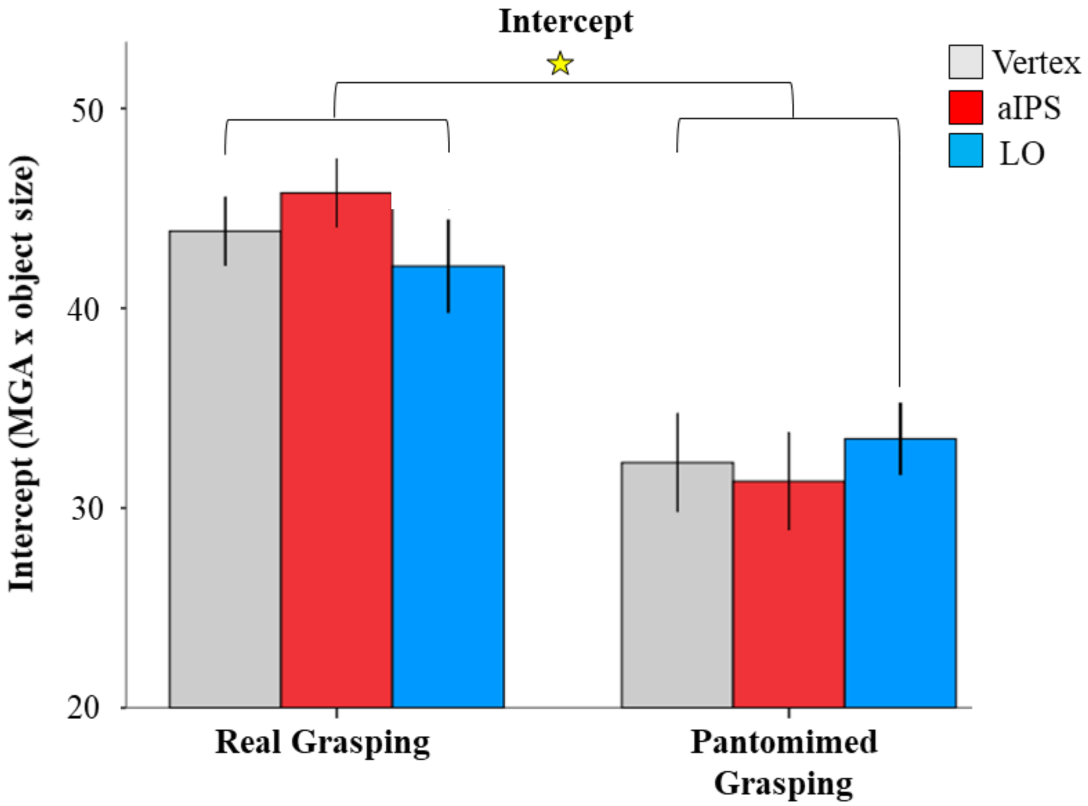


Figure 2.9 Mean intercept under each cTBS condition in each task. Error bars denote SEM. Yellow stars denote significant differences between conditions.

2.3.3 Peak velocity of grip aperture

Analysis of peak velocity of the grip aperture (PVg), revealed a significant main effect of task ($F_{(1, 15)} = 35.752$, $p < .001$, $\eta_p^2 = .704$) whereby participants reached higher velocity of their MGA for the real versus the pantomimed grasping task (mean difference = 57.14 mm/s). Also, a significant main effect of object size ($F_{(1.2, 18.1)} = 123.22$, $p < .000$, $\eta_p^2 = .891$) was observed, showing that as object size increased PVg also increased, with participants reaching a higher MGA velocity for the large compared to medium (mean difference = 22.23 mm/s) and small object (mean difference = 69.86 mm/s) and for the medium compared to the small object (mean difference = 47.62 mm/s). In contrast with Cohen et al., (2009), we did not find any effect of cTBS on PVg ($F_{(1,15)} = 287.106$, $p = .606$, $\eta_p^2 = .033$).

2.3.4 Time to maximum grip aperture

A significant main effect of task was also found for the time at which MGA occurred (tMGA: $F_{(1, 15)} = 12.379$, $p = .003$, $\eta_p^2 = .452$), showing that participants reached the MGA earlier for real compared to pantomimed grasping (mean difference = -58.74). Moreover, for tMGA, we found a main effect of object size ($F_{(2, 30)} = 27.697$, $p < .001$, $\eta_p^2 = .649$) with earlier tMGA recorded for the small versus the medium (mean difference = -23.13, $p < .001$) and versus the large objects (mean difference = -26.095, $p < .001$). No difference was observed between the medium and large objects (mean difference = -2.969, $p = 1$). No other effects or interactions were found to be significant.

2.4 Discussion

To investigate the causal role of left aIPS, a key region for grasping in the dorsal stream, and left LO, a key region for object recognition in the ventral stream, in the control of real and pantomimed grasping we used offline cTBS. Based on the perception and action model (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006, 2008), we hypothesised that cTBS to left aIPS would interfere with the participants' scaling ability in the real grasping task only, whereas cTBS to left LO would interfere with their scaling in the pantomimed grasping task only. In line with our hypothesis, we found that cTBS-to-aIPS weakened the relationship between grip aperture and object size versus cTBS-to-vertex in real and pantomimed grasping, while cTBS to left LO weakened the relationship between grip aperture and object size in pantomimed grasping. Thus, this study clarifies the role of key regions in ventral and dorsal visual streams in the control of grasping. Specifically, the findings indicate that aIPS is causally involved in hand preshaping regardless of grasping task (real or pantomimed). However, LO in the ventral stream is additionally required for pantomime grasping.

Although it might appear surprising that we found that cTBS affects the relationship between in-flight grip aperture and object's size, but not MGA, this might be explained by the fact that MGA and grip scaling variables measure different aspects of grasping. Grip scaling related variables are a measure of the participants' maximum grip aperture in relation to the object size. As such, they take into account for changes in grip aperture, object size and variability of the grip aperture. In contrast, MGA is a measure of the maximum distance between the index finger and thumb, but it does not take into account variability, nor changes in the size of the objects (Jeannerod, 1988). Thus, here participants demonstrated significant grip scaling for all cTBS conditions (e.g., opening their hands less wide for the small object compared to the medium and large objects). However, they were less precise in scaling their grip to the width of the Efron blocks for cTBS-to-aIPS (versus vertex) in the real and pantomime grasping and for cTBS-to-LO in the pantomimed grasping. Specifically, participants' grip apertures were more variable in both real and pantomimed grasping after cTBS-to-aIPS compared to vertex, while their grip apertures were less sensitive to changes in object size after cTBS-to-LO in the pantomimed compared to the real grasping. The intercept reflects how wide the grip aperture was. Thus, it is perhaps not surprising that we observed only an effect of task in the intercept, as this reflects that the participants overall opened their grip wider for real compared to pantomimed grasping, which is in line with the main effect of task observed in MGA.

It would have been interesting to additionally analyse the final position of the fingers on the objects. Davare, Andres, Clerget, Thonnard, and Olivier (2007) reported that while a virtual lesion delivered to left aIPS affects the participant's ability to apply the minimum force required to avoid the grasped object to slip, no effects on the final position (i.e. when the fingers touch the object) of the index finger and thumb were found. However, when a bilateral virtual lesion to aIPS was applied, participants could not shape their hand to the object size precisely and this was evidenced by a larger dispersion of the position of participants' fingers when they were required to grasp-to-lift an object. It is important to highlight two main differences between the experiment by Davare et al. (2007) and ours. First, they presented the stimuli in central vision, while we presented stimuli in the right peripheral visual field. Our decision to present the stimuli in the periphery was based on the observation that patients with dorsal stream lesions are usually impaired in grasping in the visual periphery, but their performance is near-normal in central vision (Perenin & Vighetto, 1988; Pisella et al., 2009; Rossetti et al., 2005; Rossit et al., 2017). Second, Davare et al. (2007) measured the hand shaping alteration based on the final position of the fingertips on the object, while we measured the maximum grip aperture reached in-flight before the fingers made contact with the objects. Importantly, the terminal position of the fingers at contact with the object and the pre-shape in flight are two different measures and might be controlled by different networks in the brain (Fukui & Inui, 2013). Thus, we could additionally analyse the final hand position in our experiment, to explore whether TBS also affects the final hand position at contact with the object.

Our findings that cTBS-to-aIPS affects hand preshaping are in line with evidence from neurophysiological studies in monkeys that have shown that neurons in area AIP specifically fire during manipulative hand movements (e.g., pull a lever, push a button;

Sakata et al., 1995) and that during visually guided grasping, AIP plays an important role in adjusting the hand posture to the object's size and shape (Gallese et al., 1994; Murata et al., 2000). Specifically, Gallese et al. (1994) have shown that transient inactivation of area AIP in the monkey produced a severe disruption of the pattern of finger movements during the period of preshaping, which resulted in a mismatch between the hand configuration and the 3D features of the object. This led to either a failure to grasp the object or to an awkward grasping, which was achieved after several corrections and contact with the object. It has been postulated that area AIP in monkeys has similar properties to area aIPS in humans (Binkofski et al., 1998; Culham et al., 2003) and seems to be specialised in computing object's properties in order to guide hand pre-shaping during grasping. However, there is controversy. In the macaque brain, area V6A, a region in the dorsomedial parieto-frontal circuit involved in reaching (Galletti et al., 2003), is also involved in the control of grasping (Desmurget et al., 1996; Smeets & Brenner, 1999). Additionally, it has been shown that surgical lesion in V6A produce both misreaching and misgrasping, with exaggerated in-flight grip aperture (Battaglini et al., 2002). Thus, whether both AIP and V6A mediate grasping is unclear. In reach to grasp movements, the transport and hand preshaping occur simultaneously during prehension movements. Area V6A, with its connection with both the AIP (Borra et al., 2008) and other posterior parietal area (Gamberini et al., 2009), is a good candidate to be involved in monitoring the direction of arm movements and grip aperture during grasping (Fattori et al., 2009). Area V6A contains a majority of visuomotor cells that respond strongly to the vision of grasping action, compared to the vision of the mere object (Breveglieri, Bosco, Galletti, Passarelli, & Fattori, 2016). On the other hand, neurons in area AIP seem to be more sensitive to simple visual stimuli, such as shapes (Romero et al., 2014). Based on these observations, Breveglieri et al. (2016) speculated that area V6A might be more involved in the fast, broad control of the hand, while AIP might be involved in the slow, finer control (Galletti, Kutz, Gamberini, Breveglieri, & Fattori, 2003; Rizzolatti & Matelli, 2003; Verhagen, Dijkerman, Medendorp, & Toni, 2013).

Here we found that a virtual lesion to aIPS weakens the relationship between the in-flight grip aperture and the width of the object, we can conclude that the left aIPS might be involved in the control of grasping movements, similarly to what has been suggested for AIP in the macaque brain. While we have shown that a virtual lesion to aIPS disrupts grasping, in the future it would be interesting to further explore whether a virtual lesion to SPOC would also impair grasping. If SPOC is the human homolog of area V6A, we should expect to observe cTBS effects on the hand and fingers transport components when cTBS is applied to SPOC. Moreover, based on AIP-V6A connections in the macaque brain, future avenues of research should implement a dual-coil TMS paradigm (De Gennaro et al., 2003) to explore how SPOC and aIPS are interconnected during grasping movements. To investigate the timing of these connections further, other techniques that could be implemented in a similar experimental setting, are EEG and event related potentials (ERPs) or functional neurospectroscopy (fNIRS), which allows for high resolution mapping of temporal dynamics and therefore might be particularly well suited to investigate connections between aIPS and SPOC.

Using TMS, Cohen et al. (2009), reported that TMS-to-aIPS (versus no-TMS) led to earlier peak velocities of the hand opening in-flight to match object size in real and delayed grasping, while TMS-to-LO (versus no-TMS) resulted in higher peak velocities of the hand opening in the delayed grasping task. The authors argued that, although the dorsal stream and in particular aIPS is critical for the online control of grasping, an intact ventral stream cannot completely compensate for a damaged dorsal stream in the performance of memory-guided delayed grasping movements. In Cohen et al.'s (2009) experiment, participants had to retrieve information about object size from memory in delayed grasping, while here, no memory was required as the object was in front of the participants. Thus, based on our findings, we conclude that even when no memory is needed to complete the task, information from LO is additionally required to pantomime grasping and that this information is specifically critical for hand preshaping.

Our results that cTBS-to-aIPS disrupts hand preshaping, provide some support for the role of aIPS in grasping (whether real or pantomimed) versus reaching (whether real or pantomimed) arisen from fMRI (Kroliczak et al., 2007). However, our results seem at odds with Kroliczak et al.'s (2007) finding that LO did not show any differential activation between real and pantomimed actions, whether grasping or reaching. Although speculative, this observation might be related to the fact that in Kroliczak et al. (2007), the object was illuminated for only 150 ms, and the movements were performed in the dark, while here the object was visible until the participant started the grasping movement. Grill-Spector, Kushnir, Hendler and Malach (2000) demonstrated that there is a correlation between an individual's ability to name objects and the activation in the LOC. They showed that when the exposure duration of masked images was varied between 20 and 500 ms, both recognition performance and activity in LOC were non-linear functions of image duration. Thus, shortening the exposure reduced the activation in the LOC (Grill-Spector et al., 2000). Additionally, it is important to highlight that fMRI and TMS measure different aspects. In fact, while fMRI measures the correlation between brain activation and a specific task, TMS measures the causal relationship between a brain region and a task, and this needs to be taken into account when comparing results across the two techniques.

What is the exact role of LO in pantomime grasping? One possibility is that LO plays a crucial role in allocentric visuospatial coding. In particular, our results could be interpreted in the view that the location of objects in the environment can be either coded in an egocentric (i.e. centred on our body) or allocentric (e.g., centred on the relationship with other objects in the surroundings) frame of reference. Milner and Goodale (Goodale & Milner, 1992; Goodale, 2014; Milner & Goodale, 1995, 2006, 2008), proposed that the ventral stream might play a crucial role in allocentric visuospatial coding and creates long-term representations of objects (Milner & Goodale, 2006, 2008; Schenk, 2006), whereas the dorsal stream generates egocentric representations necessary to guide actions (Milner & Goodale, 1995, 2006). During a grasping task, we have to compute and continuously update the information about the position of our body and our fingers in relation to the target object, however, when we have to pantomime, we additionally need to compute the distance between our fingers in relation to the object size (figure 2.10).

Schenk (2006) has shown that there was no difference in DF's performance when compared to controls in both perceptual and motor egocentric tasks, whereas she was impaired in both perceptual and motor allocentric tasks. Schenk (2006) argued that this dissociation showed in DF's performance was between the way she codes egocentric and allocentric coordinates and not between perception and action as suggested by Milner and Goodale's model of the two visual streams (Goodale & Milner, 1992; Goodale, 2014; Milner & Goodale, 1995, 2006, 2008). However, Schenk's tasks had some limitations: for instance, the tasks could have been conceived to tap into visuomotor and perceptual processing. In fact, the tasks used do not rule out the possibility that DF might have been imagining performing the pointing tasks in order to help her judge which of the two stimulus was closer (Milner and Goodale, 2008).

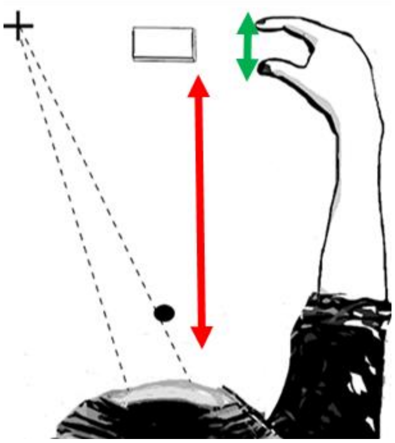


Figure 2.10 Coding of objects in the surroundings. The red arrow indicates egocentric coordinates and the green arrow allocentric coordinates.

Moreover, our results would be in line with studies of allocentric versus egocentric reaching. Thaler and Goodale (2011), using fMRI, have shown that contralateral LO is more activated in allocentric versus egocentric pointing tasks, while left IPS was activated in both egocentric and allocentric pointing tasks. In our experiment, participants might have coded information about the position of the object in an egocentric frame of reference in real and pantomimed grasping, which relies on the dorsal stream, therefore when cTBS was applied over aIPS, their performance was weakened compared to cTBS-to-vertex. On the other hand, in pantomimed grasping, additional allocentric coordinates (e.g., distance between the index finger and the thumb) need to be computed to successfully guide the movement. Perhaps, LO is causally involved in allocentric space representations required for pantomimed grasping. Future studies should investigate the role of LO in allocentric tasks. For example, future studies could combine TMS with virtual reality to explore the role of LO in the representation of allocentric space. As such, using virtual reality, it is possible to create a task in which participants grasp an object in virtual reality, using and egocentric frame of reference. As there is no contact of the hand with the object in real life, this would resemble a pantomimed grasping, however this may not require allocentric coding.

Another possibility is that LO is required in grasping tasks that have no haptic feedback available at the end of the movement, such as our pantomimed grasping task. In fact, it has been recently claimed that DF's spared ability to grasp might be driven by haptic feedback (Schenk, 2012a; for a description of the task see section 1.7). According to Schenk (2012a), DF uses haptic feedback to compensate her deficit in the perception of size and that her grip scaling relies on the integration of visual and haptic feedback and when haptic feedback is missing, her damaged ventral stream cannot support visually guided grasping. However, this hypothesis has been recently questioned.

Recently, Whitwell, Milner et al. (2014) re-tested DF and a group of healthy controls using the same mirror set-up implemented by Schenk (2012a) (for a description of the task see section 1.8). Whitwell, Milner et al. (2014) reported that DF scaled her in-flight grip aperture to object size independently of whether the visual size of the object was matching the haptic feedback derived from hand-object contact. Moreover, they showed that her performance was not significantly different from the performance observed in the control group. Even when the size of the cylinder behind the mirror was uninformative, DF continued to scale her grip to the size of the viewed cylinder (and showed the same reduction in grip scaling observed in the control group). These findings seems to contradict Schenk's (2012a,b) hypothesis that DF needs to have access to veridical haptic feedback in order to scale her grip aperture. Whitwell, Milner et al. (2014) argued that, haptic feedback provided at terminal location of a target directed action, and not object size per se, was sufficient to allow DF to calibrate her visuomotor system. Thus, when no haptic feedback was provided, the task switched to a pantomimed task, instead (Whitwell, Milner et al., 2014). Whitwell, Milner et al. (2014), concluded that the visual processing in the dorsal stream is sufficient to mediate accurate grasping in DF, and also in healthy individuals, which is in support of the original proposal by Milner and Goodale. Based on these observations and on our findings, in future studies, it will be interesting to combine the paradigm used by Withwell, Milner et al. (2014) with TMS-to-aIPS and TMS-to-LO to further test our findings that LO is required in grasping tasks that have no haptic feedback available.

Evidence from neuropsychological patients provide a great contribution to our understanding of the role of a region on a given behaviour. However, after brain damage, the brain normally reorganises its functions and therefore the patients may acquire compensatory strategies (Robertson & Murre, 1999). Therefore, using TMS we were able to recreate a virtual lesion in the healthy brain to reproduce the basis of the deficit under investigation and help in understanding the networks underling an observed behaviour in the healthy brain. Moreover, using a virtual lesion approach, we were able to test the same participants on the same tasks and to manipulate the specific region to which TMS is applied. This could help understanding the nature of the double dissociation observed in patients with optic ataxia and visual form agnosia. In fact, one of the criticisms (Pisella et al., 2006; Rossetti et al., 2003) to the proposed double dissociation observed between optic ataxia and visual form agnosia, (Milner and Goodale 1992), is that these patients have not been tested under the same conditions. As such, DF has been tested systematically under central vision conditions, whereas optic ataxia patients have been tested systematically under visual periphery conditions in grasping tasks (but see Cornelsen, Rennig, & Himmelbach, 2016). Recently, Rossit et al. (2017) tested patient DF under different reaching conditions, to explore whether DF's misreaching was biased towards fixation and her ability to perform online reaching corrections towards moving targets under free and fixation-controlled vision. Performance in these tasks is typically impaired in optic ataxia (e.g., McIntosh, Mulroue, Blangero, Pisella, & Rossetti, 2011; Milner, Paulignan, Dijkerman, Michel, & Jeannerod, 1999; Rossetti et al., 2005; Rossit et al., 2017). Rossit et al. (2017), reported that DF was impaired in peripheral, but not in central visual field reaching, and for the first time they showed that DF was impaired also in performing online corrections during reaching, thus showing a behaviour similar to optic ataxia patients. The authors suggested that the most likely explanation for DF's performance in these tasks is that her SPOC, a region that has been shown to be activated in healthy participants during reaching, especially toward peripheral targets (Martin, Karnath, & Himmelbach, 2015; Prado et al., 2005), is bilaterally damaged (Milner et al., 1991). The authors concluded that DF presents signs of optic ataxia and therefore cannot be considered a pure visual form agnosia patient and suggest that further testing is required to test the dissociation between optic ataxia and visual form agnosia. Here we show that TMS seems to be a reliable technique to further test the assumptions of the model, and to understand the causal role of different brain regions in a given behaviour. Future experiments should combine the tasks used in Rossit et al. (2017) with offline TMS to understand the causal role of SPOC, aIPS and LOC in reaching and in the online corrections in the visual periphery and the central visual field, which would help understand which brain regions are involved in DF’s behaviour.

Our study supports the view that the two streams contribute to grasping movements under different action modes and provides support to Milner and Goodale’s hypothesis of the two visual streams. Specifically, we found that area aIPS in the dorsal stream is necessary for fine hand preshaping to object’s size under real or pantomimed grasping movements, however, for pantomimed actions, information regarding object size processed in LO is additionally required to grasp efficiently. In particular, we propose that in the real grasping condition, the dorsal stream acts independently from the ventral stream to control the grasping movement by computing information in an egocentric frame of reference. However, under the pantomimed grasping condition, in addition to the computations performed by the dorsal stream, the ventral stream is additionally required, as the distance between the index finger and thumb need to be computed in relation to the size of the object in an allocentric frame of reference.

Our results that the ventral stream is involved in pantomimed grasping, seem in line with recent accounts that suggest the involvement of the ventral stream in prehension (Lingnau & Downing, 2015; Verhagen, Dijkerman, Grol, & Toni, 2008;Verhagen, Dijkerman, Medendorp, & Toni, 2012). Area LO lies within the lateral occipitotemporal cortex (LOTC), which although is not close to classical motor-control region, it has been recently shown that represents varied aspects of actions (for a review see Lingnau & Downing, 2015). Based on this evidence, Lingnau and Downing (2015) hypothesised that

LOTC has a role in the perception, understanding and production of actions, including manipulation of tools. Our findings that LO is causally involved in pantomimed grasping, seem in line with the hypothesis that LOTC is involved in action. Additionally, we could further suggest that a sub-region of LOTC, LO, is involved in hand preshaping, which will be further investigated in chapter 3.

Contrary to previous TMS studies, we did not find any effect of TMS on velocity of the peak grip aperture nor on time to maximum grip aperture variables (Tunik et al., 2005; Rice et al., 2006; Cohen et al., 2009). This might be explained by the fact that online TMS-induced effects show a time-dependence on the kinematics of grasping (Rice et al., 2006; Rice et al., 2007; Cohen et al., 2009). Specifically, Tunik and colleagues in a series of experiments (Rice et al., 2006; Rice et al., 2007; Cohen et al., 2009) have shown that online TMS disrupts kinematics variables that are measured approximately within 350 ms of TMS administration. It would be interesting to further investigate when LO is critical in pantomimed grasping, for example by using an online TMS protocol to deliver the stimulation at different action stages (e.g., viewing, planning, movement onset).

Critically, differences in the effects observed could also be related to the fact that we used a different localisation approach. Here, we implemented a novel technique. In particular, instead of using anatomical landmarks only to localise aIPS and LO only (as in Cohen et al., 2009; Rice et al., 2006; Tunik et al., 2005), we implemented a novel approach to define the regions of interest combining overlapping meta-analytic maps downloaded from NeuroSynth on each participant's structural image of the brain and anatomical landmarks. Recently, Sack and colleagues (2008) to localise a region in the IPS involved in magnitude processing, compared 4 different approaches for TMS stimulation such fMRI-guided, MRI guided, Talairach group coordinate (extracted from fMRI activation of a different group of participant) and 10-20 EEG system. They reported that, although all the approaches attempted to denote the same area within the IPS, the strongest behavioural effects (e.g., effect sizes) were found when the region was localised using fMRI activation from each single participant, followed by MRI-guided TMS, Talairach group coordinates and 10-20 EEG system. While using fMRI-guided TMS localisation, allows to account for functional and anatomical variability across participants, using MRI-guided localization allows to account only for anatomical variability across participants. In contrast with the procedure implemented by Sack et al. (2008), we did not acquire fMRI activations from each single participant to localise aIPS and LO. However, we used a large database of fMRI activations [in Sack et al. (2008) they had only 5 participants] and we extracted the peak of activation close to the anatomical landmarks in each participant. This was done to account for anatomical variability and for functional variability across participants. Thus, here we show that using population-based fMRI activations combined with individuals' anatomical landmarks, is a reliable method to localise LO and aIPS in TMS studies. In the future it would be important to compare different methods to localise aIPS and LO and compare the resultant behavioural effects (e.g., effect sizes). This is important, as using population-based activations will help save money and time as well as avoiding scanning participants multiple times.

Although the existing literature suggests that cTBS applied to the motor cortex lasts for up to 60 minutes (Huang et al., 2005), there are not many studies investigating the time course and the magnitude of TBS effects on cortical excitability when it is applied to other brain regions (see Wischnewski & Schutter, 2015 for a review). Based on Huang et al. (2005) and Wischnewski and Schutter (2015), we made sure that our tasks were under 60 minutes in duration after the stimulation was delivered (specifically our tasks together were no longer than 35 minutes to allow breaks). However, our design did not allow us to investigate the time course of cTBS-induced effects on aIPS and LO, therefore, in the future, it would be crucial to investigate if participants performance at different time intervals after the initial stimulation is different (i.e., compare the performance in the first 10 minutes, with the last 10 minutes). Nevertheless, our results contribute to expand the list of brain areas on which cTBS could successfully be used to investigate the causal link between brain and behaviour.

In conclusion, our results have important implications for Milner and Goodale's perception and action model (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006, 2008). According to the authors, the dorsal stream mediates the visual control of online action directed towards an object by continuously evaluating and updating the coordinates of the object in relation to the body and the fingers, while the ventral stream transforms visual information into perceptual representations of objects and their spatial relationships. While our results provide further support for the model, that is, that the dorsal stream is crucial in the control of online actions, we proposed that under pantomimed grasping, in addition to the dorsal stream involvement, inputs from the ventral stream are required to guide the dorsal stream. We also propose that under real and pantomimed grasping, the dorsal stream controls online grasping, by continuously evaluating in real time the position of the objects in relation to the body and the fingers and comparing this information with the location and size of the objects. However, under pantomimed grasping additional information from the ventral stream, such as allocentric computations of the distance between the fingers and the actual size of the object, is required. We could hypothesise that the fact the aIPS contributes to both real and pantomimed grasping may suggest that perceptual information from the ventral stream reaches the dorsal stream, and here merges with action information to control online grasping (as suggested by Cohen et al., for real and delayed grasping). Future studies, should implement a dual coil TMS paradigm (De Gennaro et al., 2003) to explore how LO and aIPS are interconnected during pantomimed grasping.

In this task, we used meaningless wooden blocks (Efron, 1969) to specifically investigate the role of the aIPS in the dorsal stream and area LO in the ventral stream in hand preshaping. However, Efron blocks are meaningless shapes and therefore there is no functional or manipulation knowledge associated with them. However, in our everyday interactions with the surroundings, we usually interact with tools, that have a specific meaning associated with them as well as functional and manipulation knowledge. As highlighted by Milner and Goodale (2006, 2008), tools are a particular category of objects that require the cooperation between the dorsal and the ventral stream. As such, to successfully carry out actions towards and with tools, information from both the dorsal and the ventral stream are necessary. Investigation of patient DF’s ability to reach out to grasp tools reported that although she was able to grasp a tool based on its size, she was unable to grasp the tool in the appropriate place to show its function, unless she was allowed to use her hands to explore the object identity first (Carey et al., 1996). This suggests that she could use visual information to guide her grasp, however, she was unable to use functional information which is linked to object recognition (e.g., grasp a knife by the handle to cut) to guide her hand movements (Carey et al., 1996). These findings suggest that structural and functional manipulation knowledge about tools can dissociate in the brain (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010). However, the neural correlates of these objects' properties are still unclear. In the next chapter, using fMRI, I will investigate the neural mechanisms underlying viewing tools and pantomiming tool actions and how different types of tool manipulation knowledge (structural and functional) are coded in the brain.

Chapter 3

3. The representation of tool identity and action properties in the human brain for viewing and pantomiming

3.1 Introduction

Every day we constantly recognise and interact with objects in our surroundings and in particular tools. Although many animals are able to use simple tools (e.g., a stick for reaching) to achieve a goal, humans are able to create and use complex tools (e.g., a spoon, a hammer). Tools are man-made handled artefacts that can be functionally used to particular goals (Frey, 2007) as they have specific functions associated with them which are not inter-changeable (e.g., a knife is for cutting or spreading, but is not for hammering). Nearly all our everyday activities involve interactions with tools (e.g., brushing our teeth), which we perform easily. However, multiple lines of evidence in the field of neuroscience and psychology have highlighted how tool use must rely on complex interactions between specialised brain areas, organised in networks of cortical and subcortical regions (Johnson-Frey, 2004; Rothi, Ochipa, & Heilman, 1997). In fact, training a robot to successfully reach, grasp and use tools, using brain-computer interfaces (BCIs), requires multiple complex algorithm to interface (e.g., Andersen, Kellis, Klaes, & Aflalo, 2014).

According to Milner and Goodale’s (1992) influential view of the human cortical visual system, a dorsal visual stream projecting from the occipital to the posterior parietal cortex, uses visual information to guide hand actions. Whilst a ventral stream, projecting from the occipital to the inferotemporal cortex, uses visual information for the purpose of creating perceptual representations of objects, such as the information critical for the visual recognition of objects. The advent of human functional neuroimaging has led to additional support to this account, identifying several dorsal stream areas that are specialised for the visual control of actions (for a review, see Culham & Valyear, 2006;Vingerhoets, 2014) and several ventral stream areas that are specialised for visual recognition (for a review, see Grill-Spector & Malach, 2004).

Milner and Goodale (1995, 2006, 2008), hypothesised, that tool use would require the dorsal and ventral visual pathways to cooperate and speculated that the ventral stream, implicated in the recognition of tools, would be involved in the selection of where and how the tool should be grasped according to the intended use of the object and its function (Milner & Goodale, 1995, 2006, 2008). This hypothesis was further supported by the observation that patient DF could grasp and use objects on the basis of their physical properties, however, she did so in a way that was not often compatible with how they were used (Carey et al., 1996). According to Milner and Goodale, while the ventral stream allows us to recognise a target and to select the motor plan according to our previous experience and knowledge of the object, the dorsal stream mediates the motor outputs and controls the online movements (Goodale & Humphrey, 1998; Milner & Goodale, 2006).

Milner and Goodale (1995, 2006, 2008) stressed that the visuomotor transformations performed by the dorsal stream are computed in real time and therefore are not likely to rely on stored representations, however, tool use is very much thought to rely on the stored representations of actions (for review, see Rothi & Heilman, 1997). Thus, unlike other objects, tools are tightly linked to predictable action routines (e.g., a hammer is for hammering; Frey, 2007) and efficient tool use is a particular kind of visuomotor behaviour that requires the collaboration between the two streams (Milner & Goodale, 1995, 2006, 2008). In fact, tool use depends not only on tool recognition and on processing structural manipulation knowledge (e.g., physical properties of the objects such as size, orientation and shape), but also on stored semantic knowledge about the specific function associated with it (Creem & Proffitt, 2001; Frey, 2007; Hodges, Bozeat, Ralph, Patterson, & Spatt, 2000; Hodges, Salmon, & Butters, 1992) which includes the retrieval of the knowledge related to sensory (e.g., size and location) and motor representations (e.g., the motor act associated with it; Kiefer & Pulvermüller, 2012; Martin, 2007). Moreover, it has been hypothesised that the dorsal stream is further sub-divided into a dorso-dorsal stream with a reach and a grasp sub-network for structural manipulation knowledge (e.g., how the tool is grasped) connecting frontal and parietal regions and a ventro-dorsal stream connecting frontal, parietal and temporal regions for functional manipulation knowledge (e.g., how the tool is grasped to be used; Figure 1.4, Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010; Rizzolatti & Matelli, 2003). In other words, the dorso-dorsal stream is thought to be characterised as the “grasp” system, while the ventro-dorsal stream is thought to be characterised as the “use” system (Binkofski & Buxbaum, 2013).

Here, I used fMRI and multivoxel pattern analyses to investigate how different tool properties, such as tool identity, structural and manipulation knowledge are represented within the dorso-dorsal, ventro-dorsal and ventral stream and if these representations vary according to the task (viewing or pantomiming) and stimulus presentation (pictures or words).

A central role in tool processing and use is played by object features that are relevant for grasping (i.e., affordances). According to Gibson (1979), the content of visual perception includes a description of how the environment and objects within it can potentially impact our actions. Critically, unlike many other objects, such as furniture, buildings, animals or body parts, tools can be grasped and are linked to specific actions (Mruczek et al., 2013). For example, according to Gibson (1979) the mere vision of tools, naturally involves activation of correspondent motor representations for grasping (e.g., motor affordances). As such, images of tools activate not only areas in the ventral stream implicated in tool identification, but also areas in the dorsal stream, implicated in the visual control of actions (Lewis, 2006).

Behaviourally, it has been shown that viewing pictures of tools can automatically potentiate motor actions associated with the use of the tool, even if no overt action is performed (Tucker & Ellis, 1998). In an elegant experiment, Tucker and Ellis (1998), asked participants to decide whether or not picture of familiar graspable objects with handles (e.g., pan) were inverted or upright. The authors observed that when handles were facing right, right hand responses were facilitated (i.e., faster reaction times), while left-facing handles, facilitated responses with the left hand even though the orientation was irrelevant to the task. Taken together these results indicate that the orientation of the handle automatically gives rise to the activation of corresponding motor plans for grasping (Tucker & Ellis, 1998).

Tucker and Ellis have since observed a similar compatibility effect for object size (Ellis & Tucker, 2000; Tucker & Ellis, 2004). In a series of experiments, participants were presented with either man-made tools or natural objects (e.g., fruit, vegetables or nuts), which required either precision (e.g., grasping with the index finger and thumb) or power (e.g., grasping with the five digits and the palm) grasps and they were asked to decide if objects were man-made or natural. Using a novel apparatus to simulate precision and power grasping (Ellis & Tucker, 2000; Tucker & Ellis, 2004) the authors showed that small objects facilitate precision-type responses while large objects facilitate power grip responses. Importantly, as in the authors' previous experiment (Tucker & Ellis, 1998), the task to decide if objects were man-mad or natural, did not require explicit attention to the size of the object.

Tucker & Ellis (2004) observed the same effect when words of objects, instead of images were presented (Tucker & Ellis, 2004). Thus, they proposed that objects' visual properties important for grasping, such as orientation and size, automatically trigger the activation of corresponding motor representations. Moreover, for size and grip type, the same effect was observed even when words were presented (i.e., action-related visual inputs were absent), thus the authors suggested that how the motor representations for grip are generated, depends more upon stored knowledge of the object and the actions associated with it, than the physical parameters of the stimulus used (Tucker & Ellis, 2004).

Evidence to support the idea of motor affordances as integral to the visual perception of objects comes from neurophysiology studies in monkeys and neuroimaging studies in humans. Electrophysiological recordings in monkeys have shown that grasp-related neurons within the anterior intraparietal area (AIP) often respond to the mere visual presentation of objects, even if no movement is required (Murata et al., 1997; Murata, Gallese et al., 2000; Rizzolatti et al., 1988; Taira, Mine, Georgopoulos, Murata, & Sakata, 1990). In addition, for some of these cells, a match between the visual and the motor response has been observed. Specifically, neurons that respond to precision grasping, also respond to the sight of small objects, which requires precision grasping versus bigger objects that require power grasps (Murata et al., 2000).

Similarly, fMRI studies in humans, have shown that viewing graspable objects activate regions not only in the ventral stream, but also in the dorsal stream (Lewis, 2006). In a meta-analysis of human neuroimaging studies, Lewis (2006) analysed results from 35 imaging studies across 64 different tasks, including perceptual (e.g., reading words, answering questions, hearing tools), motor tasks (e.g., pantomime and imagining tool use) and tool use and identified a network of frontoparietal and occipitotemporal regions that was consistently activated when viewing, hearing, imaging and pantomiming tool actions. Critically, he observed there was a large extent of overlap of activated brain regions across the various paradigms (Lewis, 2006), consistent with the idea that motor actions associated with tool use and perception of tools rely on similar cortical networks.

In the occipitotemporal cortex several areas have been identified to be implicated in tool-related tasks. Specifically, the fusiform gyrus (FG) (Chao et al., 1999; Garcea & Mahon, 2014; Mahon et al., 2007; Whatmough et al., 2002), the lateral occipitotemporal cortex (LOTC) (Bracci et al., 2012; Lingnau & Downing, 2015; Perini et al., 2014) and the middle temporal gyrus (MTG) (Boronat et al., 2005; Chao et al., 1999; Emmorey et al., 2004; Kellenbach, Brett, & Patterson, 2003; Macdonald & Culham, 2015; Martin, 2007; Valyear & Culham, 2009). Areas typically activated in tool-related tasks in the frontoparietal network include the intraparietal sulcus (IPS), the inferior parietal lobule (IPL), the superior parietal lobule (SPL) (Boronat et al., 2005; Buxbaum & Saffran, 2002; Chao & Martin, 2000; Hermsdorfer, Terlinden, Muhlau, Goldenberg, & Wohlschlager, 2007; Macdonald & Culham, 2015; Mruczek et al., 2013), the ventral (PMv) and dorsal (PMd) premotor cortex (Chao & Martin, 2000; Creem-Regehr & Lee, 2005; Johnson-Frey et al., 2005; Kellenbach et al., 2003).

To summarise, tool processing is thought to involve both dorsal and ventral visual stream regions and is thought to reflect access to structural manipulation knowledge (e.g., how to grasp a tool) and functional manipulation knowledge (e.g., the identity and function movement associated with it), respectively (Lewis, 2006). Structural manipulation knowledge is considered a long-term knowledge based on previous experience and contains the parameters associated with the manipulation of familiar tools, such as, for example the hand posture. Moreover, it provides this information every time we interact with objects, avoiding the need for each movement to be reconstructed every time (Reynaud, Lesourd, Navarro, & Osiurak, 2016). The structural manipulation knowledge has been originally associated with left IPL (Binkofski & Buxbaum, 2013; Buxbaum, 2001; Buxbaum & Kalénine, 2010; Daprati & Sirigu, 2006; Gainotti, 2012; Handy, Grafton, Shroff, Ketay, & Gazzaniga, 2003; Reynaud et al., 2016). On the other hand, it is thought that functional manipulation knowledge stores the function associated with a tool that can be retrieved for future uses (Vaesen, 2012). In a recent review of fMRI studies, Reynaud et al. (2016) identified the left pMTG as a potential key regions for the storage of functional manipulation knowledge.

To date, not much is known about the exact role that different areas within the frontoparietal and occipitotemporal cortex play in processing information about tools (Almeida et al., 2013; Almeida, Mahon, & Caramazza, 2010; Boronat et al., 2005; Buxbaum et al., 2000; Buxbaum & Saffran, 2002; Carey et al., 1996; Goldenberg & Spatt, 2009). Important insights come from neuropsychological research. For example, damage to the MTG and the lateral occipital complex affects knowledge about tool identity and function (Buxbaum & Saffran, 2002; Negri et al., 2007). On the other hand, damage to the IPL, specifically the SMG, disrupts the ability to functionally manipulate tools (Randerath et al., 2010) while damage to the SPL and the posterior IPS impairs structural manipulation knowledge (Wood, Chouinard, Major, & Goodale, 2017).

It is clear that, to efficiently use a tool for a specific purpose (e.g., use a spoon to stir the coffee), our visuomotor system must determine the properties of the tool and use them to select the appropriate structural manipulation (i.e., how to shape the hand to grasp it) and its functional manipulation (i.e., how to move it for use). For example, a key is typically grasped between the index finger and the thumb (i.e., precision grip) and inserted in the door hole and turned anti-clockwise to open the door (i.e., rotation movement), while when we use a screwdriver, we typically grasp the tool with the palm and all the five fingers (i.e., power grip) and rotate our wrist to use it (i.e., rotation movement). While both a key and a screwdriver involve a wrist rotation movement for using them (i.e., functional manipulation knowledge), the hand postures for grasping them (i.e., structural manipulation knowledge) are quite distinct (precision versus power).

In 1956, Napier (1956) divided handgrips from a functional and evolutionary perspective into precision and power grips. In the power grip, all digits are flexed around the object to provide high stability, whereas the precision grip requires independent finger movements to provide stability and involve fine control of the directions and the forces of the fingertips (Flanagan, Burstedt, & Johansson, 1999; Johansson, 1996). In primates and humans, the primary motor cortex is crucial for the execution of skilled manipulatory tasks, especially those that involve a precision grip (Porter & Lemon, 1993). Moreover, two key regions have been identified in monkeys to be involved in grasping, the anterior intraparietal area (AIP) and the premotor area F5 (Jeannerod et al., 1995; Murata et al., 1997, 2000; Taira et al., 1990). In a series of studies in monkeys, Baumann and colleagues (Baumann, Fluet, & Scherberger, 2009; Fluet, Baumann, & Scherberger, 2010) showed that both AIP and area F5 contained neurons selective for grip and object orientation. Specifically, during movement execution, the majority of neurons in area AIP decoded both grip type and orientation of the handle (Baumann et al., 2009), while the majority of neurons in area F5 decoded grip information only (Fluet et al., 2010). In humans, aIPS has been identified as the homologous of the macaque AIP, while PMv has been identified as the homologous of area F5 (Ferri et al., 2015).

Interestingly, similarly to what has been observed in monkeys, neuroimaging studies have shown that aIPS and PMv are more activated during grasping versus reaching movements (Binkofski et al., 1999; Cavina-Pratesi et al., 2010; Culham et al., 2003; Frey et al., 2005). As reviewed above, Tucker and Ellis (2004) reported that the smaller objects facilitated precision grip responses, while bigger objects facilitated power grip responses. This effect was observed even if no overt movement was required, nor the size of the tool was relevant for the task. Thus, the mere viewing of tools of different sizes seems to facilitate responses based on their structural manipulation (e.g., power versus precision) knowledge.

In humans, fMRI evidence has shown that both precision and power grips activate the primary sensory cortex (S1), the dorsal premotor cortex (PMd), the ventral premotor cortex (PMv), the supplementary motor area (SMA) and regions within the post-central sulcus (Ehrsson et al., 2000). One of the aims of the present fMRI and MVPA study is to explore whether power and precision grip (e.g., structural manipulation knowledge) can be decoded in the regions highlighted above independently of the task (view or pantomime) and stimulus presentation (pictures or words).

In the last decade, the use of multivoxel pattern analysis (MVPA) to analyse and interpret fMRI data has become more common (Poldrack & Farah, 2015). While conventional univariate fMRI analyses relates how experimental variables affect the activation of individual voxels voxel separately (e.g., Friston et al., 1995; Poldrack & Nichols, 2011), MVPA uses patterns of classification algorithms to differentiate the fine-grained spatial voxels pattern of activity in a given region elicited by different stimuli, which might be missed by traditional analysis approaches (Fabbri et al., 2014; Gallivan & Culham, 2015; Gallivan et al., 2011; Kriegeskorte, Goebel, & Bandettini, 2006; Mur, Bandettini, & Kriegeskorte, 2009; Pereira & Botvinick, 2011; Pereira, Mitchell, & Botvinick, 2009). In other words, whereas conventional univariate fMRI analyses examine each voxel separately, typically by smoothing and averaging the activity across several voxels, MVPA uses classification algorithms to test for information contained within voxel patterns of activations. In the last years, MVPA has been applied in the domain of visual-perceptual research and showed that visual and auditory stimuli can be decoded from voxel patterns of activity in visual (Haxby, Hoffman, & Gobbini, 2000; Haynes & Rees, 2006; Haynes & Rees, 2005; Kamitani & Tong, 2005; Williams et al., 2008) and auditory cortex (Formisano, De Martino, Bonte, & Goebel, 2008; Meyer et al., 2010). More recently, MVPA has been used to successfully decode tool processing (Bracci et al., 2012; Chen, Garcea, Jacobs, & Mahon, 2017; Chen et al., 2016; Peelen et al., 2013; Peelen & Caramazza, 2012), target-directed actions (Fabbri, Caramazza, & Lingnau, 2012; Fabbri, Strnad, Caramazza, & Lingnau, 2014) and to discriminate between pantomimes of tool use (Chen et al., 2017).

Critically, to grasp an object we need to move the arm toward it and plan the appropriate hand configuration. Previous fMRI studies suggested that the dorsomedial pathway (e.g., SPOC, medial intraparietal, PMd) is specialised for transport component while the dorsolateral pathway (aIPS, PMv) is specialised for the grip component (e.g., Culham et al., 2006; Jeannerod et al., 1995; Vesia and Crawford, 2012). More recently, using MVPA and fMRI Fabbri et al. (2014) showed that a widespread network of areas within the dorsomedial pathway, including SMA, the superior portion of PMd, SPL coded for reach direction. On the other hand, regions in the dorsolateral pathway, including the inferior portion of PMd, M1 and S1 coded grip type. Additionally, they observed that PMv, SPL and aIPS coded both reach direction and grip type. The authors concluded that their results provided evidence against the view that there is a clear distinction between a reach and a grasp subnetwork within the dorso-dorsal stream. They suggested that the two subnetworks may be involved in both components but with a different temporal involvement and identified the SPL as a candidate to combine information from the reach and the grasp component of the movement.

In another experiment, Fabbri et al. (2016), asked participants to passively view or grasp six 3D objects of different shapes (i.e., plates, disks, spheres, cubes, cylinder and bars) and sizes (small, medium and large) using a precision grip (precision 2), using all five fingers to precisely grasp the object (precision 5) or to grasp the object coarsely in a whole-hand grasp using all five digits (coarse 5). Using representational similarity analysis (RSA) the authors found that object elongation is the most strongly represented object property during grasping and is coded preferentially in the primary visual cortex, the anterior SPOC as well as posterior SPOC. On the other hand, the primary somatosensory cortex, the motor cortex and PMv coded preferentially the number of digits while regions within the ventral stream and the dorsal stream coded for both visual and motor dimensions. The authors suggested that elongation is a critical property of the object to grasp and along with the number of digits used is represented within both parietal and occipitotemporal regions. They concluded that the communication between the dorsal and the ventral streams about object visual and motor properties may be critical for the execution of grasping actions and that the preference for object elongation in the grasping task may reflect that elongation is critical in selecting the appropriate grip type and wrist orientation.

Despite the advances made in our understanding of the regions that code hand grip, the studies reviewed so far presented blocks or meaningless objects, thus whether these regions are responsible for grip selection when processing tools is unclear. When we interact with tools in our surroundings, we have to know their identity and to select not only the appropriate grip to pick them up (i.e., structural manipulation knowledge), but also the appropriate subsequent movement (i.e., functional manipulation knowledge) following our grasp. For example, a key and clothes peg are both picked-up with a precision grasp, but distinct rotating and squeezing movements are associated with their opening/closing and hanging functions.

Recently, Peelen and Caramazza (2012), implemented fMRI and multivoxel pattern analysis (MVPA) to explore which regions in the human brain carry information about conceptual object properties such as functional properties (rotation versus squeeze) and location (kitchen vs garage). The authors showed that the activity patterns in the anterior temporal cortex carry conceptual information about how (e.g., rotation versus squeeze) and where (e.g., kitchen or garage) an object is typically used, while the posterior occipitotemporal cortex carry information about perceptual similarities (e.g., how similar two objects look like). Moreover, they found that information about object location and functional action (e.g., rotation versus squeeze) was independent of whether participants made location or action judgements. The authors concluded that object conceptual properties (e.g., functional and location properties) carried in the anterior temporal lobe were retrieved even when they were irrelevant to the task and suggested that conceptual object representations in this region are independent of the perceptual properties of the object (Peelen & Caramazza, 2012).

More recently, Wurm and Lingnau (2015) used MVPA to investigate the degree to which action-specific representations (e.g., to open or to close) in regions within the tool network generalise according to different level of abstraction (e.g., concrete, intermediate and abstract). While in the scanner, participants watched videos of open and close actions with different exemplars of bottles and boxes, that required different kinematics. The authors found that bilateral IPL and LOTC coded actions at all levels of abstraction, while bilateral PMv coded action only at a concrete level. Moreover, they observed that decoding accuracies for intermediate and abstract levels were significantly higher in bilateral IPL and LOTC versus bilateral PMv. Additionally, they found that bilateral LOTC showed significantly stronger decoding for the concrete compared with intermediate and abstract levels, whereas the bilateral IPL showed similar decoding accuracy across the three levels of abstraction. Searchlight MVPA revealed that actions at a concrete level were decoded bilaterally in the occipitotemporal cortex, the post-central sulcus, the IPS, PMd and PMv, while bilateral pMTG, the inferior temporal sulcus and post-central sulcus at the junction to the anterior IPS coded action sat intermediate and abstract levels. The authors concluded that inferior parietal and occipitotemporal cortices code actions at abstract level of representation (open/close regardless of objects), while the premotor cortex codes action at a concrete level only and concluded that the occipitotemporal and the inferior parietal cortices, but not premotor regions, are involved in action understanding (Wurm & Lingnau, 2015).

Although there is some understanding of the broad computations that are carried out by regions within the frontoparietal and occipitotemporal cortices, it remains unclear what tool's structural and functional manipulation properties are represented within each region and how these representations overlap or change according to the task used. In the current fMRI study, we use multivoxel pattern analysis (MVPA; Haxby et al., 2001) to explore the role of different areas in the tool processing network in representing tool identity, structural manipulation knowledge (e.g., power versus precision grip – how to position the hand to grasp) and functional manipulation knowledge (e.g., squeeze versus rotation – how to grasp the object to use) while participants passively viewed images of tools and executed tool use pantomimes.

Recently, Chen et al (2016), using fMRI and MVPA explored the role of regions within the frontoparietal and the occipitotemporal cortex in representing actions and functional knowledge. Participants were asked to pantomime the use of six different items while were in the scanner: scissors, pliers, knife, screwdriver, corkscrew and bottle opener. The classifier for MVPA was trained to discriminate for example, the pantomime of screwdriver from the pantomime of scissors (i.e., rotation versus squeeze movement) and then tested on another pair of tools that matched the same squeeze versus rotation movement (i.e., corkscrew versus pliers). Moreover, as tools were also matched across items for function, they could also test whether regions in the brain coded for function (i.e., scissors and knife are for cutting; corkscrew and bottle opener are for opening). For the ROIs MVPA analysis, the authors defined the left somatomotor hand area and tool-selective regions within the left parietal lobe, the left pMTG and bilaterally in the medial fusiform gyrus. They reported that for action pantomimes (i.e., rotation versus squeeze), successful decoding was observed in the left somatomotor representation of the right hand and in the left aIPS. No action decoding was observed in the left pMTG or in the right medial fusiform gyrus. For tool function, they reported no significant decoding in any of the regions. Moreover, they conducted a whole-brain searchlight analysis, which revealed action decoding in motor and premotor area bilaterally, left aIPS, left anterior temporal lobe, bilateral putamen, right cerebellum and in a region posterior to the functionally defined middle temporal gyrus. They observed significant decoding for function bilaterally in the medial temporal cortex, in the left perirhinal cortex, in the right hippocampus, in the right PMd and in the right retrosplenial cortex. Additionally, they observed higher decoding accuracies for action versus function in left premotor and motor cortex, the left aIPS and bilaterally in the occipital cortex and in the right cerebellum. Higher decoding accuracies for object function than rotation versus squeeze movements were observed only in the left parahippocampal gyrus. The authors concluded that frontoparietal and medial temporal areas represent respectively rotation versus squeeze movements and the object function (i.e., corkscrew is used to open) (Chen et al., 2016).

While we were analysing our results, Chen et al. (2017) published a paper in which using fMRI MVPA, investigated whereas functional manipulation knowledge (rotation versus squeeze) and object function (open versus cut) similarity between objects can be decoded independently of the task applied (viewing or pantomime) and stimulus format (images or words) in the IPL. These items were chosen as they could be analysed in triads, in which two of the three items were similar either in their function (i.e., scissors and knife are for cutting; corkscrew and bottle opener are for opening) or in their functional manipulation knowledge (i.e., rotation versus squeeze). In the viewing task, participants were instructed to look at the images and think about the features of the objects (i.e., name, function, actions, weight, context in which is found, material properties), while in the pantomime task, participants were presented with tool names in text format and instructed to pantomime the tool use with their right hand. The authors reported successful classification of functional manipulation knowledge in the pantomime task in frontoparietal areas, including bilateral motor and premotor cortex, left IPL (the left supramarginal gyrus and the aIPS), the left SPL, the bilateral putamen, the right insula and the right cerebellum. In the viewing task, for rotation versus squeeze, they reported significant decoding in the left IPL (the supramarginal gyrus at the junction with the aIPS), the left SPL, the bilateral posterior parietal lobule, the bilateral pMTG and the right inferior temporal gyrus. Based on the fact that pMTG represents functional manipulation knowledge in the viewing task, but not in the pantomime task (e.g., when tools and hands are not visible), the authors suggested that decoding in pMTG is driven by tools and hand perceptual properties (e.g., viewing a tool/the hand). For cross-task classification they observed that the supramarginal gyrus showed above chance classification for functional manipulation knowledge. For tool function in the pantomime task, the authors reported significant classification in the medial aspect of the left ventral temporal cortex and the middle and orbital frontal gyri bilaterally; while during the viewing task, significant decoding was found in the bilateral medial aspects of the ventral temporal cortex, the bilateral middle frontal gyrus, the left precentral gyrus and the bilateral occipital pole. Thus, the authors suggested that tool function is represented in the temporal lobe and not in the parietal cortex. The authors concluded that the left inferior parietal lobule represents functional manipulation knowledge independently from the task. On the other hand, the SPL represents functional manipulation knowledge in both tasks, but not in a cross-task manner. Thus, the authors hypothesised that the SPL represents functional manipulation knowledge, but this is task specific manner. Moreover, as all functional manipulation knowledge decoding was carried out across different pairs and significant cross-task decoding was observed across different tasks and stimulus formats, the authors concluded that the IPL represents functional manipulation knowledge in an abstract manner and is not based on visual structural properties of the stimuli.

In the studies reviewed above, the focus was on tool-selective regions, however, when interacting with tools in our surroundings, our hands play a crucial role in action execution and online visuomotor control is applied to guide, monitor and correct actions. Several neuroimaging studies have investigated whether the brain activity in tool networks regions is modulated by what is used to grasp and object (i.e., the hand or a tool) as well as whereas the hand is selectively represented in the human brain. For example, Jacobs, Danielmeier and Frey (2010) showed that planning grasping action with the tool or the hand increased activity within the same regions in the parietal and premotor cortex, such as the aIPS and PMv and concluded that grasping actions involving the hand or a novel tool depend on representations that are supported by the same brain regions (Jacobs et al., 2010).

Similarly, Gallivan, McLean, Valyear and Culham (2013) showed that tool use is subserved by numerous action-centred neural representations that are both shared and distinct from the representations of hand actions without tools in hand. At an effector-specific level, they found that SPOC and the extrastriate body area (EBA) discriminated between planning grasping versus reaching for movement performed with the hand only, while SMG and pMTG discriminated upcoming movement performed with the pliers only. Additionally, the aIPS and the motor cortex discriminated planned actions with both the hand and the pliers but did not show cross-decoding between the effectors. On the other hand, at an effector-independent level, they identified regions, such as the PMd, PMv and the middle and posterior IPS, that represented the planning of reaching versus grasping for movements performed with both the hand and the pliers. The authors concluded that brain regions that represent planning of actions with the hand or with pliers may be organised according to a motor hierarchy that distinguish between various level of abstraction required to perform actions. Specifically, they suggested that at a lower level there are hand-selective regions like SPOC and EBA, which represents movement with the hand but not with the tool, tool-selective regions such as SMG and pMTG and parietal areas such as aIPS and motor cortex, which although represented upcoming movements with the hand and the pliers, did not generalise across effector. In contrast, they suggested that areas that discriminated movement plans for the hand and the pliers and across effectors, such as posterior and middle IPS, PMd and PMv, were at higher-levels within the hierarchy. The authors concluded that action performed with the hand and the pliers are represented separately at earlier levels of motor and sensory processing and that these representations become integrated in the frontoparietal cortex.

According to Napier (1956), humans' manual dexterity is an important ability that sets humans apart from other species. It is clear that the hand plays a critical role in our everyday interactions with our surrounding (e.g., to grasp objects, but also to communicate and guide attention), therefore several studies have investigated whether there are specific hand-selective regions in the brain (Bracci et al., 2012; Bracci, Cavina-Pratesi, Connolly, & Ietswaart, 2016; Bracci et al., 2010; Op de Beeck, Brants, Baeck, & Wagemans, 2010). For example, Op de Beeck et al. (2010) have shown that regions within the ventral visual stream showed a significant difference in the activation patterns between hands and torsos in regions such as the extrastriate body area, the ventral occipitotemporal cortex and the fusiform cortex and concluded that there is a distributed selectivity for specific subordinate categories within the ventral stream, and that this selectivity is particularly strong for body parts, including hands.

In the same year, Bracci et al. (2010) conducted two fMRI experiments to test for hand-preferring responses in the human visual cortex using pictures of different body parts (e.g., hands, fingers, feet, whole body parts, assorted body parts and robotic hands) and objects. The authors localized a new hand-selective region in the left occipitotemporal cortex (LOTC), which although is partially overlapping with the extrastriate body area (EBA) was functionally dissociated from it. Whilst hand-selective LOTC responded more strongly to hands, followed to robotics hands, fingers and feet, EBA responded more strongly to body parts, followed by hands and feet. The authors concluded that there is a region that contains representation of the human hand in the lateral occipitotemporal cortex (LOTC), which is separate from the EBA (Bracci et al., 2010).

In two subsequent fMRI studies, Bracci et al. (2012) compared the distribution of activity within the left LOTC in response to tools and hands to explore the degree in which the functional activity in response to these two categories overlapped. In experiment 1, they compared the responses to hands and tools, relative to animals, to localize hand- and tool- selective regions in LOTC. Moreover, they localized motion-responsive (using the contrast moving versus static dots) and object responsive (using the contrast intact versus scrambled objects) regions in LOTC. The authors then compared the location and functional representations of these regions. In experiment 2, the authors tested whether the overlap between tool- and hand- selective regions was specific to hands or related to more general body parts. The authors observed that activity within hand-selective and tool-selective left LOTC overlapped, however, hand- and tool-selective LOTC did not overlap with responses to whole bodies, body parts, objects, or motion. Using MVPA, the authors observed a higher degree of similarity between response patterns to tools and hands in LOTC, but not between hands and other body parts or tools and other body parts. Additionally, they observed that similarity between tools and hands response patterns was specific to LOTC and was not observed in the occipital cortex or in the fusiform area and suggested that the overlap was therefore not related to low-level visual or shape similarities between hands and tools, which would have been expected in the fusiform area and in the occipital cortex. Moreover, using functional connectivity contrasting the whole brain connectivity, they showed that hand- and tool- selective LOTC (versus body-, motion- and object- selective LOTC regions) were connected with regions in the left intraparietal sulcus (which showed significantly higher responses to hands and tools versus animals and scenes) and left premotor cortex. The authors suggested that hands and tools share a primary involvement in object-directed actions, which is reflected in the organisation of the occipitotemporal cortex. Regarding the overlap between tools and hands in LOTC, the authors postulated that although each selective region represents only one category (e.g., tools or hands), each category may indirectly activate the representation of the other category (e.g., viewing a picture of a tool may indirectly activate the representation of hands). Alternatively, they proposed that LOTC may represent the semantic information that represent the meaning of the action. The authors concluded the overlap between hands and tools in LOTC is not related to share visual properties, but reflect action-related dimensions, and may reflect the organisation of parietal downstream networks due to the differences observed in the connectivity between LOTC and these networks (Bracci et al., 2012).

To further investigate the role played by these occipitotemporal areas, Bracci et al. (2016) presented pictures of tools, hands, bodies, non-manipulable objects and scrambled images of objects to the participants while in the scanner. Using an ROI approach, they identified a network of areas in the left hemisphere, including the IPS, the LOTC and the ventral OTC (VOTC), that was preferentially activated for tools versus scrambled objects. Similarly, using a contrast of hand versus scrambled images, they identified regions within the left IPS, LOTC and VOTC preferentially activated for hands and that were partially overlapping with the tool-selective activation. Thus, hand-related and tool-related responses were observed in both the parietal (i.e., IPS) and occipitotemporal cortex (i.e., LOTC and VOTC). To further investigate the representational content of the different regions, the authors implemented correlation-based MVPA. They computed the distribution of the responses to hands and tools images as two categories that are functionally associated within the action domain (e.g., both are involved in object manipulation), but distinct within the category domain (e.g., tools are inanimate objects, whereas hands are animate objects). They observed that while images of hands and tools activated similar areas in the parietal and the occipitotemporal cortex, the representational content in these regions was remarkably different. In fact, activity patterns in left LOTC revealed high response pattern similarities for the action (i.e., hands and tools) as well as the category domain (i.e., inanimate and animate), while IPS coded for the action domain only. On the other hand, VOTC decoded the object's domain only. The authors concluded that while IPS seem to represent the implementation of hand and tool interactions, the VOTC seem to represent aspects of category knowledge such as animate versus inanimate. Moreover, LOTC seems to bridge category representations from VOTC and action representations from IPS by representing both types of information. The authors concluded that there is a network of overlapping hand-related and tool-related responses within the tool network in the left hemisphere which represent different properties (Bracci et al., 2016).

Inspired by these findings, here, we explored which properties, such as tool identity, structural and functional manipulation knowledge, are represented within the tool network and how these representations overlap or change according to the nature of the task. For this purpose, we implemented two tasks: in the viewing task, participants were presented with pictures of tools, while in the pantomime task they were presented with the printed name of the same tools presented in the view task. The two tasks differed in both the response that was required (passive viewing versus pantomime) and stimulus presentation.

Moreover, by presenting tools that afforded different grasp types (e.g., power versus precision) and different functional use movements (e.g., rotation versus squeeze), we manipulated structural manipulation knowledge and functional manipulation knowledge respectively. In our experiment we compared pictures versus words as well as passive view versus pantomiming. This was done as we were interested evaluating the hypothesis that regions within the occipitotemporal and frontoparietal networks represents actions in a manner that is independent from the specific task participants are performing. Successful classification of action properties (e.g., functional and manipulation knowledge) within tasks and across objects would constitute evidence that within these regions, action properties are accesses independently of task context and stimulus format.

Based on Gibson's (1979) theory of affordances, we hypothesized that viewing pictures of tools should automatically activate the motor plans for actions in the frontoparietal network. Thus, in the view task we would expect structural manipulation knowledge (power versus precision), as well as functional manipulation knowledge (rotation versus squeeze) to be coded in frontoparietal regions. Based on the perception and action model (Milner & Goodale, 1995, 2006, 2008) and on the existence of two pathways for grasp and use in the dorsal stream (figure 1.4; Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010), we hypothesised that tool identity would be represented within the ventral stream as well as within the ventro-dorsal stream (e.g., pMTG, SMG and PMv). Moreover, as in chapter 2 we observed that LO is involved in hand preshaping in pantomime grasping, we would expect that regions within the lateral occipital cortex code for structural manipulation knowledge. In the pantomime task, we would also expect that regions within the dorso-dorsal grasp network, such as IPS and PMv, represent structural manipulation knowledge, while regions within the ventro-dorsal use network, such as pMTG, SMG and PMv, represent functional manipulation knowledge. Additionally, as Lewis (2006) hypothesised that the motor and the semantic system overlap, thus if the function and the identity of the tools needs to be retrieved to successfully produce motor actions, we hypothesized that regions within the ventral stream should code tool identity in the pantomime task as well. If decoding can be found regardless of tasks and stimulus presentation format (i.e., images versus printed name of tools), this would show that the decoding observed within each task is not simply driven by the visual structural properties of the tools. As recent fMRI studies have identified an extensive left-lateralised cortical network implicated in real every-day tool use in humans, which includes areas that encode both tool identity and the manipulations that are performed (Brandi, Wohlschlager, Sorg, & Hermsdorfer, 2014) we focused our analysis on the left hemisphere.

Moreover, as Bracci et al. (2012) showed that there is hand- and tool-selective regions within the occipitotemporal cortex and that they represent action and identity related properties differently, we were interested in exploring whether and how these regions represent tool identity, structural and functional manipulation knowledge associated with manipulation of tools. Such insight would help us understanding how tools and tool related actions are represented within the tool network.

3.2 Methods

3.2.1 Participants

Eighteen participants (7 males; mean age = 24.6 years old, S.D. = 4.1 years old; mean education = 17.5 years, S.D. = 1.8 years) recruited from the University of Maastricht (Maastricht, Netherlands) took part in a neuroimaging experiment at the Scannexus MRI scanning facilities (Maastricht, www.scannexus.nl). All participants were healthy, had normal or correct-to-normal vision and were right-handed (Oldfield, 1971). The study was approved by the Ethics committee of UEA (Norwich, UK; ref: 2015-0058-000146) and conducted in accordance of the Declaration of Helsinki (1964). Participants were reimbursed for their time. Although most of the participants we tested were not English native speakers, all participants were consented, instructed, tested and debriefed in English. As not all the participants were native English speakers, before taking part in the experiment all participants took part in a training session (see section 3.2.5) to ensure they were familiar with the word presented as well as with the expected movement associated with the tools.

3.2.2 Stimuli Selection

To select the most appropriate tools for our experiment, we selected 12 tool identities included in previous normative, behavioural and fMRI studies (Brodeur, Dionne-Dostie, Montreuil, & Lepage, 2010; Brodeur, Guérard, & Bouras, 2014; Chen et al., 2016; Garcea & Mahon, 2012; Guérard, Lagacé, & Brodeur, 2015; Lagacé, Downing-Doucet, & Guérard, 2013; McNair & Harris, 2012). First, from a dataset of 296 stimuli from Lagacé et al. (2013), we excluded the objects that did not have a specific action associated with them (e.g., ashtray), leaving us with 161 tools. Lagacé et al. (2013) presented participants with 5 possible grip types: power, intermediate, index-thumb, fingers-thumb and parallel extension (see appendix D). Thus, for the purpose of the study, from the list of 161 we extracted only tools that afforded power (N = 87) and precision (N = 43) grip. These tools were selected, based on Lagacé et al. (2013) 's ratings in the grip use rating task (e.g., grasp to use the object) and grasp rating task (e.g., grasp the object). From this list, we selected only tools which were rated to afford between 0.9 and 1.5 actions on average, which left us with 58 power grip and 33 precision grip tools. This was done to make sure we selected tools that afforded a number of actions as close as possible to 1 (thus excluding tools with no actions associated with them, or tools with many actions associated with them). From this list of 91 tools, we excluded tools if they included actions involving an interaction with the upper part of the body (e.g., lipstick, toothbrush, cup) or throw actions (e.g., ball). This was done to avoid excessive movements during pantomime actions in the scanner. Moreover, tools that had more than one exemplar, but were functionally similar were only reported once (e.g., pen and fountain pen, spoon and wooden spoon). This left us with 44 tools: 9 precision grip tools and 34 power grip tools. The remaining 34 power grip tools and 9 index-thumb grip tools were compiled in a table with other tools used in previous studies from Chen et al. (2016), Garcea and Mahon (2012) and McNair and Harris (2012), totalling 60 tools. All tools in the list were matched with the grip rating extracted from Lagacé et al. (2013) and the familiarity rating extracted from (Guérard et al., 2015). Tools that were not rated in any of these two studies or were given different ratings according to use or grasp were excluded (N = 33). Tools were then divided according to power (N = 19) and precision (N = 8) and were separately grouped according to the functional action. Within precision grip tools were grouped according to rotation, squeeze and writing/colouring actions. Tools within the power grip group were grouped in a similar manner. Tools that could not be grouped within the three categories were excluded. This left us with pliers, tongs, screwdriver, tweezers, peg, key, screw, nutcracker, corkscrew, clippers and measuring spoon. We additionally selected the bolt as its movement was similar to the screw. The bolt was originally excluded because it was presented coupled with a nut in Lagacé et al. (2013), but we decided to present it separately from the nut.

Using the 12 tools above, we conducted a normative study at UEA, to select our final 8 tools to use in the fMRI study. We asked 15 naïve participants (1 male; mean age = 25.6 years old, S.D. = 6.5 years old) to complete a questionnaire about the 12 different tool identities: corkscrew, key, nutcracker, peg, screwdriver, screw, tongs and tweezers, pliers, clippers bolt and measuring spoon. The questionnaire was divided into two parts. In part one participants had to name the tools, to rate how familiar they were with each tool (on a scale from 1 -"very different" to 7 -"very similar"), how many times they use each tool (on a scale from 1 – "every day" to 8 "never used2), how easy it was to pantomime the use of the tools (on a scale from 1 -"very difficult" to 7 -"very easy"), to determine the number of actions and the type of grip required to use each tools (appendix D). To select the appropriate grip to use each tool, participants were presented with photographs of five grip types: a power grip, an intermediate grip and three different precision grips, including an index–thumb grip, a fingers–thumb grip and a parallel extension grip (Lagacé et al., 2013) (appendix D). Each participant rated each object once (12 trials). Instructions and an example extracted from the questionnaire are presented in Appendix D. As we were interested in hand actions that occur in everyday life, we selected tool identities that our participants rated as highly familiar, used frequently, afforded a smaller number of possible actions and crucially that afforded either a power or precision grip. For each item, we computed the median of the group answers (Brandi et al., 2014). Descriptive statistics of the ratings are provided in Appendix F.

In part two, we asked participants to rate the similarity of the grip when required to move or use each tool (on a scale from 1 -"very different" to 7 -"very similar"), to rate how similar is the function of a pair of objects (on a scale from 1 -"very different" to 7 - "very similar") and to rate how similar is the shape of the hand when grasping a tool compared to another when grasping or using it (on a scale from 1 - "very different" to 7 - "very similar"). Each participant rated each objects pair twice (110 trials). Instructions and an example extracted from the questionnaire are presented in Appendix E.

First, we looked at the agreement in the naming task. The measuring spoon and the bolt were excluded as there was a low percentage of name agreement across participants (see Appendix F.1). Second, we looked at familiarity, use and number of actions, but we did not exclude any of the tools based on these ratings (Appendix F.3). Third, we looked at the grip rating task. The key (index-thumb = 93.3%), the peg (index-thumb = 86.6%), the screw (index-thumb = 80%) and the tweezers (index-thumb = 93.3%) were selected for the precision grip category, while the clippers were excluded as participants were not in agreement on the grip type used to grasp the object (index-thumb = 60%; see appendix F.2 for descriptive ratings of all tools). To select the tools for the power grip category, we computed the percentage of answers for each tool across the power, intermediate, fingers-thumb and parallel extension grip type. The screwdriver (100%) and the tongs (100%) were selected as tools that afforded power grip. However, as the other tools were all rated with high percentage to afford power grip, to select the most appropriate tools between the nutcracker (86.5%), the corkscrew (93.2%) and the pliers (93.2%), we looked at the ratings in part two of the questionnaire. Thus, the corkscrew was selected as it was rated to afford a grasp similar to the screwdriver (median = 3.5; range 2-7); while the nutcracker was selected as it was rated to afford a grip more similar to the tongs (median = 7; range 5-7) compared to the pliers (median = 6; range 1-7). To summarise: the screw, the key, the peg and the tweezers were selected as precision grip tools, while the screwdriver, the corkscrew, the nutcrackers and the tongs were selected as power grip tools. This selection was further confirmed by the ratings of the grasp similarity task in part two of the questionnaire (Appendix G). Based on the ratings of part two, the tools were also grouped for movement similarity. As such, the screw, the key, the screwdriver and the corkscrew were grouped in rotation movement category, while the nutcracker, the tongs, the tweezers and the peg were grouped in the squeeze movement category.

For each item, we computed the median of the group answers (Brandi et al., 2014) and selected the tools and pairs with the higher median. From the 12 tool identities, we selected 8 identities: corkscrew, key, nutcracker, peg, screwdriver, screw, tongs and tweezers. Descriptive of ratings are presented in Appendix G.

Ten exemplar images for each tool identity were selected from the BOSS database (Brodeur et al., 2010; Brodeur et al., 2014), from the Konklab database (Konkle & Oliva, 2011, 2012) and Google Images and then converted to greyscale.

3.2.3 Experimental design

Participants were presented with either black and white images (800x800 pixels; viewing task; visual angle: approx. 15 °) or words (font size 32; pantomime task) of eight tool's identities on a white background (corkscrew, key, nutcracker, peg, screwdriver, screw, tongs and tweezers) on a white background in a block design protocol (Figure 3.1 shows all the visual stimuli used in the experiment). Presentation was controlled using a PC laptop running a custom designed programme in Matlab (The MathWorks, USA) and Psychophysics Toolbox (Brainard, 1997). Visual stimuli were projected onto a screen (spatial resolution of the screen: 1920 x 1200) and viewed through a mirror mounted on the head coil (distance mirror – screen: 60 cm). Stimuli were matched for orientation (approximately 45° angle) with the handle positioned towards the right side of the screen. This was done so that the handle was oriented towards the participant's right hand, which was used to pantomime the use of the depicted tool. Each image was presented with a fixation cross at the centre.

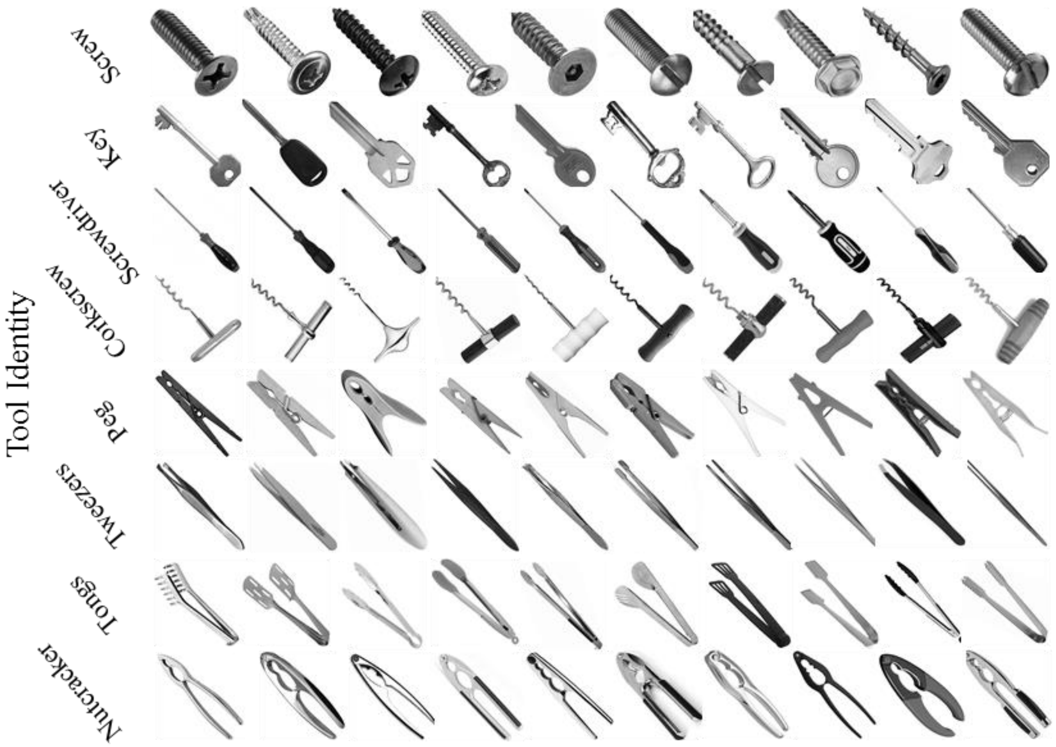


Figure 3.1 Viewing task stimuli consisted of ten exemplars for each of the eight tool identities: screw, keys, screwdriver, corkscrew, peg, tweezers, tongs, and nutcracker.

The stimuli were organised into different categories according to manipulation knowledge (power and precision) and function knowledge (rotation, squeeze). In particular, the power grip included corkscrew, nutcracker, screwdriver and tongs, all similar in terms of manner of manipulation in which the object is held only between the index finger and thumb and requires a small force (Lagace ey al., 2013); the precision grip type category included key, screw, peg and tweezers, all similar in terms of manner of manipulation in which the object is held in contact with the palm and the fingers work against the palm (Lagace et al., 2013). For function knowledge, the rotation category included key, screw, corkscrew and screwdriver, all similar as the use of the objects requires a rotation of the wrist; the squeeze category included nutcracker, peg, tongs and tweezers, al similar as the use of the objects requires to put pressure on them (figure 3.2).

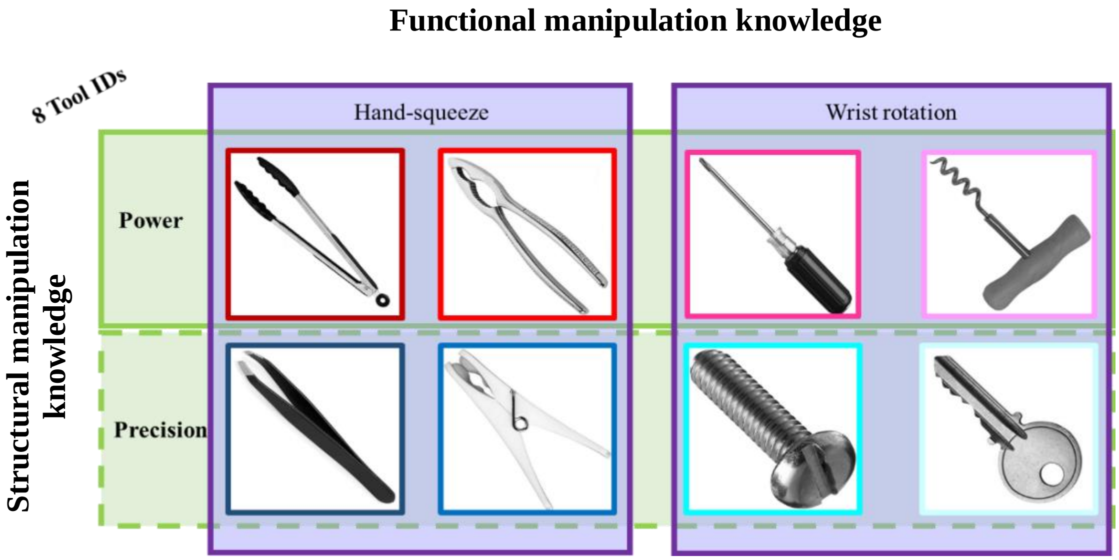


Figure 3.2 The stimuli were organised into different categories according to precision and power grip as well as squeeze and rotation movements.

3.2.4 *fMRI procedure*

In the present study, we measured the blood-oxygenation-level dependent (BOLD) signal while participants performed viewing and pantomiming tasks (in separate runs) while lying supine in the scanner. As it is well known that movements of the shoulder and upper arm may induce artefacts in the BOLD signal the upper arms were immobilised to restrict shoulder movements by means of a strap, but allowed for full rotation of the elbow and wrist (Culham, Cavina-Pratesi, & Singhal, 2006; Rossit et al., 2013).

Each participant completed two tasks while in the scanner: a viewing task and a pantomime task. To avoid the possibility that the activation could be affected by the order of which the tasks were presented, we counterbalanced the order participants were presented with the experimental runs. To give an example, participants one performed pantomime, view, pantomime, view, etc., whereas participant two was presented with view, pantomime, view, pantomime, etc. Each functional run comprised 16 stimulus blocks and 18 fixation blocks and each individual performed at least 4 runs for each task. In each task, each tool identity was presented twice per run. However, in the view condition, each exemplar was presented only once within the run (totalling 10 different pictures of each identity, figure 3.1). This was done to minimise the possibility that any effects might be driven by low-level visual features associated with the tools.

We used a block design with 10s on and 10 s off as Birn, Cox, & Bandettini (2004) showed that a block design with tasks and control durations of 10 s is minimally sensitive to task-induced motion artefacts and therefore optimal to detect blood oxygenation level-dependant signal changes without significant motion artifacts (Birn et al., 2004).

In the viewing task, within each block, 5 exemplars of each tools were presented (i.e., 5 different pegs were presented in 10s), each for 1000 ms with a blank inter-stimulus-interval (ISI) of 1000 ms. Each run lasted 5.3 minutes and was composed by 16 category blocks and each block lasted 10 s interleaved with a fixation block of 10 s (figure 3.3) and two baseline blocks of 14 s (one at the beginning and one at the end of the task). During this task, participants were presented with pictures of tools and instructed to look at the picture keeping their eyes on the bull's eye (24 pixels) at the centre of the screen. Participants performed a 1-back repetition task throughout the run, whereby responses were made whenever two successive photos were identical by pressing a button on the response box with the right index finger (2.5 x 13 x 6.4 cm, 4 coloured round buttons blue, yellow, green and red, fORP 932 response box system).

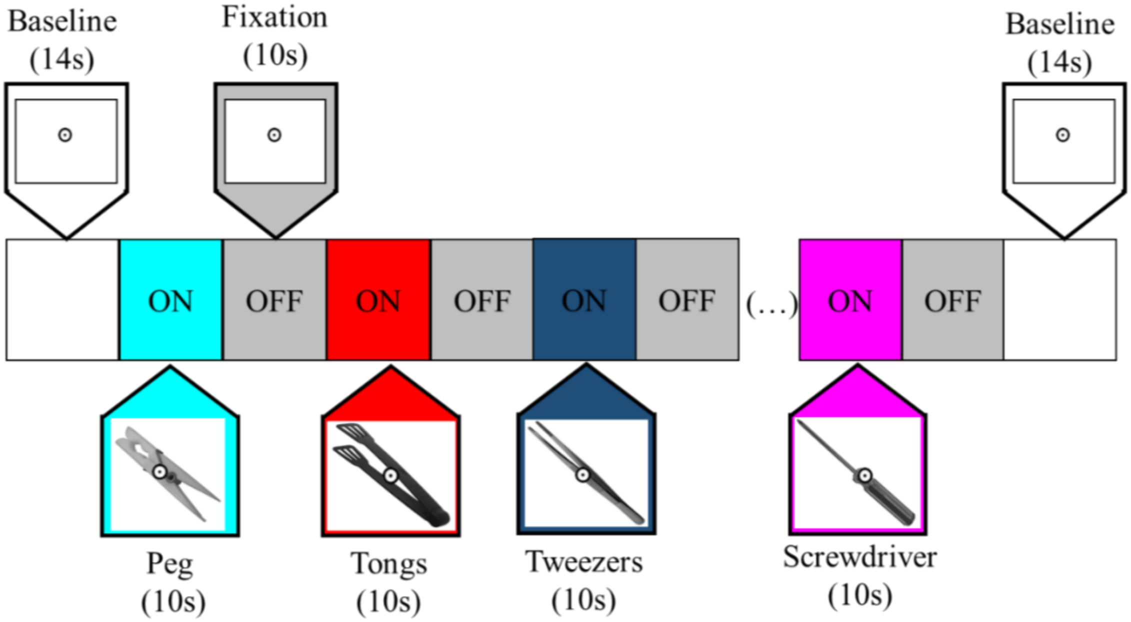


Figure 3.3 View task: block-design protocol and experimental timing.

In the pantomime task, each run lasted 5.43 minutes and was composed by 16 blocks (each tool identity was repeated twice interleaved with a fixation block of 10 s and two baseline periods of 14 s (one at the beginning and one at the end of the run). At the beginning of each block, a word (e.g., tweezers) to cue the type of pantomime was presented for 500 ms. During this time, participants were instructed to keep their eyes on the fixation and to lift up their fist from the chest and to get ready to perform the action. At the end of the 500 ms, the word disappeared from the screen and the fixation flashed green 5 times (1 s on, 1 s off) to cue the participant to perform the action (figure 3.4). Each block lasted 10 s and 5 actions were performed triggered by the fixation changing colour on the screen. At the end of the 10 s, the fixation turned red to cue the participant to place their fist on the chest. During the pantomimed condition, hand actions were recorded by means of a video camera (Panasonic HD HVC-210) placed in the control room of the scanner and videos were visually inspected before data analysis to check for participants’ errors.

The view and pantomimed task were matched in timing as much as possible (e.g., in both tasks, participants viewed the pictures or pantomimed for 10 s with 5 repetitions per block), however, each trial in the pantomime task lasted 500 ms more than the view task, which corresponded to the time in which the word cue was presented on the screen.

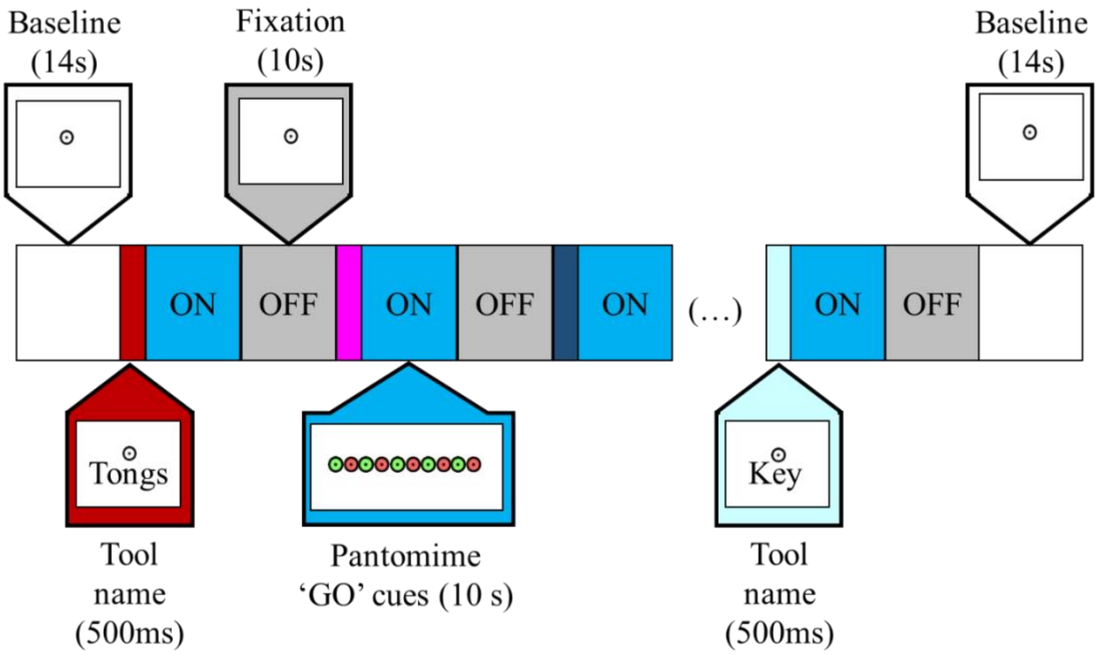


Figure 3.4 Pantomime task: block-design protocol and experimental timing.

3.2.5 *Pre-scanning training of participants*

An hour prior to entering the scanner, participants were presented with the images of all the eight categories and asked to name each tool identity, to ensure they were familiar with the name of each tool. After the naming task, participants were asked to show the experimenter how they would pantomime the use of each tool shown on the screen. At the end of this task, the experimenter showed the movement expected for each tool and asked the participant to perform each movement again in a similar way to the one shown (this procedure was adapted from Lausberg, Kazzer, Heekeren, & Wartenburger, 2015). Importantly, each participant was reminded to carry out the movement in a comfortable and natural manner. In addition, as not all our participants were native

English speakers, each participant was then shown the name of each tool on the screen and asked to perform the expected movement. They were then presented with the words of each tool in English and asked to repeat the expected movement when the word appeared on the screen. For native Dutch speakers (N = 7), the translation of each word in their native language was provided. After this task, participants were given time to familiarise with the tools' word for up to 15 minutes. Once the 15 minutes were over, the experimenter asked the participants to pantomime the expected movement for each word shown on the screen until they reached 100% correct performance. It is important to highlight that most of the participants performed the expected movement correct for each tool at the first presentation. Finally, participants were asked to complete up to 8 trials of the pantomime task to familiarise themselves with the timing of the experiment (e.g., go and stop cues). Although they were sitting at the table, they were asked to pretend they were in the scanner (Fabbri et al., 2014). This was done so that the experimenter could check if the participant did understand the task and where s/he should place the hand in between trials. All participants took part in the training to minimise any effects on the results. Moreover, to ensure that while in the scanner the participants performed the correct movement associated with each word, we used a video camera to record the movements and we visually examined the videos to check for mistakes. No trials were excluded.

3.2.6 Independent localiser stimuli and paradigm

To localise hand-, tool- and object-selective areas, we used a separate perceptual localiser in which greyscale images of whole bodies, chairs, hands, tools and scrambled (800 x 800 pixels; visual angle: approx. 15 °) were presented on a white background. Importantly, to avoid circularity, we used different stimuli from our main experiment. Stimuli were selected from a set of images used in previously published studies in the field (Bracci et al., 2010; Bracci, Cavina-Pratesi, Ietswaart, Caramazza, & Peelen, 2011; Bracci et al., 2016). For scrambled visual stimuli, each image was divided into a grid of 25 pixels square and randomly reordered. Moreover, heads were removed from whole body stimuli, to keep the concept of the whole body intact (Bracci et al., 2010). A small black bulls eye fixation (24 pixels) was superimposed at the centre of each image to provide a fixation point. Each run lasted 7.47 minutes and was composed of 6 stimulus epochs per condition (14 s each), 6 scrambled epochs (14 s each) and two fixation/baseline epochs (14 s) placed at the beginning and at the end of the run. Each picture was presented for 500 ms with 500 ms ISI. Stimulus sequences were organised into sets of four, separated by scrambled epochs with the order of the conditions counterbalanced across the total number of runs. We created two sets of stimuli for the localiser task: in each set, the category of the stimuli was the same, but included 14 different exemplars. Each participant completed 3 runs of the localizer (only one participant completed 4 runs of the localiser) after 8 runs of the main experiment. Participants were instructed to keep fixation during the whole duration of the run and to perform a 1-back task throughout the run, whereby responses were made whenever to successive photos were identical by pressing a button on the response box with the right index finger. During scrambled epochs, participants were asked to simply look at the stimuli. Figure 3.5 shows the protocol and the timing of the localiser task.

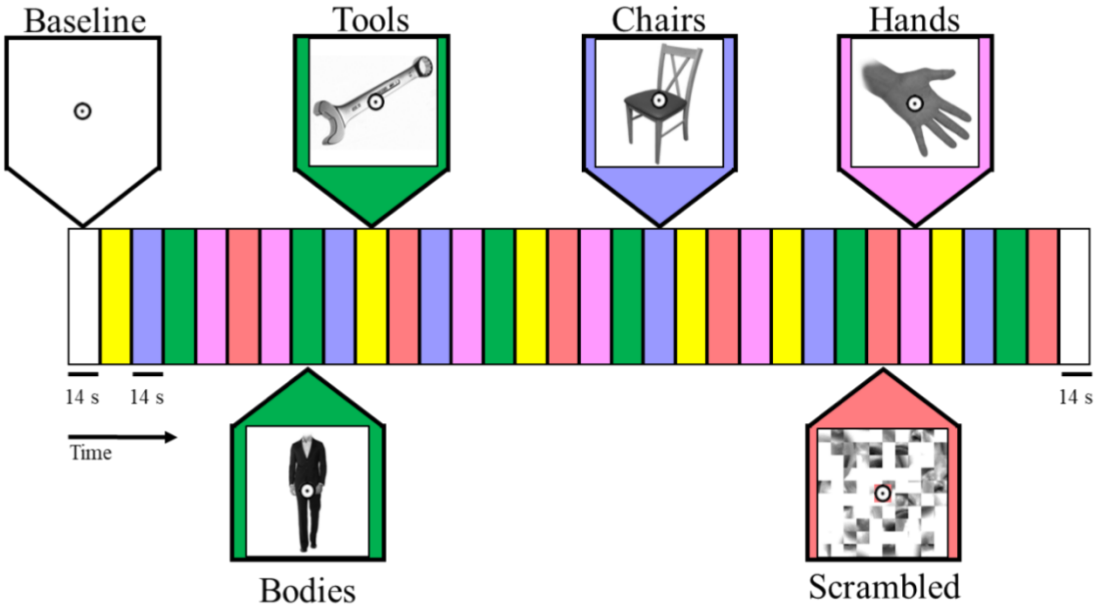


Figure 3.5 Localiser task. Block-design protocol and experimental timing. Localiser adapted from Bracci et al. (2011).

3.2.7 *fMRI data collection and processing*

All images were acquired using a Siemens whole-body 3T MAGNETON Prisma fit scanner with a 64-channel head coil at the Scannexus imaging centre, Maastricht, Netherlands. The functional T2*-weighted images (EPI) with BOLD contrast were acquired using the following parameters: repetition time (TR) = 2000 ms, echo time (TE) =30 ms, flip angle (FA) = 77°, field of view (FOV) = 216 mm, matrix size = 72 x 72 pixels. Each functional image consisted of 35 slices (sagittal left-to-right; 3 mm thickness). High-resolution T1-weighted anatomical images were collected in the same session as the functional scans. The following parameters were used: TR = 2250 ms, TE of 2.21 ms, FA = 9°, FOV 256 mm, matrix size = 256 x 256. We collected 192 slices (sagittal left-to-right) of 1 mm thickness. All experimental runs (View: Mean = 4.5; Standard Deviation 0.51; Pantomime: Mean = 4.66; Standard Deviation = 0.48) and localiser runs (Mean = 3.05; Standard Deviation = 0.23) were completed in the same session of approximately 2 hours.

Brain Voyager QX (version 2.8; Brain Innovation, Maastricht, The Netherlands) was used to pre-process the data, to perform univariate analysis and ROI selection. We used Brain Voyager's 3D motion correction (sinc interpolation) to align each functional volume within a participant to the functional volume acquired closest in time to the anatomical scan (e.g., Fabbri et al., 2016; Rossit et. al., 2013). Data from each run was screened for motion artifacts, however, no abrupt movement artifacts were detected. Functional data were superimposed on anatomical brain images, previously aligned to AC-PC and transformed into standard stereotaxic space (Talairach & Tournoux, 1988). No spatial smoothing was applied for ROIs and MVPA analysis. Moreover, for completeness, we performed a univariate whole brain analysis. For this analysis data were spatially smoothed with a Gaussian Filter function of full-width half-maximum (FWHM) of 6 mm.

3.2.8 *ROI definition*

To identify ROIs for MVPA, we used the data from our independent localizer and an orthogonal contrast with the main experiment data. The latter was used as no motor areas were identified using the perceptual localiser. Critically, to avoid the problem of "circular analysis" (Kriegeskorte, Simmons, Bellgowan, & Baker, 2009), we used an orthogonal contrast so that the activity within the ROIs was not directly biased to show and pattern related to differences between our experimental conditions. We aimed to identify ROIs in the left hemisphere previously reported to be part of the tool network (for a review see Lewis, 2006) and to be involved in the execution and planning of prehension movements (for a review see Gallivan & Culham, 2015; Turella & Lingnau, 2014). ROIs were defined in each individual participant based on criteria defined below.

Data was analysed in each participant with a random-effects general linear model for both the main experiment data and the localiser data. The statistical threshold was set at $p < .005$, $t = 3$ (e.g., Gallivan et al., 2013). For each ROI, we selected the voxels active within a volume of interest up to 15 mm^3 around the peak centred on the anatomical landmarks (Gallivan et al., 2013).

To identify ROIs we identified the activations individuated through each contrast in each individual participant's brain transformed into Talairach space. Regions were defined using a combination of anatomical and activation criteria rather than stereotaxic coordinates. Following ROI definition, Talairach coordinates of each participant were extracted and averaged to permit comparison with previous studies. Details of the ROIs are reported in table 3.1. Moreover, figure 3.6 and 3.7 show the representative anatomical location of each ROI on a Colin 27 Talairach inflated brain (http://neuroelf.net).

The following left hemisphere ROIs were identified using the following criteria:

- *Lateral Occipitotemporal Cortex Object selective* (LOTC Object) – [chairs > scrambled] – defined by selecting voxels located near the lateral occipital sulcus (LOS) (Bracci & Op de Beeck, 2016).
- *Lateral Occipitotemporal Cortex Tool selective* (LOTC Tool)– [tools > chairs] – defined by selecting voxels located near the LOS that closely overlap with LOTC hand selective area (Bracci et al., 2011).

- *Lateral Occipitotemporal Cortex Hand selective* (LOTC Hand) – [(hands > chair) and (hands > bodies)] (Bracci & Op de Beeck, 2016) – we first defined LOTC body by selecting the peak of activation near the LOS for the contrast [bodies > chairs] and then defined LOTC hands by selecting the peak of activation located near the LOS and anterior to LOTC Body (Bracci et al., 2010). LOTC body was not included in the analysis.

- *Posterior Middle Temporal Gyrus* (pMTG) – [hands > chairs] – defined by selecting the voxels on the posterior middle temporal gyrus, more lateral, ventral and anterior to EBA (Hutchison et al., 2014). We selected the peak in front of the anterior occipital sulcus (AOS), as the MTG is in the temporal lobe and the AOS separates the temporal from the occipital (Damasio, 1995).

- *Supramarginal Gyrus* (SMG) – [pantomimes > baseline] - defined by selecting the voxels along the supramarginal gyrus, lateral to the anterior segment of the IPS (Gallivan et al., 2013).

- *IPS Tools* – [tools > scrambled] (Bracci et al., 2016) – defined by selecting the voxels located close to the junction between the aIPS and the post-central sulcus.

- *IPS hand* – [hands > chairs] (Bracci & Op de Beeck, 2016) – defined by selecting the voxels located along the intraparietal sulcus posterior to IPS tools.

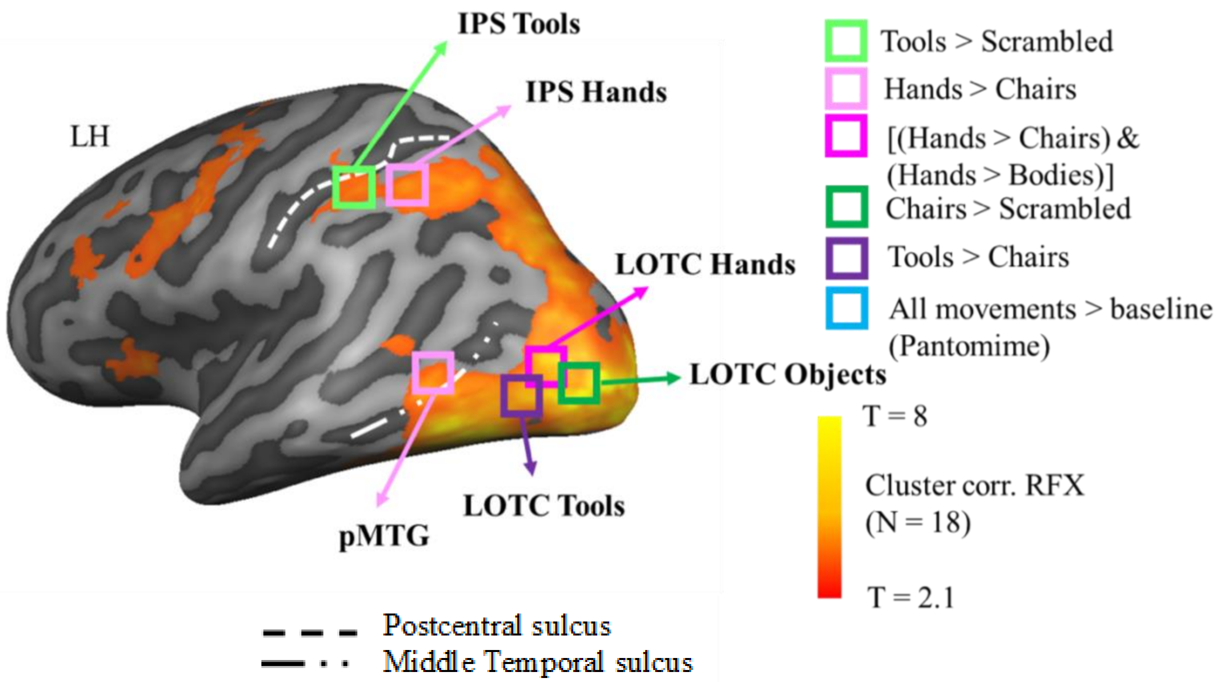
- *Motor Cortex* (MC) - [pantomimes > baseline] – defined by selecting the voxels around the "hand knob" area in the anterior bank of the central sulcus (Gallivan et al., 2013; Ariani et al., 2015).

- *Somatosensory Cortex* (SC) - [pantomimes > baseline] (Fabbri, Strnad, Caramazza, & Lingnau, 2014) – defined by selecting voxels medial and anterior to the aIPS, encompassing the post-central gyrus and the post-central sulcus (Gallivan et al., 2013).

- *Dorsal Premotor Cortex* (PMd) - [pantomimes > baseline] – defined by selecting the voxels at the junction of the precentral sulcus and the superior frontal sulcus (Gallivan et al., 2013; Ariani et al., 2015).
- *Ventral Premotor Cortex* (PMv) - [pantomimes > baseline] – defined by selecting the voxels inferior and posterior to the junction between the inferior frontal sulcus and the pre-central sulcus (Gallivan et al., 2013).
- *Supplementary Motor Area* (SMA) - [pantomimes > fixation] (Fabbri, Stubbs, Cusack, & Culham, 2016) – defined by selecting the voxels on the medial wall of the posterior frontal gyrus, anterior to the medial end of the central sulcus and posterior to the vertical projection of the AC plane (Ariani et al., 2015).

Table 3.1 ROIs with corresponding Talairach coordinates (mean x, y and z centre of mass and standard deviation (SD). Mean sizes across participants from Talairach data (in mm^3 and functional voxel).

	Tailarach coordinates						ROI size	
ROI name	Mean x	Mean y	Mean z	SD x	SD y	SD z	mm^3	Nr voxels
LOTC Object	-42.55	-74.83	-4.36	2.18	2.84	4.67	2130	79
LOTC Tools	-44.92	-67.93	-2.31	4.44	3.59	4.25	581	22
LOTC Hands	-46.69	-67.67	1.94	4.45	4.14	4.64	1027	38
pMTG	-47.24	-58.84	5.31	4.4	3.71	4.95	1034	38
SMG	-51.77	-34.57	28.75	4.5	9.05	10.33	1952	72
IPS Tools	-37.47	-38.05	40.08	4.84	6.07	5.72	787	29
IPS Hands	-36.42	-43.9	42.77	3.38	6.79	5.44	1263	47
MC	-35.31	-25.29	49.53	4	4.93	4.47	2726	101
SSC	-50.11	-25.4	43.5	4.35	3.52	4.06	2415	89
PMd	-29.19	-18.66	47.74	5.54	12.64	14.67	1748	65
PMv	-47.17	-7.95	33.66	4.64	14.84	11.11	1336	49
SMA	-6	-11.09	48.2	2.35	4.69	4.45	1735	64



Perceptual localiser: all stimuli > baseline

Figure 3.6 Brain areas activated using the contrast all stimuli > baseline in the localizer task shown on a Colin 27 Talairach inflated brain (http://neuroelf.net). The general locations of the selected ROIs are outlined in squares (please note that actual ROIs were anatomically defined separately in each participant). Each colour corresponds to the contrast used on localizer data as defined in the legend. Sulcal landmarks are denoted by white lines (stylised according to the corresponding legend). ROI acronyms are spelled out in main text. LH = left hemisphere.

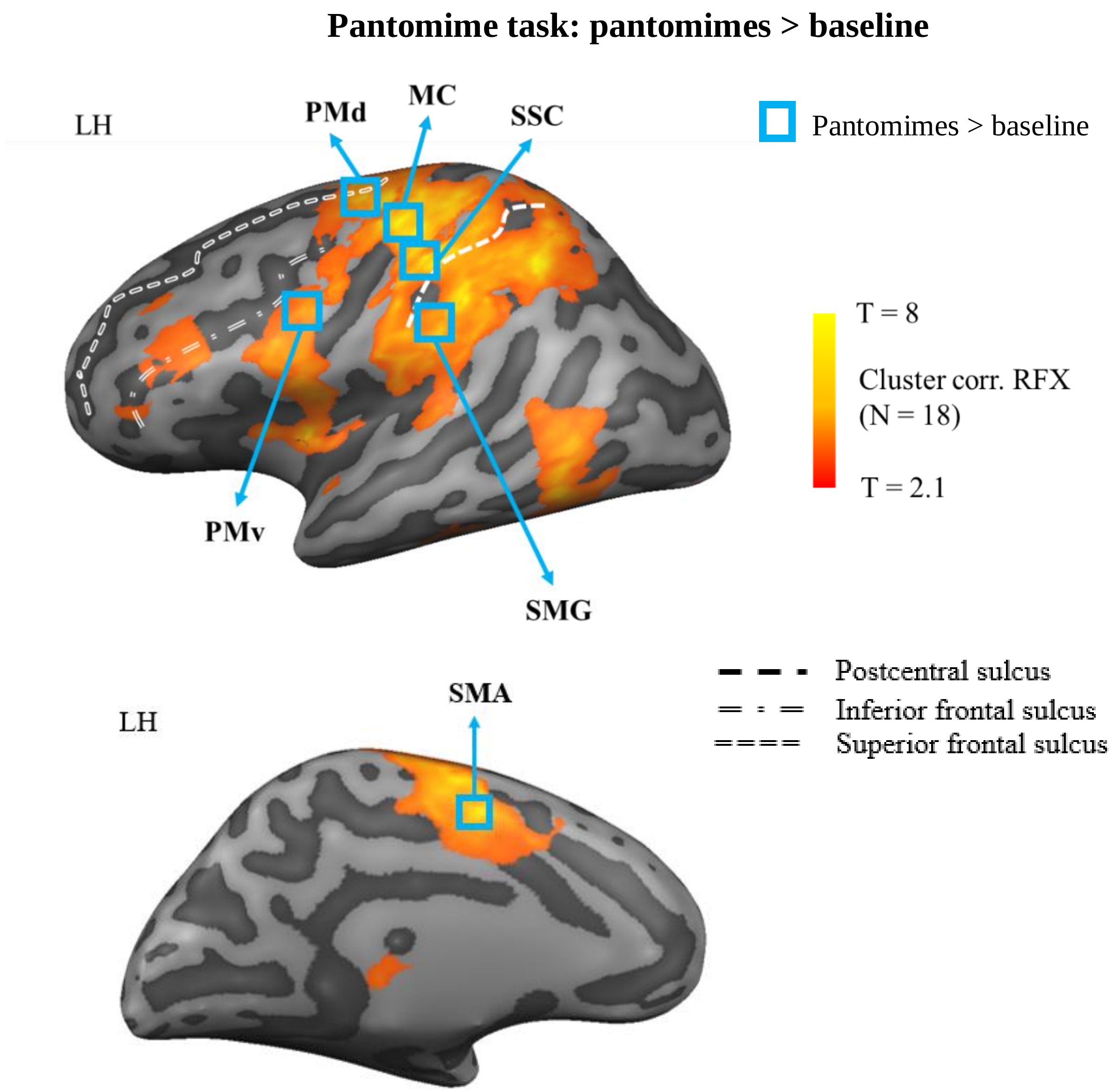


Figure 3.7 Brain areas activated using an orthogonal contrast in the pantomime task pantomimes > fixation shown on a Colin 27 Talairach inflated brain (http://neuroelf.net). The general locations of the selected ROIs are outlined in squares (please note that actual ROIs were anatomically defined separately in each participant). Sulcal landmarks are denoted by white lines (stylised according to the corresponding legend). ROI acronyms are spelled out in main text. LH = left hemisphere.

3.2.9 *Univariate whole-brain voxel-wise analysis*

To investigate possible areas that may demonstrate univariate differences for structural or functional manipulation knowledge, we conducted a whole brain voxel-wise analysis using a random effect general linear model (RFX GLM) with separate predictors for each condition and each participant. In order to control the problem of multiple comparisons we used Brain Voyager's cluster-level statistical threshold estimator. We set the voxel-wise threshold at $p = .01$ and the cluster-wise to $p < .001$. To investigate structural manipulation knowledge, we applied the following contrast: Power > Precision in each task separately. To investigate functional manipulation knowledge, we applied the following contrast: Rotation > Squeeze in each task separately.

3.2.10 *Multivariate Pattern Classification Analysis (MVPA)*

We implemented ROI-based MVPA (Haxby et al., 2001) to explore if we could decode tool identity, power versus precision grip and rotation versus squeeze movements in our ROIs. We performed MVPA within the view and pantomimed tasks (within-task decoding) and then we implemented MVPA across the two tasks (cross-task decoding). To prepare inputs for the classifier for MVPA, a GLM was used to estimate ß-weights in each trial independently for each participant and ROI separately. Design matrices contained 16 predictors (2 for each tool identity). Moreover, we included six parameters (x, y, z translation and rotation) resulting from 3D motion correction as predictors of no interest. To perform MVPA, we used the NeuroElf v 0.9 toolbox in combination with custom software written in Matlab R2016b (MathWorks, Natick, MA, U.S.A) and a Support Vector Machine (SVM) binary classifier (libSVM toolbox, Chang & Lin, 2011). The SVM model used a linear kernel function and default parameters (a fixed regularization parameter C = 1) to compute a hyperplane that best separated the trial responses (e.g., Gallivan et al., 2013; Haynes et al., 2007; LaConte et al., 2003; Mitchell et al., 2003; Mourão-Miranda, Bokde, Born, Hampel, & Stetter, 2005; Pessoa & Padmala, 2007; Smith & Muckli, 2010). To assess the performance of the classifier we used a leave one-run out cross-validation procedure (Smith & Goodale, 2015). This involved training the SMV classifier on data from all the run – 1 in each participant and testing on the run that was previously excluded from training the classifier. MVPA was performed in each participant individually.

3.2.10.1 Within-task decoding

For each participant and for each ROI, separate SVM classifiers were estimated for MVPA (e.g., for each pair-wise comparison power versus precision, squeeze versus rotation and each tool identity, see figure 3.2). We implemented a "leave-one-run-out" N-fold cross-validation to test the accuracy of the SVM classifiers (i.e., one run was reserved for testing the classifier [2 tool identities trials, 8 grip trials, 8 movement trials] and the remaining runs were used to train the classifier). We statistically assessed decoding accuracy at a group level by performing a series of one-tailed t-tests against 12.5% chance decoding for tool identity, 50% chance decoding for grip type and movement type (e.g., Smith & Goodale, 2015; Wurm & Lingnau, 2015). To control for the problem of multiple comparisons, we used a false discovery rate (FDR) correction of $q \leq 0.05$ on all t-tests performed for each task (Benjamini & Yekutieli, 2001).

3.2.10.2 Cross-task decoding

Moreover, to test whether there was a similarity of pattern information between view and pantomime task in our ROIs, we implemented a cross-task decoding approach between the two tasks. For example, to decode functional manipulation knowledge, we trained a pattern classifier to discriminate squeeze versus rotation in one task (e.g., view) and then we tested whether the same classifier could predict the same movement type in the other task (e.g., pantomime). To continue the example, to decode manipulation knowledge, the classifier was trained to discriminate precision versus power in the pantomimed task and then we tested the classifier in the view task. In this procedure we used a leave-one-run-out procedure for training and testing the classifier (Smith & Muckli, 2010). We then computed cross-decoding accuracies by averaging together the accuracy generated by training the classifier on the view task and testing it on the pantomime task and by training the classified on the pantomime task and testing it on the view task for each participant. We repeated the same procedure for tool identity. To statistically asses decoding significance, we used a series of one-tailed t-test versus 50% chance decoding for grip and movement type and versus 12.5% chance decoding for tool identity (Smith & Goodale, 2015; Wurm & Lingnau, 2015) and we applied FDR correction of $q \leq 0.05$ on all t-tests performed (Benjamini & Yekutieli, 2001).

3.2.11 *Decoding effects of task and/or action*

To test the differences between decoding accuracies between task and action property, we entered each ROI into a 2 x 2 repeated measure analyses of variance (RM-ANOVA), with factors task (view, pantomime) and action property (manipulation, function knowledge). All comparisons in the RM-ANOVAs were analysed using the Greenhouse-Geisser correction when sphericity was not assumed and considered significant at α-level of 0.05 (two-tailed). *Post hoc* pairwise contrasts used the Bonferroni correction to control for multiple comparisons.

3.3 Results

3.3.1 *Voxelwise whole-brain analysis*

3.3.1.1 Structural manipulation knowledge

In the view task, in the univariate analysis contrast Power > Precision, we found significant activation in bilateral anterior cingulate cortex (aCingC), right precuneus and right early visual cortex (EVC) (figure 3.8). In the pantomime task, in the univariate analysis contrast Power > Precision, we found significant activation in left MC, left Intraparietal Sulcus (IPS), left FG, left SMA and bilaterally in the superior parietal occipital cortex (SPOC) (figure 3.9).

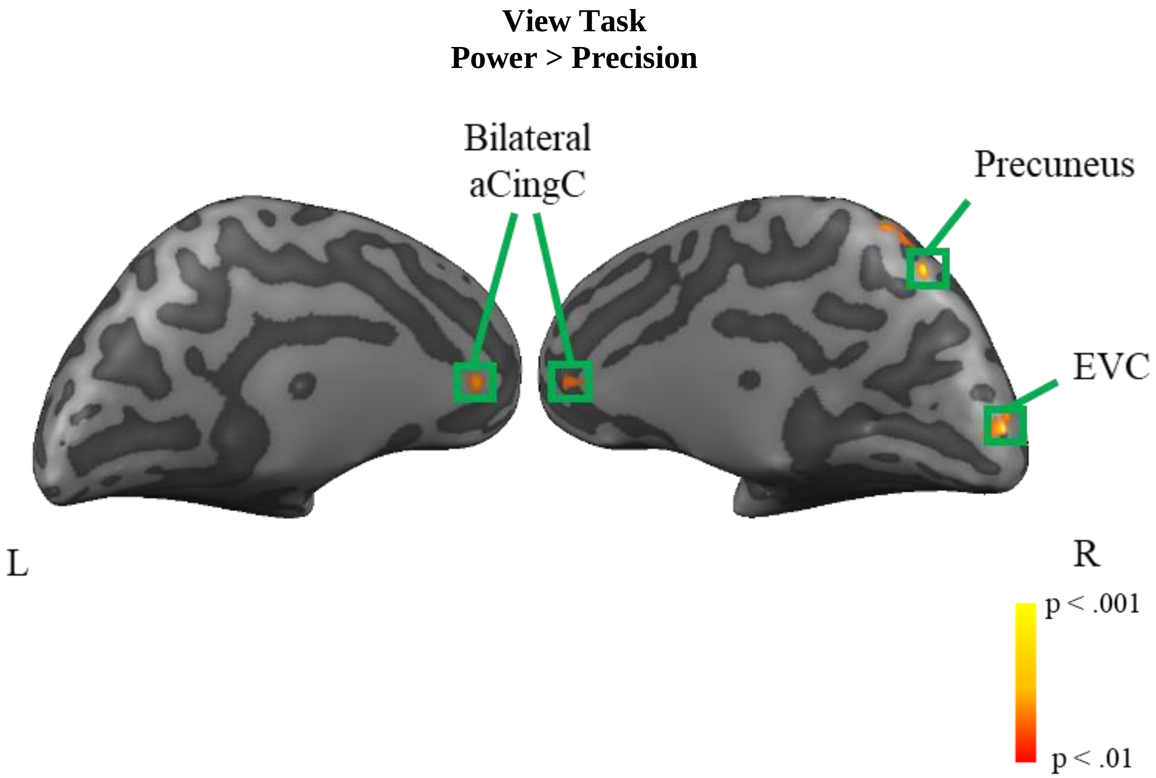
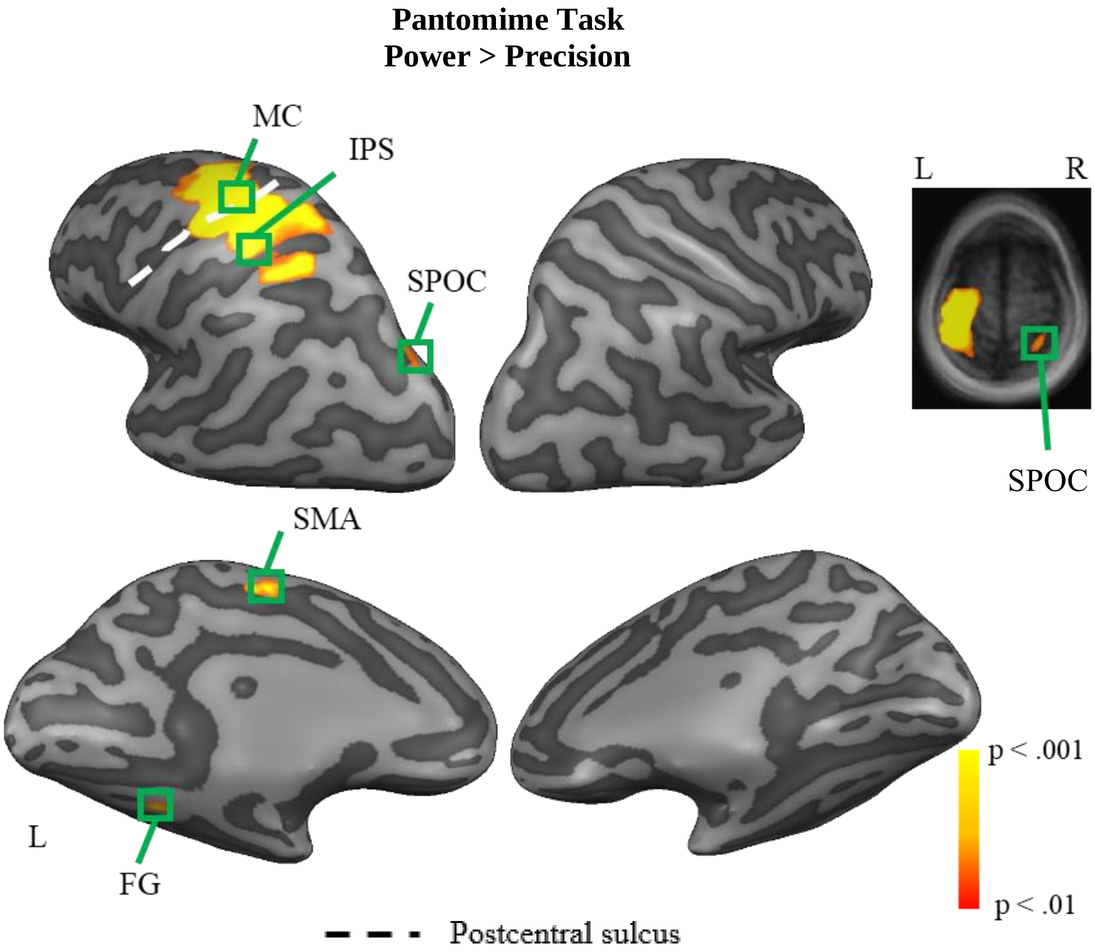


Figure 3.8 Brain areas activated using the contrast Power > Precision in the view task. The general locations of the selected ROIs are outlined in squares. aCingC = anterior cingulate cortex; EVC = early visual cortex; L = Left hemisphere; R = Right hemisphere. Regions are shown on a Colin 27 Talairach inflated brain (http://neuroelf.net).



Pantomime Task
Power > Precision

Figure 3.9 Brain areas activated using the contrast Power > Precision the pantomime task. The general locations of the selected ROIs are outlined in squares. Sulcal landmarks are denoted by white lines (stylised according to the corresponding legend). MC = Motor Cortex; IPS = Intraparietal Sulcus; FG = Fusiform Gyrus; SMA = Supplementary Motor Area; LH = Left hemisphere; R = Right Hemisphere. Regions are shown on a Colin 27 Talairach inflated brain (http://neuroelf.net).

3.3.1.2 Functional manipulation knowledge

In the view task, for the contrast Rotation > squeeze, we found significant activation in left inferior frontal gyrus (IFG), motor cortex (MC), supramarginal gyrus (SMG), fusiform gyrus and supplementary motor area (SMG). We also found significant activation bilaterally in the visual cortex and in right pre-SMA and lingual gyrus (figure 3.10). While in the pantomime task, we found significant activation bilaterally in MC, IPS, SMG, FG, pre-SMA, SMA and subcortically in the putamen. We also found significant activation in the right EVC and in the left thalamus (figure 3.11).

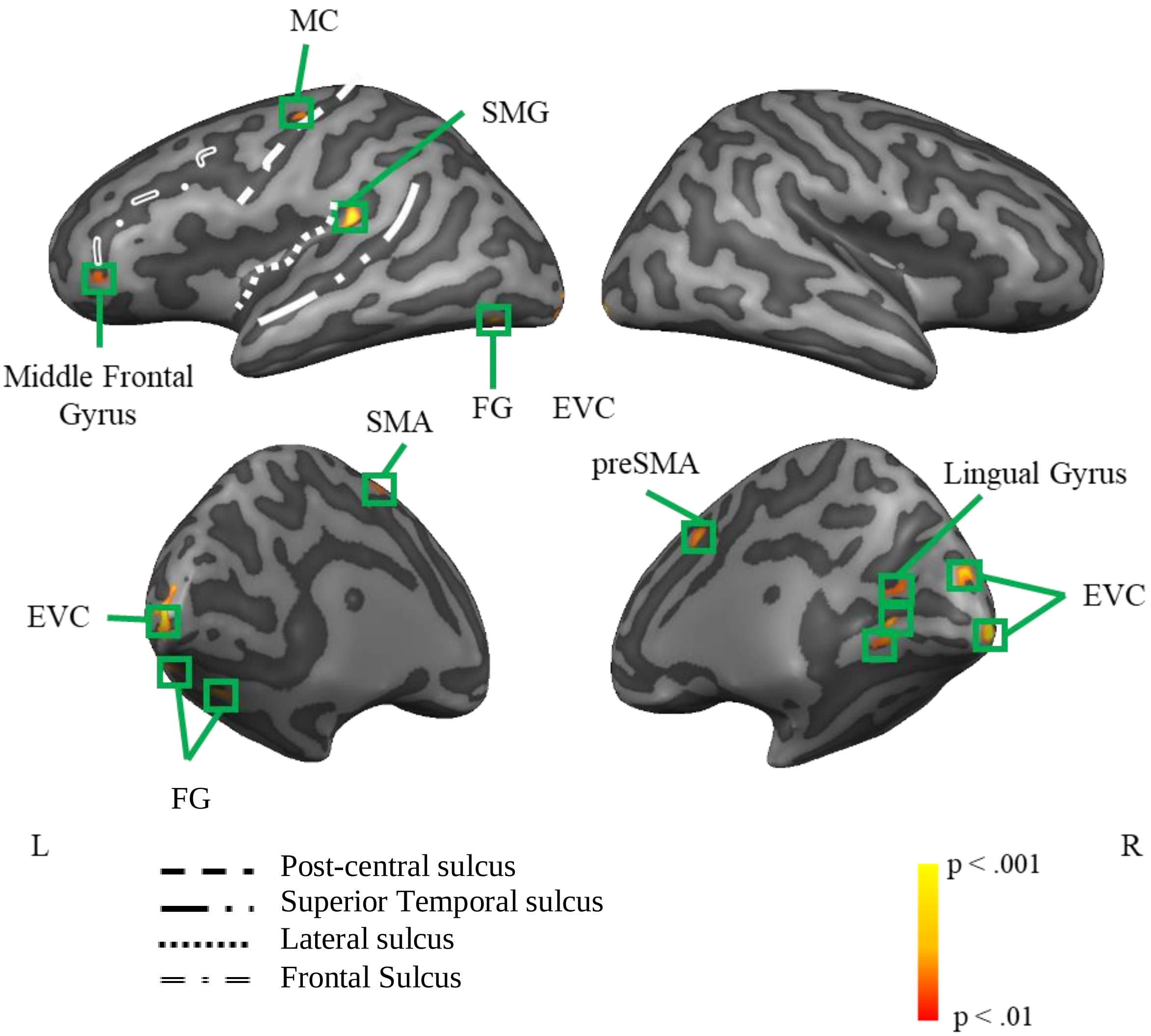
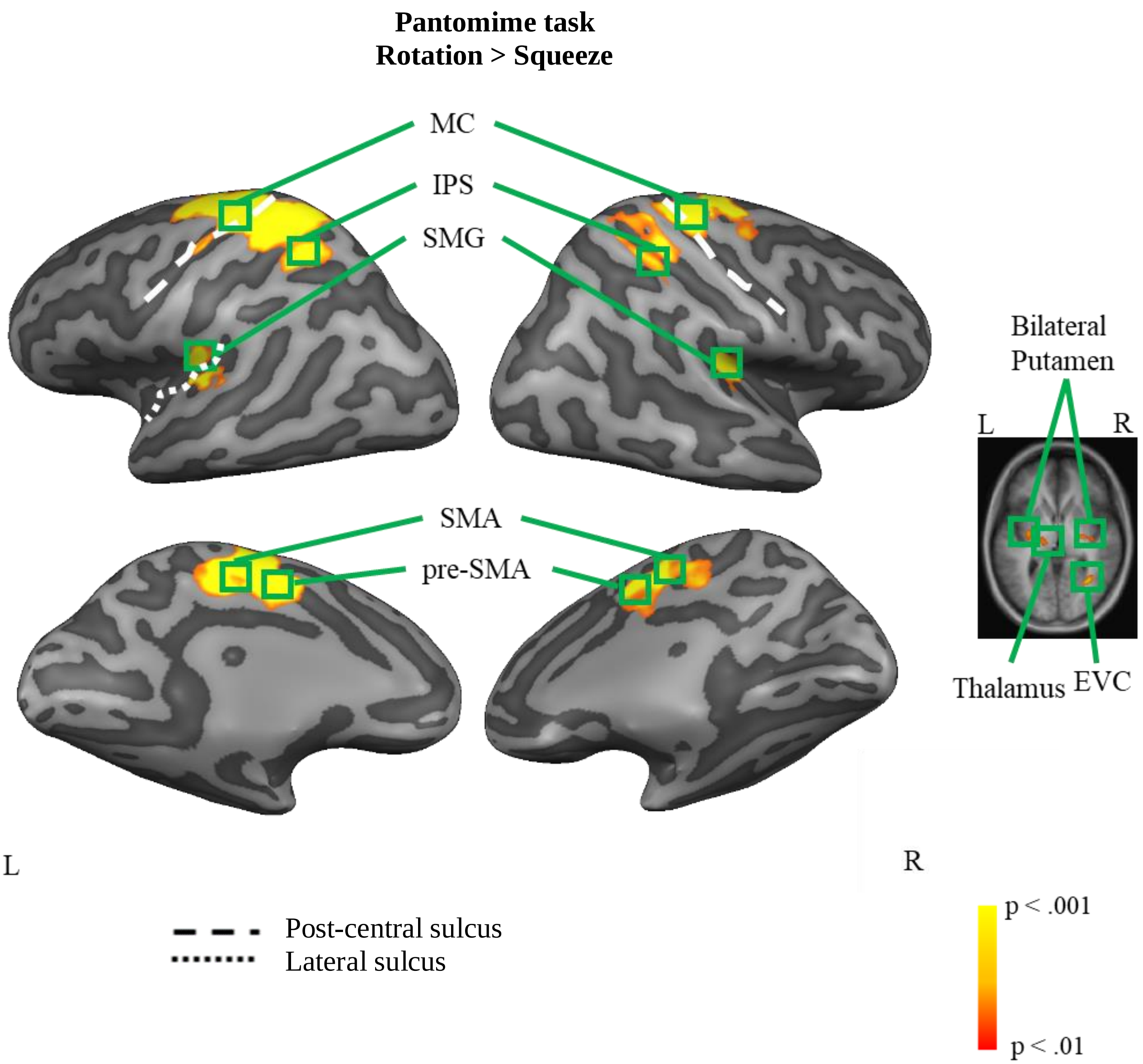

View task
Rotation > Squeeze

Figure 3.10 Brain areas activated using the contrast Rotation > Squeeze in the view task. The general locations of the selected ROIs are outlined in squares. Sulcal landmarks are denoted by white lines (stylised according to the corresponding legend). MC = Motor Cortex; SMG = Supramarginal Gyrus; FG = Fusiform Gyrus; SMA = Supplementary Motor Area; preSMA = pre-Supplementary Motor Area; EVC = Early Visual Cortex; LH = Left hemisphere; R = Right Hemisphere. Regions are shown on a Colin 27 Talairach inflated brain (http://neuroelf.net).



Pantomime task
Rotation > Squeeze

Figure 3.11 Brain areas activated using the contrast Rotation > Squeeze in the pantomime task. The general locations of the selected ROIs are outlined in squares. Sulcal landmarks are denoted by white lines (stylised according to the corresponding legend). MC = Motor Cortex; IPS = Intraparietal Sulcus; SMG = Supramarginal Gyrus; FG = Fusiform Gyrus; SMA = Supplementary Motor Area; preSMA = pre-Supplementary Motor Area; VC = Visual Cortex; LH = Left hemisphere; R = Right Hemisphere. Regions are shown on a Colin 27 Talairach inflated brain (http://neuroelf.net).

3.3.2 MVPA within-task decoding

3.3.2.1 Tool Identity

In the view task, tool identity was classified above chance in LOTC object, LOTC tools, LOTC hands, pMTG, SMG and IPS hands (figure 3.12). In the pantomiming task, tool identity was classified above chance in LOTC tools, LOTC hands, pMTG, SMG, IPS Tools, IPS hands, MC, SSC, SMA, PMd and PMv. Areas in the occipitotemporal network, such as LOTC objects and LOTC tools, showed higher decoding accuracy for view versus pantomime. In contrast, areas in the frontoparietal networks, such as SMG, IPS tools, IPS hands, MC, SSC, PMd, PMv and SMA, showed higher decoding accuracy for pantomime versus view (figure 3.12 and tables 3.2 and 3.5).

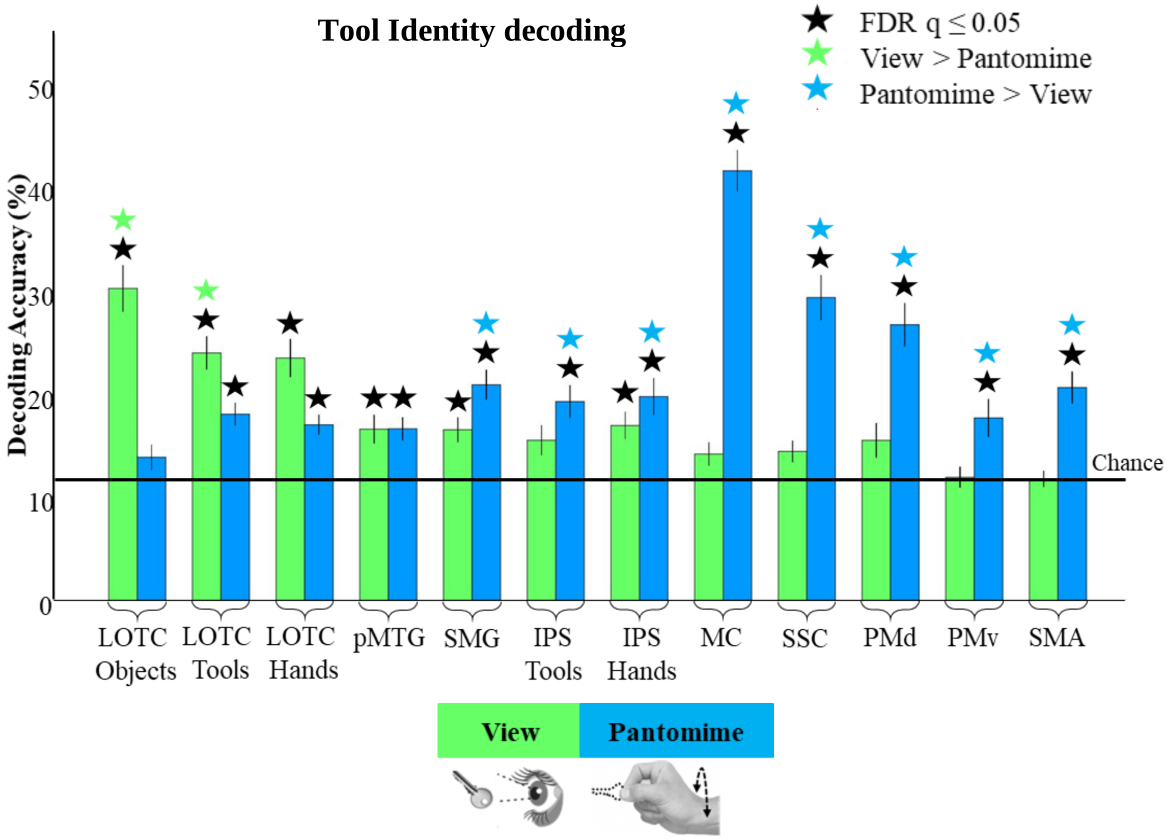


Figure 3.12 ROI MVPA results for tool identity decoding. Mean classification accuracies for decoding within the view (green) and pantomime (blue). Error bars indicate SEM. Black stars assess statistical significance across participants with respect to the chance level (FDR corrected for the number of tests). Green stars indicate significantly higher accuracy for the view task. Blue stars indicate significantly higher accuracy for the pantomime task. Solid black horizontal line represents the chance accuracy level (12.5%).

Table 3.2 ROIs and significance levels against chance for the within-task MVPA results for tool identity. T values, p-values, Cohen's d and percentage of mean accuracies are provided. * denotes p-values that are significant after FDR correction. Chance level = 12.5%

Tool identity (versus 12.5% chance level)

	View task				Pantomime task			
Region	t	*p* value (1-tailed)	Cohen's d	Accuracy	t	*p* value (1-tailed)	Cohen's d	Accuracy
LOTC Object	7.833	< .001 *	1.846	30.00%	1.074	= .149	0.253	13.80%
LOTC Tools	7.077	< .001 *	1.716	23.80%	5.056	< .001 *	1.226	17.90%
LOTC Hands	5.910	< .001 *	1.392	23.30%	4.527	< .001 *	1.066	16.90%
pMTG	2.894	= .005 *	0.682	16.50%	3.656	< .001 *	0.862	16.50%
SMG	3.312	= .002 *	0.803	16.40%	5.739	< .001 *	1.391	20.80%
IPS Tools	2.037	= .028 *	0.480	15.40%	4.237	< .001 *	0.998	19.20%
IPS Hands	3.350	= .001 *	0.789	16.80%	4.050	< .001 *	0.954	19.60%
MC	1.442	= .083	0.339	14.10%	14.675	< .001 *	3.459	41.40%
SSC	1.779	= .046	0.419	14.30%	7.691	< .001 *	1.812	29.20%
PMd	1.755	= .049	0.425	15.40%	6.734	< .001 *	1.633	26.50%
PMv	-.614	= .273	-0.149	11.90%	2.778	= .006 *	0.673	17.60%
SMA	-1.002	= .165	-0.236	11.70%	5.194	< .001 *	1.224	20.50%

3.3.2.2 Structural manipulation knowledge (power versus precision)

In the view task, images of objects associated with different grip types were classified above chance in LOTC objects, LOTC tools and LOTC hands (figure 3.13). In the pantomime task, objects with different grip types were decoded above chance in LOTC tools, LOTC hands, pMTG, SMG, IPS tools, IPS hands, MC, SSC, PMd, PMv and SMA. Area LOTC objects, in the occipitotemporal network, showed higher decoding accuracy for view versus pantomime. In contrast, areas in the frontoparietal networks, such as SMG, IPS tools, MC, SSC, PMd, PMv and SMA, showed higher decoding accuracy for pantomime versus view (figure 3.13 and tables 3.3 and 3.5).

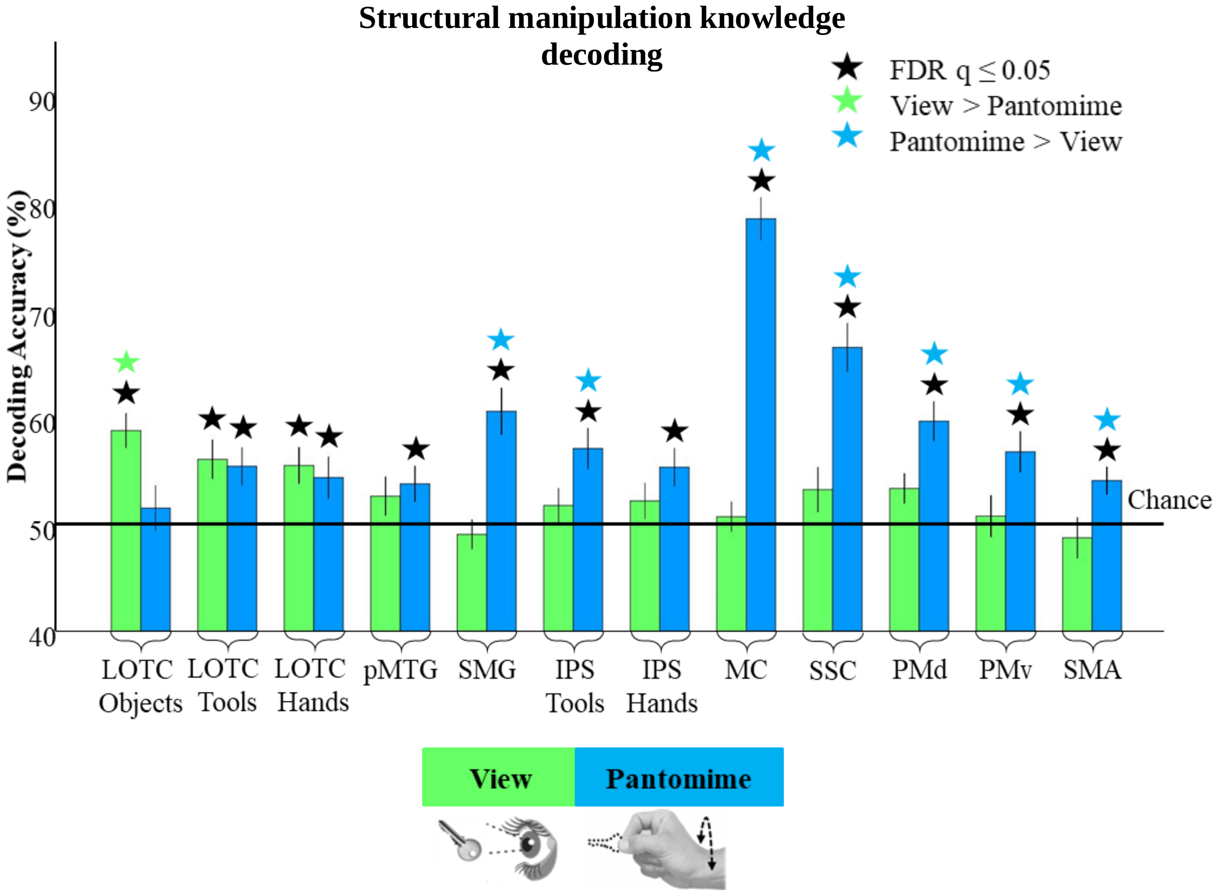


Figure 3.13 ROI MVPA results for structural manipulation knowledge. Mean classification accuracies for decoding within the view (green) and pantomime (blue). Error bars indicate SEM. Black stars assess statistical significance across participants with respect to the chance level (FDR corrected for the number of tests). Green stars indicate significantly higher accuracy for the view task. Blue stars indicate significantly higher accuracy for the pantomime task. Solid black horizontal line represents the chance accuracy level (50%).

Table 3.3 ROIs and significance levels against chance for the within-task MVPA results for structural manipulation knowledge. t values, p-values and Cohen's d and percentage of mean accuracies are provided. * denotes p-values that are significant after FDR correction. Chance level = 50%

Structural manipulation knowledge (versus 50% chance level)

	View task				Pantomime task			
Region	t	*p* value (1-tailed)	Cohen's d	Accuracy	t	*p* value (1-tailed)	Cohen's d	Accuracy
LOTC Object	5.406	< .001 *	1.274	58.70%	-.391	= .350	-0.092	51.40%
LOTC Tools	3.289	= .002 *	0.797	56.00%	3.034	= .003 *	0.735	55.30%
LOTC Hands	3.166	= .003 *	0.746	55.40%	2.190	= .021 *	0.516	54.30%
pMTG	1.415	= .087	0.333	52.50%	2.216	=.020 *	0.522	53.70%
SMG	-.720	= .241	-0.174	49.00%	4.775	< .001 *	1.158	60.40%
IPS Tools	1.069	= .150 *	0.558	51.70%	3.699	< .001 *	0.871	57.00%
IPS Hands	1.271	= .110	0.299	52.10%	2.973	= .004 *	0.800	55.20%
MC	.472	= .321	0.111	50.60%	14.284	< .001 *	3.366	78.30%
SSC	1.516	= .073	0.357	53.10%	7.238	< .001 *	1.706	66.40%
PMd	2.330	= .016 *	0.565	53.20%	5.178	< .001 *	1.255	59.50%
PMv	.368	= .359	0.089	50.70%	3.491	= .001 *	0.846	56.70%
SMA	-.685	= .251	-0.161	48.70%	3.097	= .003 *	0.729	54.00%

3.3.2.3 Functional manipulation knowledge (rotation versus squeeze)

In the view task, functional manipulation knowledge was classified above chance in LOTC object, LOTC tools, LOTC hands, pMTG, SMG, MC IPS tools, IPS hands, MC and SSC (figure 3.13). In the pantomiming task, movement was classified above chance in LOTC object, LOTC tools, LOTC hands, pMTG, SMG, IPS tools, IPS hands, MC, SSC, PMd, PMv and SMA. Areas in the occipitotemporal network, such as LOTC objects and LOTC tools, showed higher decoding accuracy for view vs pantomime. In contrast, areas in the frontoparietal networks, such as SMG, IPS tools, IPS hands, MC, SSC, PMd, PMv and SMA, showed higher decoding accuracy for pantomime than view. Moreover, all region in the occipitotemporal network showed higher decoding accuracy for function versus structural manipulation knowledge in both tasks. Areas in the frontoparietal network such as IPS tools, IPS hands and MC showed higher decoding accuracy for movement vs grip in both tasks, whereas PMd and SMA showed higher decoding accuracy for movement vs grip in pantomime task only (figure 3.13 and tables 3.4, 3.5 and 3.6). *Post hoc* paired sample t-test were conducted for each interaction observed between task and property. In PMd, the main effect of task and the main effect of property were further explained by an interaction ($F_{(1-16)} = 36.306$, $p < .001$, $\eta_p^2 = .688$) which revealed higher decoding for functional (mean = 74%) compared to structural manipulation knowledge (mean = 59%) within the pantomime task. In SMA, the main effect of task and the main effect of property were further explained by an interaction ($F_{(1-17)} = 32.403$, $p < .001$, $\eta_p^2 = .656$) which revealed higher decoding for functional (mean = 70%) compared to structural manipulation knowledge (mean = 54%) within the pantomime task. In IPS hands, the main effect of task and the main effect of property were further explained by an interaction ($F_{(1-17)} = 6.573$, $p < .020$, $\eta_p^2 = .279$) which revealed higher decoding for functional manipulation knowledge within the pantomime (mean = 67%) versus the view task (mean = 55%).

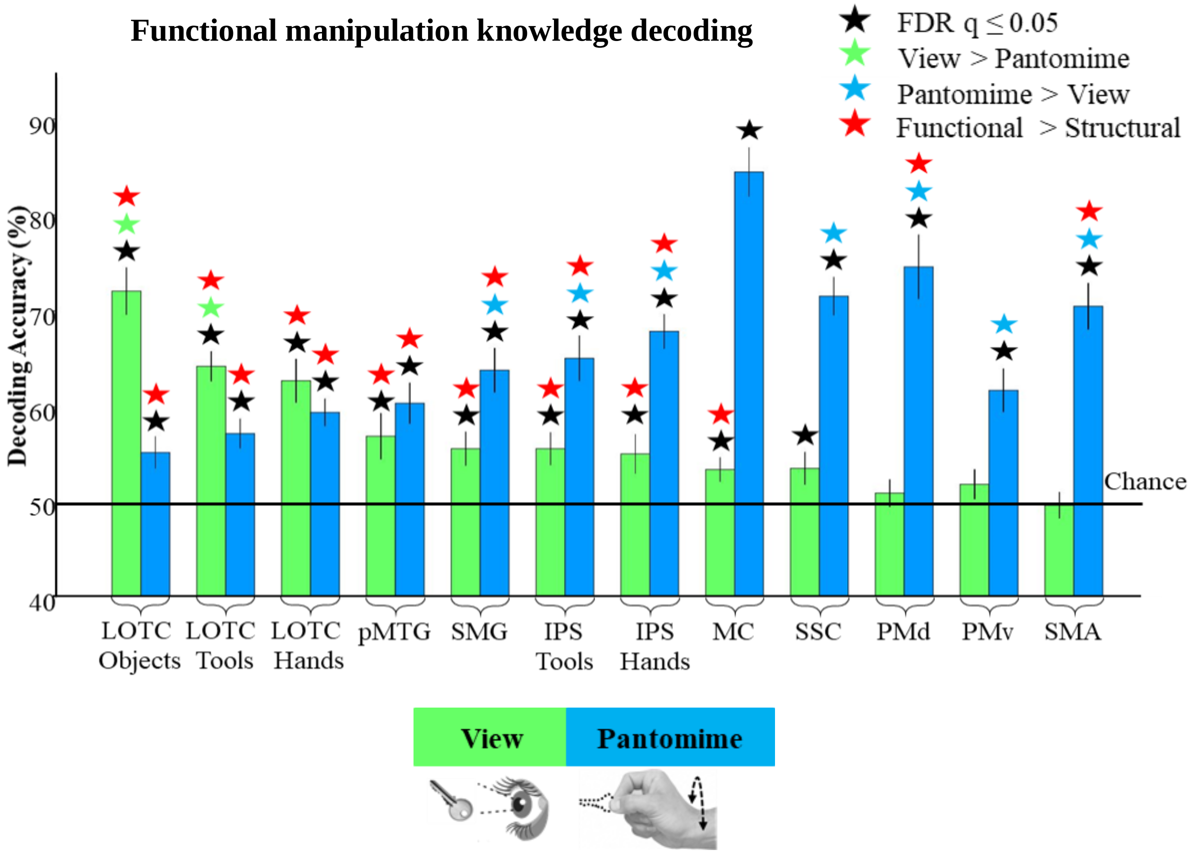


Figure 3.14 ROI MVPA results for functional manipulation knowledge decoding. Mean classification accuracies for decoding within the view (green) and pantomime (blue) task. Error bars indicate SEM. Black stars assess statistical significance across participants with respect to the chance level (FDR corrected for the number of tests). Green stars indicate significantly higher accuracy for the view task. Blue stars indicate significantly higher accuracy for the pantomime task. Red stars indicate significantly higher accuracy for functional manipulation knowledge. Solid black horizontal line represents the chance accuracy level (50%).

Table 3.4 ROIs and significance levels against chance for the within-task MVPA results for structural manipulation knowledge. t values, p-values, Cohen’s d and percentage of mean accuracies are provided. * denotes p-values that are significant after FDR correction. Chance level = 50%

Functional manipulation knowledge (versus 50% chance)

	View task				Pantomime task			
Region	t	*p* value (1-tailed)	Cohen's d	Accuracy	t	*p* value (1-tailed)	Cohen's d	Accuracy
LOTC Object	8.933	< .001 *	2.105	72.10%	3.161	= .002 *	0.745	55.30%
LOTC Tools	9.090	< .001 *	2.204	64.20%	4.732	< .001 *	1.147	57.20%
LOTC Hands	5.571	< .001 *	1.131	62.70%	6.639	< .001 *	1.564	59.40%
pMTG	2.883	= .005 *	0.679	56.90%	4.856	< .001 *	1.144	60.40%
SMG	3.205	= .002 *	0.777	55.70%	5.970	< .001 *	1.557	64.80%
IPS Tools	3.297	= .002 *	0.777	55.60%	6.355	< .001 *	1.497	65.10%
IPS Hands	2.502	= .011 *	0.589	55.10%	9.914	< .001 *	2.336	67.90%
MC	2.760	= .007 *	0.650	53.50%	13.455	< .001 *	3.171	84.40%
SSC	2.120	= .024 *	0.449	53.60%	10.821	< .001 *	2.550	71.50%
PMd	.714	= .242	0.173	51.00%	7.344	< .001 *	1.781	74.60%
PMv	1.246	= .115	0.302	51.90%	5.160	< .001 *	1.251	61.70%
SMA	-.165	= .435	-0.038	49.80%	8.445	< .001 *	1.990	70.50%

3.3.3 *Decoding effects of task and/or action*

A summary of main effects and interactions form the 2x2 ANOVA are reported in tables 3.5 and 3.6. Effects are reported separately for tool identification (figure 3.11), power versus precision grip (figure 3.12) and rotation versus squeeze movement (figure 3.13). *Post-hoc* paired sample t-test were conducted for each interaction observed and are reported within MVPA within-task decoding section below.

Table 3.5 Summary of main effects from the 2 tasks x 2 properties ANOVA on decoding accuracies. F values, degrees of freedom (df), p-values, Eta squared values and mean differences (MD; expressed as percentage) are reported. v – p = mean difference between view and pantomime task accuracies; f – s = mean difference between functional and structural manipulation knowledge accuracies.

	Task						Property					
	F	df	p		Eta squared	MD (v - p)	F	df	p		Eta squared	MD (f - s)
LOTC Objects	38.77	1-17	< .001	*	.695	13%	14.1	1-17	.002	*	.453	10%
LOTC Tools	9.103	1-16	.008	*	.363	38%	9.927	1-16	.006	*	.383	5%
LOTC Hands	1.142	1-17	.300		.063	22%	10.83	1-17	.004	*	.389	6%
pMTG	0.998	1-17	.332		.055	-2%	8.219	1-17	.011	*	.326	5%
SMG	43.16	1-16	< .001	*	.730	-9%	10.5	1-16	.005	*	.369	5%
IPS Tools	23.21	1-17	< .001	*	.577	-7%	7.4	1-17	.017	*	.293	6%
IPS Hands	11.44	1-17	.004	*	.402	-8%	45.57	1-17	<.001	*	.728	7%
MC	309.6	1-17	< .001	*	.948	-29%	3.744	1-17	.070		.180	4%
SSC	41.52	1-17	< .001	*	.710	-15%	1.890	1-17	.187		.100	2%
PMd	35.31	1-16	< .001	*	.688	-14%	8.893	1-16	.009	*	.357	6%
PMv	28.85	1-16	< .001	*	.643	-7%	1.58	1-16	.181		.109	3%
SMA	57.22	1-17	< .001	*	.771	-13%	23.18	1-17	< .001	*	.577	8%

Table 3.6 Summary of interactions from the 2x2 ANOVA on decoding accuracies. F values, degrees of freedom (df), p-values and Eta squared values are reported.

	Task x Property				
	F	df	p		Eta squared
LOTC Objects	2.344	1-17	.144		.121
LOTC Tools	3.045	1-16	.100		.160
LOTC Hands	0.714	1-17	.140		.040
pMTG	0.415	1-17	.528		.024
SMG	0.729	1-16	.406		.044
IPS Tools	0.977	1-17	.337		.054
IPS Hands	6.573	1-17	.020	*	.279
MC	1.231	1-17	.283		.068
SSC	0.186	1-17	.190		.099
PMd	36.72	1-16	< .001	*	.697
PMv	1.12	1-16	.306		.065
SMA	32.4	1-17	< .001	*	.656

3.3.4 *Task cross-classification decoding*

Cross-classification MVPA analysis was used to test whether there was similarity in pattern information between view and pantomime tasks, but this was not significant in any ROI for functional manipulation knowledge (figure 3.16) and tool identity (figure 3.15). For structural manipulation knowledge, we found that decoding was significantly above chance in PMd ($t_{(16)} = 2.627$, $p = .009$, one-tailed), however, it did not survive FDR correction (figure 3.17).

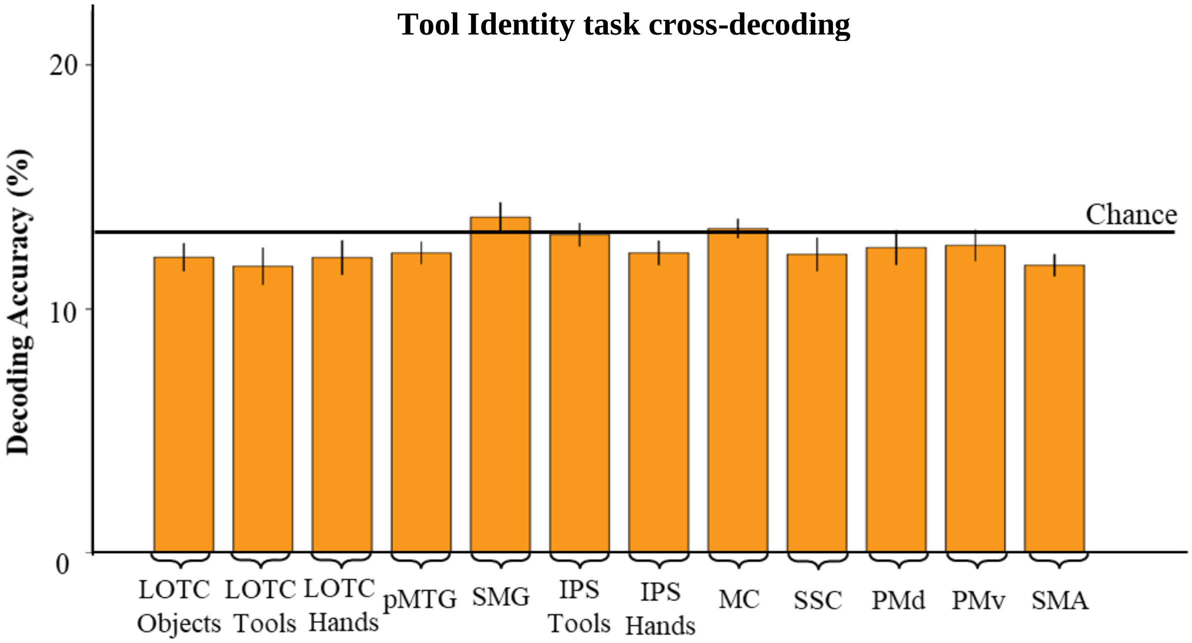


Figure 3.15 Task cross-classification decoding accuracy for tool identity. Error bars represent SEM. Solid horizontal black line represents the chance accuracy level (12.5%).

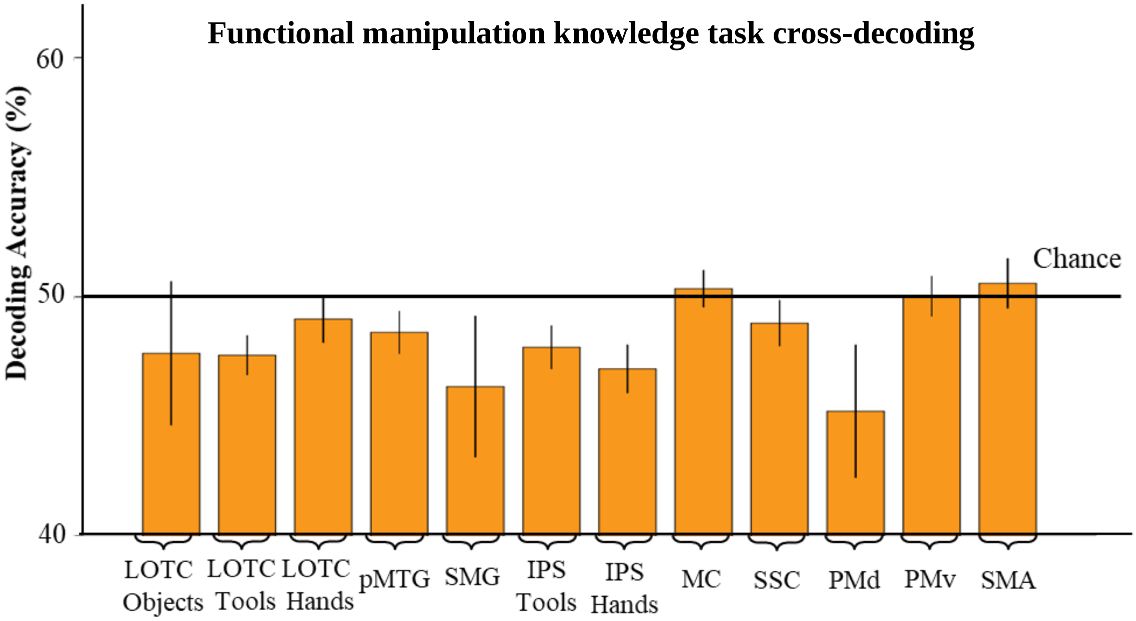


Figure 3.16 Task cross-classification decoding accuracy for functional manipulation knowledge. Error bars represent SEM. Solid horizontal black line represents the chance accuracy level (50%).

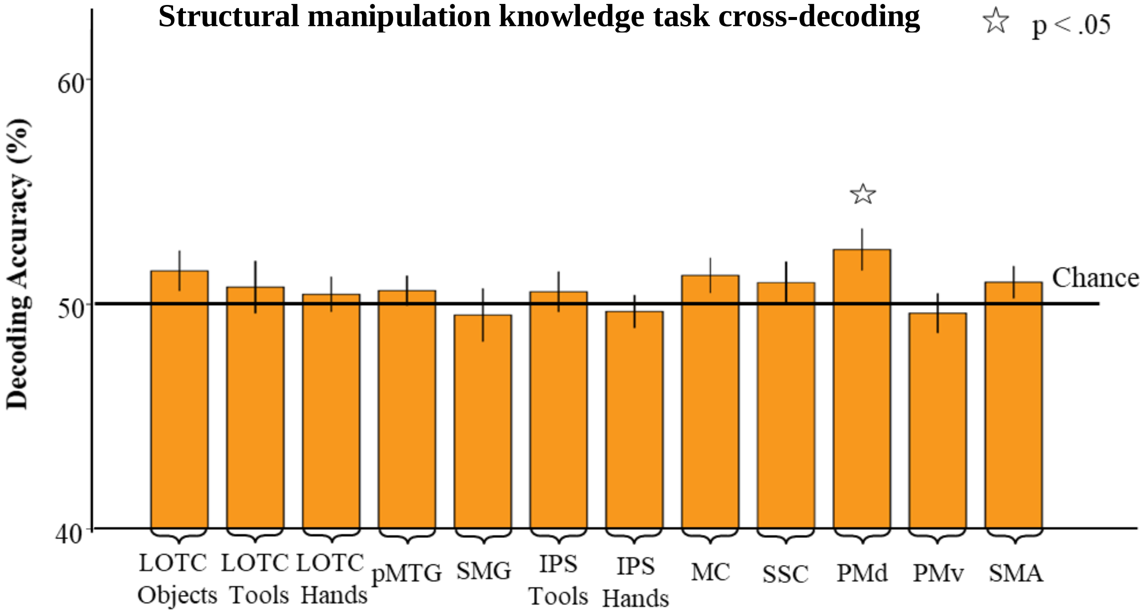


Figure 3.17 Task cross-classification decoding accuracy for structural manipulation knowledge. Error bars represent SEM. Solid horizontal black line represents the chance accuracy level (50%). White star represents accuracy above chance, not FDR corrected.

3.4 Discussion

In the current study, to explore whether different tool identities are coded in regions within the tool network for different tasks we employed a viewing task and a pantomime task, and we used multivariate pattern analysis over fMRI data. Moreover, by using tool identities grouped according to structural and function manipulation knowledge (e.g., how to position hand to grasp versus how to move for use), we could test whether tools that afford similar actions produce similar activity patterns during viewing versus pantomime tasks. Additionally, by using two different tasks, we explored whether different tool identities and structural and functional manipulation knowledge are accessed independent of task and the format in which the stimulus is presented. As we were able to decode action properties (e.g., functional and manipulation knowledge) within tasks and across objects, this could be taken as evidence that action properties are accessed independently of task or representation context (e.g., picture or words). The principal findings are that: 1) different regions within the dorsal and the ventral streams represent both tool identity, structural and functional manipulation knowledge; 2) patterns of activity in the tool network are modulated by task and type of manipulation knowledge the tool affords.

Univariate analysis revealed a network of left lateralised parietofrontal regions that were preferentially activated by power versus precision grip in the pantomime task, while in the view task we observed activations bilaterally in the anterior cingulate cortex, right precuneus and right early visual areas. On the other hand, for rotation versus squeeze, we observed activations bilaterally in frontoparietal regions (including MC, IPS, SMG and SMA) in the pantomime task, while in the view task we observed left lateralised activation in parietofrontal regions, including MC, SMG and SMA and in the FG in the occipitotemporal cortex. Moreover, we observed bilateral activations in EVC. While in the univariate analysis we found regions that overlapped with our ROIs analysis, showing that univariate analysis is likely to be consistent with MVPA, however, MVPA was more sensitive to the representations of the information processed. For instance, while univariate analysis showed that IPS, MC and SMG exhibited activation for power versus precision and for rotation versus squeeze in the pantomime task, MVPA reflects the representation of specific structural and functional manipulation knowledge in these regions.

3.4.1 Decoding in the occipitotemporal network

Interestingly, we could decode not only tool identity, but also structural and functional manipulation knowledge in both tasks in several areas in the occipitotemporal network, more closely associated with the ventral stream. Specifically, regions in the ventral stream presented stronger decoding for tool identities not only in the view condition, but also in the pantomime condition, in which no visual stimuli were presented. These findings could be viewed as evidence for sensitivity within the ventral stream of semantic and/or conceptual knowledge and in particular to the knowledge of tool-specific actions. Moreover, hand and tool-selective LOTC in the ventral stream coded tool identity as well as functional and structural manipulation knowledge during both the view and pantomime tasks.

Our results demonstrate that object- , tool- and hand-selective LOTC represent tool identity but also structural (i.e., power versus precision grip) and functional (i.e., rotation and squeeze movements) manipulation knowledge associated with tools. Critically, tool identity, structural and functional manipulation knowledge could be decoded in both the view and the pantomime task in tool- and hand- selective LOTC, while only function manipulation knowledge could be decoded in object selective LOTC in both view and pantomime tasks. Although LOTC is not a motor region, we could decode manipulation properties that tool affords by simply viewing pictures of objects. Moreover, the fact that patterns of activity in regions within LOTC represent not only tool identity, but also structure and functional manipulation knowledge, even when no visual images are presented, is in line with evidence from congenitally blind individuals. Specifically, Peelen et al. (2013), found that left tool-selective LOTC shows a similar activity in congenitally blind and sighted participants when they hear words referring to tools compared to words related to animals and non-manipulable objects. Based on their results, the authors speculated that LOTC-tool stores action-related tool properties, such as the posture and the movement of the hand associated with a specific tool (Peelen et al., 2013).

Our results suggest that tool- and hand- selective LOTC contain neural codes that represent tool-related actions associated with both tool pantomimes and passive view, which is in line with Peelen et al.’s (2013) account that LOTC stores action-related tool properties.

Moreover, Oosterhof, Tipper, & Downing (2012) have shown that multivoxel patterns of activity in LOTC distinguish between meaningless hand actions (e.g., open versus close the hand) as well as object-directed actions, such as punch versus lift a cup-shaped object, while participants were either seeing short movies of a hand performing the actions or performing the action themselves. While performing actions, participants were also instructed to either use the fingers or the whole hand. In the meaningless hand action condition, the authors observed that both the left anterior parietal cortex and the LOTC bilaterally carried information that discriminates between meaningless actions in both the visual and motor domains. Thus, the authors speculated that the patterns of activity that code the action must be similar across the visual and motor tasks (Oosterhof et al., 2012). Similar patterns were also observed in the object-directed experiment for LOTC and anterior parietal cortex, additionally, they observed regions around the post-central gyrus that carry information about actions. The authors concluded that there is a common neural coding in these areas across visual and motor aspect of actions (Oosterhof et al., 2012). Our results, confirm and further expand these findings. In particular, we show that regions within the LOTC discriminate between structure and function manipulation knowledge in both the view and the pantomime task. Taken together, these findings may suggest that LOTC contains patterns of activity that code for hand actions during tool use.

Moreover, Valyear and Culham (2010) have shown that regions within the occipitotemporal cortex, including LO and pMTG, were more active when participants viewed videos of hands grasping tools in a functionally appropriate manner (typical grasping) versus videos of hands grasping tools in a way that would not easily allow the actor to use the tool without further postural adjustment (atypical grasping). In their experiment, areas localized in the posterior occipital and lateral temporo-occipital cortices, including both ventral stream areas such as LO and MT+ and the tool-selective pMTG, showed a preferential response for typical grasping actions versus atypical grasping actions. The authors suggested that areas in the ventral stream, as well as tool-selective pMTG, might play a critical role in coupling stored perceptual and semantic knowledge about tools. These results seem in line with our finding. Here, we observed that in both the view and the pantomime task, manipulation and function knowledge, as well as tool identity could be decoded in hand- and tool- selective LOTC. This suggests that during the perception of tool images and during overt pantomime actions without the object in hand, the ventral stream contains patterns of activity that represent information about semantic knowledge of tools and how they are used based on previous interactions, which is in line with Valyear and Culham's (2010) account.

It is also worth mentioning that we observed a close overlap between LOTC hand and LOTC tool, similarly to Bracci et al. (Bracci et al., 2011; Bracci & Peelen, 2013). Additionally, we observed similar decoding accuracies between LOTC-tool and LOTC-hand, which were distinct from the nearby LOTC-object regions. In fact, both regions decoded tool identities and action-related properties similarly in both tasks. These findings suggest that these regions might represents properties that are common to hands and tools, such as for example the size of the object, the hand posture, or semantic information related to the meaning of the actions (Bracci et al., 2011; Valyear & Culham, 2010).

We observed that during the view task, patterns of activity in LOTC-object contained information about tool identity, structural and functional manipulation knowledge. However, the same pattern was not observed in this region for pantomiming, as during this task only functional knowledge about tools could be decoded above chance. In contrast with LOTC- object, LOTC-tool contained patterns of activity that represented tool identity, function and structural manipulation knowledge regardless of task. These observations of the differences observed between LOTC-object and LOTC-tool, further confirm the account that LOTC has different subregions which play different role in action-related processes (Lingnau & Downing, 2015). A possible explanation for these differences between LOTC-object and LOTC tool could be related to the fact that objects are not perceived as being controlled by and used as an extension of the body, while tools are (Bracci & Peelen, 2013). The fact that LOTC-object contains patterns of activity that codes for function manipulation knowledge, but not for structural manipulation knowledge in the pantomime task suggests that this region does not contain information about the specific shape of the hand (e.g., grip). Instead, LOTC-object may contain information regarding conceptual knowledge about the movement sequences involved in using a tool (which is a property perhaps strongly linked with identity). This observation seems to be in line with Gallivan, Johnsrude, and Flanagan's (2016) observation that manipulatory sequences of actions, that occur after an object has been grasped to be held or placed, are represented in the occipitotemporal cortex. Gallivan et al. (2016) instructed participants to execute different object-directed action sequences that varied in the number of movement components (e.g., grasp to hold or grasp to place) and varied in their final spatial position (e.g., grasp to place on the left or grasp to place on the right) while they were in the scanner. The authors analysed the preparatory pattern of fMRI activity that form prior to movement onset and they could decode which of the 3 action sequences (e.g., place to the left, place to the right or grasp to hold) were to be performed within the occipitotemporal and frontoparietal regions. In particular they found that object-selective LOTC appeared to represent sequence-related information. The authors concluded that action sequences were not represented only in frontoparietal regions, but also within regions in the ventral visual stream.

Our results shed new light on the functional organisation of LOTC and in particular, how object-, tool- and hand -selective areas process tool identity, functional and structural manipulation knowledge about tools during view and pantomime. As we observed decoding within LOTC regions during both the view and the pantomime task, it is unlikely that the decoding is attributable to low-level visual features alone. Thus, our findings seem to be in line with the growing evidence that the organisation of these regions is independent from low-level visual features (Mahon, Anzellotti, Schwarzbach, Zampini, & Caramazza, 2009; Mahon & Caramazza, 2009; Peelen et al., 2013). However, more research is needed to investigate how these regions within the LOTC are functionally related to each other and how they represent actions. For example, future fMRI studies could implement an event-related design combined with MVPA to understand the involvement of regions within LOTC during the planning and the execution of real actions with 3D tools.

It is worth mentioning that our stimuli were not controlled for properties such as elongation, material nor the size and shape of the handle. For example, tools affording a power grip had more straighter handles, while tools affording precision grip did not. Additionally, while tools affording a squeeze functional movement were straighter, some tools affording rotation also had a rounded part (e.g., screw). Finally, while some tools were entirely made of metal, other were made of metal and/or plastic. Thus, in future studies it would be important to introduce control objects to control for these properties. This is important especially as Chen et al. (2018) recently demonstrated that images of elongated tools (versus stubby tools) preferentially activated the MTG and the SPL (for a description of task and results see section 1.10.4).

Another region in the occipitotemporal network, the pMTG is considered important for knowing about tool-specific actions (e.g., Martin, 2007; Martin, Wiggs, Ungerleider, & Haxby, 1996). Left pMTG is active during the generation of words associated with tool-specific actions (Kellenbach et al., 2003; Lewis, 2006; Martin, Haxby, Lalonde, Wiggs, & Ungerleider, 1995), when viewing and naming tools (Lewis, 2006; Martin, Wiggs, Ungerleider, & Haxby, 1996; Valyear et al., 2007), when pantomiming tool use (Fridman et al., 2006; Johnson-Frey et al., 2005; Lewis, 2006), during the retrieval of semantic information about tool function and manipulability (Boronat et al., 2005; Kellenbach et al., 2003) and is also responsive when sounds of familiar tools in action are presented (Beauchamp, Argall, Bodurka, Duyn, & Martin, 2004; Beauchamp, Lee, Argall, & Martin, 2004; Lewis, 2005; Lewis, 2006). Here, we show that patterns of activity in pMTG contains information about tool identity and function during both view and pantomime tasks, while structural manipulation knowledge could only be decoded during pantomimes. Gallivan et al. (2013), using MVPA have shown that pMTG discriminates upcoming object-directed actions (e.g. grasping versus reaching) when participants were performing the actions with a tool only (compared to the hand). The coding for functional and structural manipulation knowledge in the pantomime task provide an extension of these previous findings. Here, we demonstrate that area pMTG plays an important role in generating the appropriate goal-directed movements and is also involved in generating the appropriate grips when there is no visual feedback of the hand available. Thus, suggesting that the information might be retrieved from memory of previous experience with the tool.

It is also important to mention that the human pMTG is anatomically in a location to receive various types of visual, auditory and sensory-motor inputs (e.g., Beauchamp, Argall et al., 2004; Beauchamp, Lee et al., 2004, Martin, 2007) and is believed to mediate interactions between the dorsal and the ventral stream (van Polanen & Davare, 2015). Brandi et al. (2014), presenting real tools and bars while participants were in the scanner, observed that the middle temporal gyrus was more activated when tools were grasped to be used (compared to the bars). The authors suggested that tool use requires complex movements as well as conceptual knowledge of the tools and relies on interactions between the dorsal and the ventral stream (Brandi et al., 2014).

Moreover, Valyear and Culham (2010) suggested that areas in the ventral stream, as well as tool-selective pMTG, might play a critical role in coupling stored perceptual and semantic knowledge about tools. Here, we observed that tool identity and functional manipulation knowledge could be decoded in the view condition in pMTG, which seem in line with Valyear and Culham (2010) account that this region might be representing the knowledge associated with the tool's function.

Here, we showed that patterns of activity could be decoded in pMTG for both the view and the pantomime tasks for manipulation and function knowledge and tool identity, which might indicate that processing of tool motion in pMTG (Martin, 2007) includes both knowledge of how tools are used (e.g., squeeze vs rotation) as well as the movement required by specific body parts (e.g., hand and wrist). Additionally, as we observed higher decoding accuracies for function versus manipulation knowledge, this might suggest that pMTG is preferentially involved in processing functional movements, rather than the shape of the hand, which is more likely represented in the aIPS, as observed in chapter 2. Moreover, grip could be decoded in pMTG during pantomime but not during view. This might suggest that information about the appropriate hand shape selection may be processed within the ventral stream. This information is then passed to the dorso-dorsal stream via the ventro-dorsal stream, likely via the pMTG, only when actual tool-related actions are required. Further experiments should investigate the role played by the pMTG in selecting the appropriate hand movements during hand-tool interactions, for example by using online TMS during the planning and the performance of the movement. Our results expand the knowledge about the important role of pMTG in processing how tools and body effectors are likely to move and interact in the surrounding based on our previous experience of actually using them.

Overall, our findings in the occipitotemporal cortex seem in line with Gibson's (1979) theory of affordances. In particular, we have shown that the mere sight of pictures of tools automatically evokes tool-related representations associated with their use even when this is irrelevant to task performance (Gibson, 1979; Tucker & Ellis, 1998).

3.4.2 Decoding in the frontoparietal network

The regions in the parietal lobe that are usually activated during tool-use and by viewing pictures of tools are located in the vicinity of regions involved in coding the grip component of hand actions (Gallivan et al., 2013). The SMG, a region located near the grasp-selective anterior part of the IPS (Chao & Martin, 2000; Gallivan et al., 2013; Valyear et al., 2007; Culham, 2006) shows both tool- and grasp- selective responses (Gallivan et al., 2013). Although both pMTG and SMG are thought to be part of the ventro-dorsal stream (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010), SMG showed significantly higher decoding accuracies for pantomimes in decoding tool identity, functional and structural manipulation knowledge, while decoding accuracies in pMTG were similar across the two tasks. Here, we show that patterns of activity within the SMG contain representations of tool identity and functional manipulation knowledge in both view and pantomime, while in the pantomime task, the SMG additionally contains patterns of activity that represent structural manipulation knowledge. Damage to SMG is linked to an impairment in pantomiming or performing tool use actions known as apraxia (Haaland et al., 2000). The fact that SMG contains patterns of activity that represent tool identity, functional and structural manipulation knowledge during pantomime provide an important extension of previous neuropsychological observations.

Interestingly, but perhaps unsurprisingly, here we show that the motor cortex contains neural codes that represent tool identity, movement and grip of tool pantomimes.

This is in line with the evidence that the motor cortex is more engaged when individuals execute an action, compared to when they are observing it performed by someone else (Hari et al., 1998). Moreover, the fact that patterns of activity in M1 contain information regarding tool identity suggest that, although tools could require similar hand shapes or movements, the motor cortex processed tool identity for the purpose of sending appropriate motor commands to the muscles. As expected, viewing tools led to considerably lower decoding accuracy in the motor cortex compared to tool pantomimes. In the motor cortex, we observed that patterns of activity did not contain information regarding tool identity or structural manipulation knowledge (power versus precision grip) while participants were simply viewing pictures of tools. However, the patterns of activity contained information regarding functional manipulation knowledge (rotation versus squeeze movements). Although it might initially seem surprising to observe significant decoding of motor properties of objects in a motor region even when no overt movement is required, Gallivan et al. (2011), reported a similar patterns of results. They showed that hand movement could be decoded from the preparatory responses in the motor cortex, prior to action execution. These results raise the question of why is the motor cortex not decoding grip when viewing pictures of tools? We know from behavioural investigations that viewing pictures of tools automatically trigger motor affordances (Tucker & Ellis, 1998). The fact that we could decode rotation versus squeeze movements, but not power versus precision grip nor tool identity, might suggest that, viewing picture of tools elicit patterns of activity that are related to more general motor programs, such as the movement of the hand and the wrist. On the other hand, the grip type might require the involvement of more specialized areas such as the IPS. In line with this observation, evidence from TMS studies (including our own results in chapter 2, e.g., Cohen et al., 2009; Davare et al., 2007; Le et al., 2014; Rice et al., 2006; Tunik et al., 2007; Tunik et al., 2005) as well as fMRI (e.g., Cavina-Pratesi, Ietswaart, Humphreys, Lestou, & Milner, 2010; Culham et al., 2003; Gallivan et al., 2011; Gallivan et al., 2013) have shown that the left aIPS is involved in hand shaping during grasping.

Nevertheless, we cannot exclude that the decoding observed in the motor cortex during the view task is related to participants imagining the use of tools. In fact, Pilgramm et al. (2016), asked participants to imagine three different types of hand actions (e.g., an aiming movement, an extension-flexion movement and a squeezing movement) while in the scanner. They showed that the action type could be decoded significantly above chance level in the motor and premotor cortex, as well as in SPL, IPS and IPL. However, we do not believe imagery can explain our findings as we were not able to decode power versus precision grip nor tool identity, which also involve different actions. To further explore this, future studies could compare decoding of accuracies during motor imagining of tool use versus pantomimes and passive viewing, which so far has been explored univariately (e.g., Creem-Regehr & Lee, 2005; Imazu, Sugio, Tanaka, & Inui, 2007).

Similar to the decoding observed in the motor cortex, we observed higher decoding accuracy for tool pantomime versus viewing images of tools in the somatosensory cortex. Traditionally, the terms somatosensory cortex refers to the upper bank of the lateral sulcus the anterior parietal cortex (Keysers, Kaas, & Gazzola, 2010), which includes 4 different areas that are known to have different connections and functions: area 3a deals with proprioceptive information, area 3b with tactile information, area 1 with a second level of tactile analysis, area 3 combines information from the other areas (Keysers et al., 2010). Thus, the function of the somatosensory cortex are manifold including (but not limited to) providing proprioceptive information for action related process, as well as tactile input if hand-object interaction is involved (Dijkerman & de Haan, 2007). Many studies have demonstrated that visual stimuli that imply sound, touch or smell can activate the somatosensory cortex (Blakemore, Bristow, Bird, Frith, & Ward, 2005; Ebisch et al., 2008; Pihko, Nangini, Jousmki, & Hari, 2010; Schaefer, Xu, Flor, & Cohen, 2009) and that the somatosensory cortex is also modulated by vision of hands performing actions (Avikainen, Forss, & Hari, 2002; Cross, Hamilton, & Grafton, 2006; Julie Grèzes et al., 2003; Meyer et al., 2010; Molnar-Szakacs, Kaplan, Greenfield, & Iacoboni, 2006; Oouchida et al., 2004; Pierno et al., 2009). Activation in the somatosensory cortex has been observed in response to tool pantomimes (Johnson-Frey et al., 2005; Lewis, 2005). Additionally, it has been shown that passive viewing and perceptual discrimination of familiar graspable objects (e.g., a glass, a phone) with no explicit action knowledge associated with them also recruit the somatosensory cortex (Creem-Regehr & Lee, 2005;

Smith & Goodale, 2015). Surprisingly, in the somatosensory cortex we could not decode tool identity, which might seem at odds with Smith & Goodale's (2015) findings. Smith & Goodale (2015) presented participants with visual images of familiar objects (e.g., wine glasses, mobile phones, apples) or unfamiliar objects (e.g., cubies, smoothies, spikies) to test whether the earliest regions of the somatosensory (S1 and S2) cortex contain content-specific information about visual object categories. They showed that MVPA revealed significant above chance decoding of familiar, but not unfamiliar, visual object category bilaterally in S1 and right S2. The authors concluded that the earliest areas of the somatosensory cortex carry information about the category of visually presented familiar objects. A difference between our experiment and Smith & Goodale's (2015) experiments is that they did not present tools, but familiar objects. Another difference between our study and Smith & Goodale (2015) is that they defined early somatosensory cortex (S1), using a mask, while we defined the somatosensory cortex based on fMRI activation in the pantomime task. A possible interpretation is that by selecting voxels using the contrast pantomimes > baseline, we might have targeted a region within the somatosensory cortex more associated with proprioception which could explain why we could decode tool identity, functional and structural manipulation knowledge during pantomimes, but we could only decode movement from the view task. Further work is needed to ascertain the specific role of the somatosensory cortex in tool recognition, for example in a future study we could use a specific localizer to identify S1 and S2 to understand which specific regions within the somatosensory cortices contain activity patterns that code for tool identity and functional manipulation knowledge.

Our results show that both structural and functional manipulation properties are represented in tool- and hand- selective IPS, PMd, PMv, somatosensory cortex and SMA during pantomimes of tool use. While the reported structural manipulation knowledge selectivity in these regions is in line with similar findings in monkey area AIP (Murata et al., 2000; Taira et al., 1990), area F5 (Fluet et al., 2010; Rizzolatti et al., 1988; Umilta et al., 2007), PMd (Raos, 2004) and M1 (Muir & Lemon, 1983; Umilta et al., 2007) and also in human aIPS, PMv (Binkofski et al., 1999; Cavina-Pratesi et al., 2010; Culham et al., 2003; Frey et al., 2005), PMd, M1 and S1 (Ehrsson et al., 2000), the reported functional manipulation knowledge selectivity is in line with directional tuning reported in parietal areas in the human brain during reaching movements towards 3D objects (e.g., half-spheres; Fabbri et al., 2010, 2012; Fabbri et al., 2014; Lingnau et al., 2014). Our data suggests that tool- and hand- selective IPS play a critical role in identifying and controlling hand movements, including the grip during overt movements. This is in line with our results from chapter 2, in which we show that TBS-to-aIPS disrupts hand preshaping during target-directed actions.

Alongside with parietal areas, we observed the involvement of premotor areas. We show that PMd codes for identity, power versus precision grip and rotation versus squeeze movements during pantomiming and also for grip type during the view task. Although it might seem surprisingly that a motor region codes for grip during passive view of tools, Grafton et al. (1997) have previously shown activity in left PMd when tools are viewed passively. It is thought that PMd is crucial in accessing, maintaining and translating an action into a sequence of motor commands (Fink et al., 1999) whereas PMv has a somatotopic organisation (Rizzolatti, Luppino, & Matelli, 1998) and is involved in spatial perception, imitation and understanding actions, especially with manipulable objects (Rizzolatti, Fogassi, & Gallese, 2002). Critically, rotation and squeeze movements require different movement of the hand and the wrist. Thus, we could speculate that this region not only code for reach direction (Fabbri et al., 2014) and structural manipulation knowledge, but also contains patterns of activity that code for functional hand movements.

PMv is a frontal region that is thought to be necessary for hand grasping and object manipulation (Binkofski et al., 1999; Davare, 2006; Grèzes, Armony, Rowe, & Passingham, 2003). The observation that PMv contains patterns of activity that represent actions only during overt tool use pantomiming is consistent with the findings from Chen et al. (2017). In their experiment, Chen et al. (2017) found that when participants were performing pantomimes of tool use but not when participants were performing a tool identification task, PMd and PMv coded for object-directed actions (e.g., pantomime the use of scissors).

We also found that SMA contained patterns of activity that code for tool identity, power versus precision grip and rotation versus squeeze movement during pantomimes only. SMA lies within the superior frontal gyrus and has reciprocal connections with the primary motor cortex and PMd (Cona & Semenza, 2017; Luppino, Matelli, Camarda, & Rizzolatti, 1993; Tanji, 1996) and is directly related to motor output (Nachev, Kennard, & Husain, 2008). It is thought that SMA makes an important contribution to motor planning and execution and it is involved in representing action sequences (Halsband, Ito, Tanji, & Freund, 1993; Tanji, 2001) and action execution (Nachev et al., 2008; Tanji, 1996). Evidence from monkey neurophysiology has shown that SMA neurons respond preferentially to specific order of movements, such as turn - pull – push, rather than others, such as turn – push – pull (Shima & Tanji, 2000; Tanji & Shima, 1994). Moreover, SMA inactivation studies in monkeys have shown that monkeys were impaired in performing action sequences (e.g., turn – pull – push) previously memorised, however, where still able to complete single movements (e.g., reaching) (Shima & Tanji, 1998). In humans, Wymbs and Grafton (2013), using repetitive TMS over SMA, have shown that participants were less accurate during the retrieval of previously learned action sequences compared to no-TMS. Moreover, Wiestler and Diedrichsen (2013) using fMRI and MVPA have shown that trained sequences were classified more reliably versus untrained finger sequences in the supplementary motor cortex. The fact that SMA contains patterns of activity that code for tool identity, structural and functional manipulation knowledge, might reflect the fact that this region plays a critical role in implementing previously learned action sequences when using tools. Future fMRI studies should look at patterns of activation within the SMA when participants are functionally demonstrating the use of tools versus performing atypical movement with tools, to disentangle whether SMA contains patterns of activity that differentiate between new and learned action sequences.

We observed an extensive involvement of the frontal and parietal cortices in coding rotation versus squeeze movements, power versus precision grip and tool identity during pantomimes, which is in line with previous evidence from different fields showing that aIPS, SMG, PMd and PMv are generally implicated in hand preshaping and tool-related actions (Culham et al., 2006; Lewis, 2006; Rizzolatti, & Luppino, 2001; Umilta et al., 2008) Moreover, neuroimaging evidence has shown that areas in the frontoparietal network are activated in the absence of any overt movement, such as when imaging tool use (Lewis, 2006), suggesting that the frontoparietal network creates representations of actions upon viewing tools, which might then be used for action generation, understanding and learning (Rizzolatti & Luppino, 2001). However, our results seem at odds with this. Although we show that MC and SSC contain patterns of activity that decode for functional manipulation knowledge in both the view and the pantomime task, we did not observe above chance decoding accuracy in the other regions for the view task. Specifically, in our experiment we found that structural manipulation knowledge and tool identity could not be decoded above chance in motor region within the frontoparietal network, such as MC, SSC, PMv, PMd and SMA during the view task, although decoding was above chance in the pantomime task. Thus, it may be that although these regions show activation during imagining of tool use, however, this activation may be related to the imagined movement. Here, we expand upon these observations and we have shown which specific regions within the frontoparietal network contains patterns of activity that represent function and manipulation knowledge during tool pantomimes.

Recently, Binkofski & Buxbaum (2013), proposed that there is a distinction between a dorso-dorsal and a ventral-dorsal circuit. This hypothesis comes from the observation of two parallel parieto-frontal networks in the macaque monkey. A dorso-dorsal pathway leading from visual area V6 over the superior parietal lobule towards the dorsal premotor cortex and a ventro-dorsal pathway running from the middle temporal and medial superior temporal areas through the inferior parietal lobule to the ventral premotor cortex (Rizzolatti & Matelli, 2003; Rossetti et al., 2003). According to this hypothesis, while dorso-dorsal regions (including the aIPS, SPL and PMd) contribute to the planning of online reaching and grasping movements, ventro-dorsal regions (including SMG and PMv) contains long-term representation specialized for the processing of learned and skilled movements such as tool-use and integrate grasp-related information (Binkofski & Buxbaum, 2013). Here, we have shown that with tool pantomimes, regions in both ventro-dorsal and dorso-dorsal pathways contain patterns of activity that code for both functional and structural manipulation knowledge. These findings support the account that there is no clear separations between the two pathways and leaving open the possibility of alternative explanations for the involvement of the two sub-circuits in the execution of object-directed actions, including the possibility that the two pathways have different temporal involvements in skilled tool-use. Future experiments should implement MEG, which has higher timing and spatial resolution compared to both fMRI and EEG to investigate the temporal involvement of the two pathways when participants are interacting with tools. Additionally, implementing online TMS at different phases during planning and execution of tool use pantomimed in regions within the dorso-dorsal stream, such as middle IPS and PMd, or the ventro-dorsal stream, such as aIPS and PMv, could help us to shed new light on the temporal involvement of these pathways in tool interactions.

3.4.3 Task Cross-Decoding

Surprisingly, we could not cross decode between view and pantomime in any of our regions. Although we found above chance task cross-decoding accuracy for structural manipulation knowledge in PMd, it did not survive FDR correction. The fact that patterns of activity in PMd represent structural manipulation knowledge across tasks may be in line with evidence that show that this region plays a role in accessing and maintaining information in semantic working memory (Gabrieli, Poldrack, & Desmond, 1998; Wagner, Paré-Blagoev, Clark, & Poldrack, 2001). Moreover, although the PMd is considered part of the reach subnetwork of the dorso-dorsal stream (e.g., Binkofski & Buxbaum, 2013), it is also though that the PMd contains representation of hand digits (Dum, 2005). Moreover, multiunit recordings in monkeys have shown that reach and grasp can be predicted from PMd (and PMv) accurately. Thus, the fact that we observed a trend in decoding accuracy across tasks in PMd may suggested that this region contains sematic information about the sequence of the grasp and that this information is available independently of whereas an overt movement is required.

In Chen et al.'s (2017) experiment classifiers were trained and tested across tasks, stimulus format and specific tools. Implementing searchlight MVPA and ROI MVPA analyses, they found that the only brain regions in which action relations among objects could be decoded across tasks, stimulus format and tools was the inferior parietal lobule, suggesting that this area has access to abstract action information, even when no overt action is required. A difference between Chen et al. (2017) and our experiment is that they used triads of objects, in which 2 of the 3 items were similar by manner of manipulation or by function. Our task was designed so that we had 4 objects out of the 8 objects in each category of interest. For example, in the power (or precision) category we have 2 objects that required a rotation movement and 2 that required a squeeze movement. Similarly, in the rotation (or squeeze) category, we had 2 objects that afforded precision and 2 that afforded power. Thus, in each group, even if the objects were similar for type of movement (e.g., rotation or squeeze), they were different for type of grip, which might have had an impact on the way the classifier was trained and tested. Thus, in further analysis we should look at training and testing the classifier using objects that are matched for both grip and movements type. For example, to test whether we could decode power versus precision grip in our brain regions we should train the classifier within the rotation and the squeeze category separately and then average the accuracies. For example, we should train the classifier on screw versus screwdriver and test on key versus corkscrew and vice versa. Similarly, in the squeeze category we should train the classifier on tweezers versus nutcracker and test on peg versus tongs. Another difference is that Chen et al. (2017) instructed participants to think about the function of the tools, while in our task participants were focusing on the identity of the tools as they had to perform a 1-back repetition task. It may be that instructing participants to think about the function of the objects facilitated the decoding across tasks.

Although we could not implement searchlight analysis due to time constraints, we would like to implement searchlight MVPA (Kriegeskorte, Goebel, & Bandettini, 2006) to explore other areas than our ROIs that potentially represent power versus precision grip, rotation versus squeeze movements and identity across the two tasks. Additionally, we could also implement whole-brain multivoxel representational similarity analysis (RSA) (Kriegeskorte, 2008; Kriegeskorte & Kievit, 2013). RSA is a widely used approach to characterise the correspondence between brain activity patterns and behavioural measurement (Kriegeskorte, 2008) and it consists in constructing representational dissimilarity matrices (RDMs) for both measures and calculating the correlation between them. Thus, we could combine the behavioural ratings with our ROIs and whole-brain fMRI analysis to test whether the information recorded in our behavioural tasks, such as grip ratings, object familiarity and similarities between objects (e.g., use and grasp) influence the functional organisation of regions within the dorsal and ventral stream.

3.4.4 Concluding remarks

To conclude, we observed that patterns of activity in both visual streams contain information about the identities of tools and how to grasp and use them. Moreover, we observed that the tool network is modulated by task. That is, although frontoparietal and occipitotemporal networks contain patterns of activity that coded for tool identities and functional and structural manipulation knowledge, accuracies in regions within the occipitotemporal were higher for the view task, while accuracies in frontoparietal regions were higher in the pantomime task. Moreover, we showed that not only regions within the dorsal stream showed decoding for motor properties, but also regions in the ventral stream. On the other hand, visual properties were decoded not only in ventral, but also in dorsal stream regions. These results suggest that visual perception is not a characteristic of the ventral stream only, but that also the dorsal stream plays a role visual perception (Freud, Plaut, & Behrmann, 2016). This will be further expanded in the general discussion.

One of the limitations of the current experiment is that in the viewing task we implemented a working memory component (e.g., 1-back task) but we did not have a similar task in the pantomime task. The 1-back task is commonly used in fMRI experiments (e.g., Bracci et al, 2010; Bracci et al., 2016; Smith & Goodale, 2015), based on our analysis we cannot exclude that the task may have had an effect on the network of region analysed. However, we believe that here it was not the case. First, several lines of evidence (for a review see Critchley, 1953; Pisella & Mattingley, 2004) suggest that is the right posterior parietal cortex, but not the left, that is critically involved in visual functions. As here we run our analysis on the left hemisphere only and our task involved visual working memory, is unlikely that the task may have had an impact on the regions analysed. Second, we did not find cross-decoding between the two tasks, therefore it is unlikely that the working memory task used in the viewing task but not in the pantomiming task had an impact on the network of regions involved. Indeed, our ability to interact with tools requires that the information about the sequence of the actions is integrated with information about object properties as well as maintained over time and evidence has demonstrated that parietal mechanisms are important for visual working memory (e.g., Berryhill & Olson, 2008; Kastner, Chen, Jeong & Mruczek, 2018; Todd and Marois, 2004). Therefore, in the future it would be interesting to investigate whether implementing a working memory task affected the network of brain regions involved in the two tasks, for example this could be done by identifying the regions involved in working memory using an independent localiser and run both univariate and MVP analyses in both the left and right hemisphere.

For the purpose of our experiment, we selected tools that were associated with specific action plans (e.g., a nutcracker is to open nuts) and participants were specifically trained to perform the expected action plan before entering the scanner, however, familiar everyday graspable objects may, in fact, be associated with multiple action plans. For example, grasping a spoon based on its physical properties (e.g., handle size shape and orientation) may differ from grasping based on knowledge and intention of use (Daprati & Sirigu, 2006; Frey, 2007). So far, we have shown that functional and manipulation knowledge are represented in a network of regions and that these representations are modulated by task, but what about grasping real tools with the intention of use? In the next chapter, using grasp-to-use (GTU) and grasp-to-move (GTM) tasks we will further investigate how knowledge and intention of use modulates the kinematics of grasping by using different 3D everyday tools.

Chapter 4

4. Tool identity and subsequent use affect the kinematic of grasping movements

4.1 Introduction

In our everyday activities we interact with numerous objects, which vary in the extent to which they offer functional interactions. For example, while preparing our breakfast we use the knife to slice the bread, but also to butter the bread. As noted in chapter 3, tools are a unique class of objects as they are man-made artefacts that afford specialised actions that are tied closely to their identity. Here, I explored how tool identity and action end-goal modulates grasping kinematics even when structural differences between objects are controlled for. My interest focused on whether grasping kinematics towards the same tool are influenced by the end-goal of the subsequent action and whether tool identity is processed when grasping a tool without any subsequent movement and/or when the tool is grasped to be used according to its function.

According to Gibson (1979), objects have specific properties that convey relevance for actions, called "motor affordances". Gibson (1979) used the term affordances to refer to the fact that the visual perception of our environment is not a passive perception of the objects within it, but is instead a direct perception of the potential for action for the observer that these objects carry. In other words, when viewing a mug, we would not only perceive its colour and shape, but first and foremost we would perceive the fact that it is graspable, that we could lift it and drink from it. Importantly, object affordances depend not only on the object alone, but also on the action possibilities of the perceiving agent.

Moreover, actions afforded by tools typically consist of specific motor routines (Creem & Proffitt, 2001; Tucker & Ellis, 1998). For example, a tea-spoon affords stirring and it is wielded with a precision grip between the index finger and thumb and is typically associated with a characteristic rotation of the wrist movement to stir. The strong functional specificity associated with tools is what differentiates tools from other objects in our surroundings, which could be familiar and graspable, however whose identity is typically not associated with a specific function (e.g., a building or a flower). For example, although we could grasp an apple to throw it, or a carrot to pound something, natural objects are not typically associated with a specific function, nor a typical motor routine. In fact, only tools have been created by humans to have a specific function and address a specific problem.

In line with this functional specificity of tools, it has been shown that the mere sight of tools facilitates perceiving objects affordances that activate their associated motor responses (Ellis & Tucker, 2000; Grèzes et al., 2003; Tucker & Ellis, 1998, 2004). In 1998, Tucker and Ellis, showed that right-hand responses were facilitated when the objects handles were facing right, and left-hand responses were facilitated when the objects handles were facing left (for a description of the task see chapter 3). Based on this observation, the authors postulated that the orientation of the handle automatically gives rise to the activation of the corresponding motor plans for grasping. Subsequently, Tucker and Ellis (2004), have shown that small objects facilitate precision-type responses while large objects facilitate power types responses (for a description of the task, see chapter 3). Taken together, this evidence suggests that the visual properties of objects important for grasping, such as orientation and size, automatically facilitate the activation of corresponding motor representations.

In line with Tucker and Ellis (1998, 2004), several neuroimaging studies have shown that sensorimotor areas are preferentially activated for pictures of graspable versus non-graspable objects even when no action is required (Chao & Martin, 2000; Valyear et al., 2007). Chao and Martin (2000) compared viewing and silent naming of pictures of familiar tools with viewing pictures of animals. They showed that graspable objects elicited higher activation in both left ventral premotor and left posterior parietal cortex compared to pictures of animals. The authors suggested that the observed parietal activity represented stored manipulation and function knowledge about tools (Chao & Martin, 2000).

Moreover, Valyear et al. (2007) suggested that tool related activity in the parietal cortex does not reflect only the graspable property of the stimuli, but that the activity relates to action representations which are linked to knowledge of use and prior experience (Valyear et al., 2007) (for a description of the procedure see chapter 3).

Also, Buccino et al. (2009) using a combined TMS and EMG approach and pictures of objects with a whole or broken handle, showed that motor evoked potentials (MEP) recorded from muscles in the right hand are modulated by the handle orientation of passively viewed objects. In fact, MEPs were larger when handles were oriented to the right, in accordance to a right-hand grasp, but only when the handle was intact. The authors suggested that motor programs are tuned to the handle and that in the case of a broken handle, these motor programs are interrupted (Buccino et al., 2009).

Additional evidence that object affordances activate motor representation for actions comes from patients showing "utilisation behaviour" following damage to their frontal areas (Lhermitte, 1983). These patients are compelled to grasp and use familiar objects, even if they are told not to do so (Lhermitte, 1983; Shallice, Burgess, Schon, & Baxter, 1989). For example, Humphreys and Riddoch (2000) have shown that object affordance play a critical role in such impulsive behaviour. In their task, patient FK, who suffered bilateral lesions to the medial frontal and anterior temporal lobes was presented with a cup with the handle facing either to the left or the right. FK was instructed to grasp the cup with the left hand if the cup was placed on the left, and with the right hand if placed on the right. They observed that the patient made frequent errors when the cup was placed on the left, but with the handle facing to the right, as such FK often incorrectly grasped the cup with his right hand, although was instructed to grasp it with the left hand. According to Humphreys and Riddoch (2000), this suggested that the orientation of the handle automatically evoked a grasp response. Interestingly, when the patient was asked to point to the handle instead of grasping, no errors were observed. The findings indicate that affordances can elicit grasping and that the task end-goal (e.g., pointing or grasping) plays a determining role in the observation of the impulsive behaviour in these patients (Humphreys & Riddoch, 2000). Taken together, these evidences suggest that object affordances can lead to the activation of the motor representation relevant for grasping actions.

At a neural level, in the healthy brain, motor affordances are thought to arise due to the automatic activation of regions responsible to integrate visual and motor information (e.g., visuomotor regions; Gallivan et al., 2011; Handy, Grafton, Shroff, Ketay, &

Gazzaniga, 2003). In contrast with other classes of objects, such as non-graspable objects, animal, faces and houses (Chao & Martin, 2000; Gallivan et al., 2013; Handy et al., 2003) and meaningless shapes (Creem-Regehr & Lee, 2005), tools can be processed based on what they are and what they can be functionally used for (Creem-Regehr & Lee, 2005). As reviewed in chapter 3, brain regions activated by viewing tools overlap with brain regions activated when grasping, using, imagining and pantomiming tool use (Lewis, 2006). These findings are consistent with the idea that tool perception and actions associated with tool use rely on overlapping cortical networks (Humphreys, Riddoch, Forti, & Ackroyd, 2004).

So far, I reviewed work that indicates that object affordances relevant for grasping facilitate motor-related activity and can influence perceptual and motor responses, but what about the goal of the action (e.g., use a spoon to stir the coffee)? For example, while cooking, if I need a spatula, I reach toward my utensils holder to grasp the spatula to flip my egg. However, I might also grasp the spatula to move it closer to the hob and use it later. Although the object grasped is the same, the end goal of the reaching actions is different. When we perform actions in our surrounding our motor behaviour is influenced by the forthcoming task, and evidence for this claim comes from studies in which ongoing movements are influenced by the context and the next task demands. For example, during speech production, the articulation of a phoneme is affected by the identity of the upcoming phonemes (Liberman, 1970). Moreover, contextual effects have been reported in a variety of manual tasks, including manual aiming (Klapp & Greim, 1979), finger spelling (Jerde, Soechting, & Flanders, 2003a, 2003b), typing (Rumelhart & Norman, 1982), handwriting (van Galen, 1984) and, indeed, it has been shown that during prehension, reaching kinematics are influenced by the end goal of the action (e.g., Ansuini, Santello, Massaccesi, & Castiello, 2006; Cohen & Rosenbaum, 2004; Cole & Abbs, 1986; Gentilucci, Negrotti, & Gangitano, 1997; Marteniuk, MacKenzie, Jeannerod, Athenes, & Dugas, 1987; Naish, Reader, Houston-Price, Bremner, & Holmes, 2013; Rosenbaum & Jorgensen, 1992; Rosenbaum, Vaughan, Barnes, & Jorgensen, 1992; Schuboe, Maldonado, Stork, & Beetz, 2008; Stelmach, Castiello, & Jeannerod, 1994; Valyear, Chapman, Gallivan, Mark, & Culham, 2011).

For example, it has been shown that the intent of what an individual wants to do with an object affects both the planning and the control of the movement (Marteniuk et al., 1987) and that the shape of the hand during reach-to-grasp movement is affected by the nature of the following task (Ansuini et al., 2006).

Although these studies are informative, participants were presented with meaningless shapes that are usually not associated with specific action plans. However, in everyday life, we interact with familiar graspable objects, which may, in fact, be strongly associated with multiple action plans. For example, a plum may afford a particular grasp style based on its size and shape, but it also may afford a different grasp based on the way it is typically brought to the mouth to be eaten (Gentilucci, 2002; Naish et al., 2013) or to be placed elsewhere (Naish et al., 2013). Similarly, familiar objects may afford different grasp styles based on the task end goal. For instance, Ansuini, Giosa, Turella, Altoe and Castiello (2008) showed that changes in finger joint angles were unique for grasping a water bottle to pour water from it and that these changes appeared to reflect anticipation of the particular dynamics linked to the pouring action. The authors concluded that different after-grasp movements affect the kinematics of the preceding prehension movement (Ansuini et al., 2008).

Moreover, Schuboe et al. (2008) observed differences in reaching movements when participants were picking up a bottle in different task contexts. Specifically, the authors observed that reaching movements towards the bottle were longer in duration when the subsequent action was pouring liquid from the bottle before placing it down, compared to when the end-goal was simply placing the bottle (Schuboe et al., 2008).

Likewise, for familiar tools, grasping based on properties of the object, such as, size, shape and orientation, may differ from grasping based on the knowledge and the intention to use the tool for a specific end-goal (Daprati & Sirigu, 2006; Frey, 2007; Valyear et al., 2011; Valyear et al., 2007). Therefore, different task goals with the same tool may translate into distinct motor affordances (e.g., a knife can be used to cut but also to spread butter). It is also worth mentioning that for some objects and tools, the hand configuration based on the structure of the object is at odds with the configuration required for use (Buxbaum et al., 2003; Klatzky, McCloskey, Doherty, Pellegrino, & Smith, 1987). For example, the structure of a hotel reception service bell affords a whole-hand pinch interaction to lift it up, but in fact, the learned interaction to use it is a poke. As highlighted in the main introduction (see section 1.10.2), evidence from neuropsychology has shown that patients with ideomotor apraxia, with damages to their inferior parietal lobe, might be able to grasp objects based on their physical properties, however, they are unable to use the same object (Carey, Harvey, & Milner, 1996; Randerath et al., 2009; Sirigu et al., 1995). In contrast, patients with posterior parietal damages, which include the SPL, improve when grasping familiar objects versus shapes (e.g., cylinder) (Jeannerod, Decety, & Michel, 1994). This suggests that for familiar tools, learned functional properties (use-based), structural properties (structure-based) or both, may be critical for affordances (Bub, Masson, & Cree, 2008; Valyear et al., 2011; Valyear et al., 2007).

To further investigate use-based affordances, Valyear et al. (2011) asked healthy participants to grasp familiar kitchen tools in order to move them (grasp-to-move; GTM) or to demonstrate their common use (grasp-to-use; GTU). Actions were preceded by a short visual preview of a tool with either congruent or incongruent identity to the tool which was then acted with. Importantly, all the tools had identical handles so that priming and differences in kinematics could only be related to knowledge of identity and learned tool use, instead of structural object properties. The authors showed that priming and the kinematics of grasping depend on the goal of the grasping action as well as the context in which the tasks were presented. They reported that priming effects were observed for reaction times in GTU only when the tasks were presented in separate blocks. According to the authors, these results show that the priming effect appeared to be evident when the identity of the tool was important for the end-goal of the task (e.g., use the object). However, when the tasks were presented in a mixed order, priming effects emerged in the GTM task as well. The authors suggested that the effect of priming in GTM when the tasks were mixed was linked to the attention to tool identity effect observed in GTU. When the two tasks were mixed, the attention to tool identity was in place, and therefore priming effects emerged for GTM trials as well. Moreover, they observed longer reaction times, shorter movement durations and wider peak grip apertures in GTU compared to GTM. The authors concluded that the end-goal of the task modulates the attention to particular object features, which as a consequence modulated affordances and priming. For grasping kinematics, no effects of priming were observed. They observed wider grip apertures and shorter movement durations for GTU, regardless of the task setting. Moreover, in the block setting, they reported an interaction between tool identity and task, which showed that in the GTU task the grasping patterns differed according to the tool identity, whereas in the GTM task, grasping was similar across all tool identities. Although in the mixed design the interaction did not reach significance, the authors reported that the pattern remained, but was less pronounced. The authors concluded that priming of grasping is determined by the end-goal (e.g., GTU and GTM) of the task as well as the task setting (e.g., mix or block design), which are both likely to modulate how affordances are perceived and therefore influence the planning of subsequent actions (Valyear et al., 2011)

In a recent experiment, Cicerale, Ambron, Lingnau and Rumiati (2014) showed that participants were faster to initiate the movements and took less time to perform the movements for GTM versus GTU.. The authors suggested that the kinematic characteristics of the initial grasping movement were modulated by the precision of the end-goal of the action. Specifically, in GTU, participants took longer to prepare and execute the reach-to-grasp movement indicating that more attention was paid to the plan and control of the movement (Cicerale et al., 2014). These results confirm that the end-goal of an action has an impact on grasping kinematics of the initial reaching and grasping movement (Cicerale et al., 2014; but see also: Ansuini et al., 2008). Perhaps surprisingly, they did not observe an effect of the goal of the task on grip aperture, however, this might be related to the fact that they did not control for structural differences between tools (i.e., the tools used did not have the same size handle).

Based on evidence that there are differences in kinematic characteristics between GTU and GTM, one would expect that these differences might be reflected in the muscular activity. I have previously discussed that the mere sight of a tool activates motor affordances. Similarly, humans are predisposed to have facial reactions to the mere sight of facial expressions (Dimberg, 1982; Dimberg & Karlsson, 1997). In a series of studies, Dimberg and colleagues have shown that when people see pictures of emotional facial expressions, they rapidly, spontaneously and unconsciously react with distinct facial electromyographic (EMG) reactions in the face muscles that are relevant for the emotion displayed (e.g., Dimberg, 1990; Dimberg & Thunberg, 1998; Dimberg, 1982; Dimberg, Thunberg, & Elmehed, 2000) after only 500 ms of exposure (e.g., Dimberg & Thunberg, 1998). Moreover, it has been consistently reported that face muscles more generally automatically distinguish between negative and positive emotional reactions. Based on these observations on facial EMG and emotions, we would expect that hand muscle would spontaneously and rapidly react to the mere sight of objects, before any overt movement is initiated. Moreover, based on the difference in kinematic characteristics highlighted in the previous paragraphs, differences in EMG would be expected between GTU and GTM.

For example, Naish et al. (2013) using EMG and motion tracking showed that the initial reach-to-grasp movement in target-directed actions with objects, varies depending on both the subsequent action and on the properties of the object itself.

Inspired by these previous studies, here we explored whether and how reach-to-grasp movements differ depending on whether familiar tools are going to be grasped and placed (GTM) or functionally grasped and used (GTU) and whether tool identity affects grasping kinematics. To this end, we investigated real grasping action using familiar kitchen tools. Similar to Valyear et al. (2011), we had two tasks: grasp-to-move (GTM), whereby participants grasped a tool to move it from one location to the other and grasp-to-use (GTU), whereby participants grasped a tool to demonstrate its typical use.

Our interest focused on whether grasping kinematics towards the same tool are influenced by the end-goal of the subsequent action and whether tool identity is processed in both GTU and GTM or not. For the GTU task, the identity of the tool should play a critical role in action planning, therefore we predicted that grip aperture, peak velocities and EMG activity would differ across tools. In contrast, for the GTM task, tool identity may not play such an important role, and therefore we did not expect differences in kinematics and EMG activity across tools. According to Gibson (1979), affordances are perceived in a direct way, that is that the knowledge associated with the object does not need to be activated, as affordances are not properties of the object alone, but they are linked to the object and the effector potential for action. Therefore, based on this account, we would expect that tool identity would affect grasp kinematics in the GTU task only.

However, an alternative scenario could be expected. Gentilucci (2002) showed that grasping kinematics are influenced not only by the actual opposition space (e.g., the part of the object that has to be grasped), but by also other parts of the object. Gentilucci did not use tools, but meaningless spheres and blocks with no semantic meaning associated with them. Similarly, it is possible that when tools are grasped the business head influences how the tool is grasped and therefore it may be that the identity of a tool is always processed when interacting with it, regardless of the specific goals or motor requirements (Gentilucci, 2002, 2003). If this is the case, different kinematics of grasping and EMG activity across tools should be expected not only in the GTU, but also in the GTM task.

Importantly, we used tools with the exact same handle so that any differences in grasping kinematics could not be simply attributed to any difference in the structure of the handle of the objects. This was implemented such as the grasping kinematics would in principle be comparable for all tools in the reach-to-grasp movement and to characterise the kinematics of grasping in GTU and GTM, without the confounding of using tools with different handles (see Valyear et al., 2011). Additionally, we kept the first sequence of the movement (e.g., reach-to-grasp) constant across the two tasks, so that any differences observed in grasping kinematics and EMG were comparable across tasks and tools. Although we recorded EMG, due to time constraints, this data was not analysed.

4.2 Methods

4.2.1 Participants

Eighteen naïve participants (5 males; mean age = 21.5 years old, S.D. = ±2.7 years old; mean education = 15.7 years, S.D. = ±1.9) recruited from the University of East Anglia (Norwich, UK) took part in a motion-tracking study. In total 20 participants were recruited, however, data from 2 participants were discarded due to missing markers. All participants were healthy, had normal or corrected-to-normal vision and were right-handed (Oldfield, 1971).

The Ethics Committee of UEA, School of Psychology (reference: 2016-0058-000226), approved the study and participants informed consent was obtained in accordance with the principles of the Declaration of Helsinki (1964). The experiment took approximately 1 hour 45 minutes, and participants were compensated financially or were given SONA course credits.

4.2.2 Materials and Apparatus

Six high-resolution infrared sensitive cameras (Qualisys AB, Gothenburg, Sweden) were used to record the x, y, and z positions (179 Hz) of three lightweight markers (4 mm diameter) attached with adhesive tape to the inside tip of the thumb, the tip of the index finger and the metacarpophalangeal joint of the index finger of the participants' right hands. EMG data were acquired using a BioNomadix dual channel wireless device (W x H x D: 6 cm x 4 cm x 2 cm; weight: 54 g) and a Biopac MP-150 electromyograph (BIOPAC Systems, Inc., Goleta, CA). EMG signals from the right hand and forearm were acquired throughout the whole experiment at a sampling rate of 1kHz and band-pass filtered at 1-1000 Hz, digitalized and displayed on the computer screen. Four pairs of adhesive solid hydrogel silver-silver chloride surface cloth electrodes (2.5 cm x 2.5 cm cloth backing) were attached to the skin to record the activity of four muscles of the participants' right hand and forearm. Specifically, electrodes were placed over the first dorsal interosseous (FDI) and the abductor pollicis brevis (APB) in the hand; and the forearm flexor (i.e. flexor digitalis superficialis, FDS) and the extensor muscles (i.e. extensor digitorum communis, EDC) in the forearm. The ground electrode was placed on the styloid process of the wrist, and each pair of electrodes was placed on the skin overlaying each muscle at approximately 2 cm apart (Naish et al., 2013). Figure 4.1 represents where the electrodes were placed on the right hand and forearm.

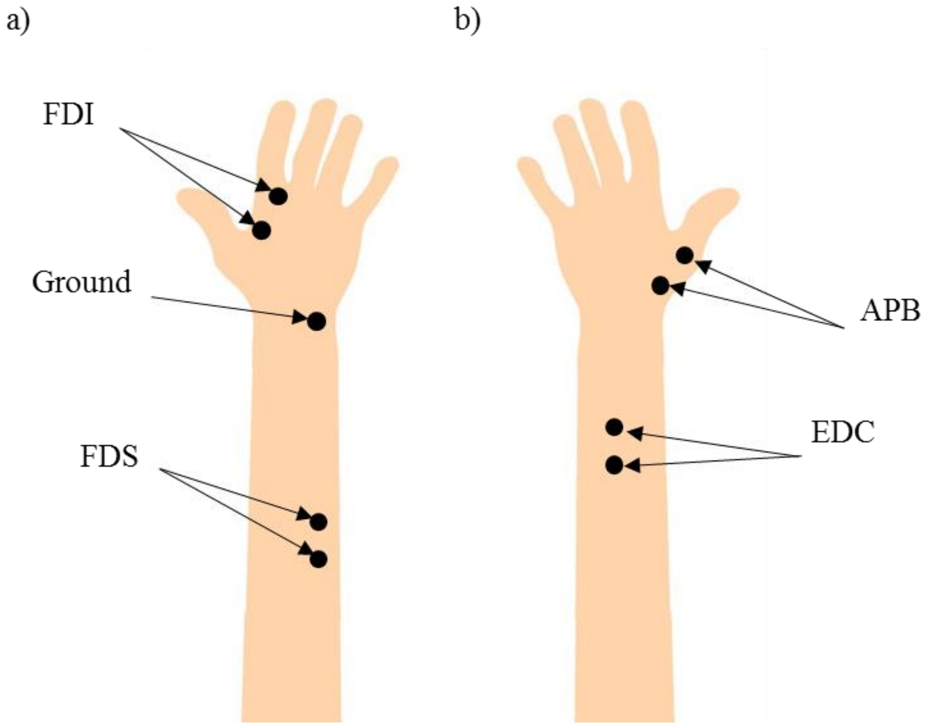


Figure 4.1 Representation of electrodes placement on the exterior (a) and interior (b) surface of the right hand and right forearm. FDI: first dorsal interosseous, FDS: flexor digitalis superficialis, ABP: abductor pollicis brevis, EDC: extensor digitorum communis.

Participants were seated in front of a grey table (1m^2) with their chin stabilised on a chin-rest to minimise head movements. They were asked to comfortably place their right hand and arm on a cushion with their index finger and thumb placed on the start position 5 cm on the right of their midline and approximately 20 cm from the edge of the table. A black rectangular platform (initial platform, 22.5 x 30 cm), used to place the tools, was positioned on the right side in front and of the participants at 38 cm from the edge of the table. The black platform in front of the participants (final platform) served as a standard position to perform the movements and had a marker on the bottom right corner where the participants were instructed to place the handle of the tool at the end of each trial (40 cm from the hedge of the table and 12 cm from the participants' midline; figure 4.2). This was done to keep the end position of each trial constant between trials and tasks. Visual feedback was controlled using liquid crystals shutter glasses (Plato System; Translucent Technologies, Toronto, Ontario, Canada). Participants were presented with three different tools: whisk, ice-cream scoop and knife. Table 4.1 lists all the tools and their features.

Importantly, all tools have the exact same handle (width: 3.2 cm). This was implemented so that the grasping kinematics would in principle be comparable for all tools in the reach-to-grasp movement and to characterise the kinematics of grasping in GTU and GTM, without the confounding of using tools with different handles (as in Valyear et al., 2011) A custom designed program written in Matlab (The MathWorks, USA) and the Psychophysics Toolbox (Brainard, 1997) were used to control the presentation of the tools, goggles, motion-tracking and EMG recordings.

Table 4.1 Tools. Table shows length, width, depth and weight of each tool. All tools have the same handle.

	Whisk	Scoop	Knife
Length (cm)	28.5	19.5	21.5
Width (cm)	5.5	4.3	2.1
Depth (cm)	5	2	2
Weight (g)	51	53	38

4.2.3 Procedure

Prior to testing, participants were asked to name the three tools and the experimenter demonstrated the expected action associated with each tool, however, participants were asked to carry out the movements in a way that was comfortable for them and not necessarily the way the experimenter showed them (Valyear et al., 2011). At the end of the experiment, participants completed a questionnaire about tool use and familiarity (see section 4.2.4 below). This was done to ensure that participants were familiar with the tool used.

In this study, we used a tool manipulation paradigm adapted from Valyear et al. (2011). Participants began each trial with their right hand and arm on a cushion with the index finger and thumb close to each other. A foam cushion was used to allow the participants to have their arm in a comfortable position and help them in relaxing their muscles in-between trials. Tools were placed on the platform in two different positions: the near position was placed 29 cm from the start position while the far position was positioned 35 cm from the start position, at an increment of 15° on the right. This was implemented to reduce the repetitiveness of the movements (Cicerale et al., 2014). Only trials in the near position were included in the analysis, while trials in the far position where used as catch trials and therefore repeated fewer times and not included in the analysis (Valyear et al., 2011).

Tasks were presented in a block order and at the beginning and at the end of each task, before recording these baselines, participants were asked to sit comfortably on the chair and relax their hand and arm muscles. When they felt they were relaxed, a one-minute task-EMG-baseline was recorded. We recorded these baselines to account for changes in factor such as how well accommodate the electrodes are to the skin, how much the equipment has heated up and potentially sweat and fatigue, which are factors that could affect the low frequency signal in the data and might affect the data even after filtering (see Cacioppo, Tassinary, & Berntson, 2007).

Each trial began with no vision of the workspace available for 1s, in which a trial-EMG-baseline was recorded, then the goggles opened, and the participants were instructed to simply look at the tool displayed on the platform for 2 s, plus a random delay (between 0 and 750 ms). At the end of the preview period, a beep (500 Hz, duration 250 ms) played to cue the participants to reach-to-grasp the tool on the initial platform. In the GTM task, participants were instructed to grasp the tool and place it on the final platform. In the GTU task, participants were instructed to grasp the tool on the initial platform, move it on the final platform in front of them and then demonstrate three cycles of the use associated with the tool, before placing it down with the handle on the final position. Figure 4.2 represents the timing of a trial. Importantly, to keep the direction of the movement consistent between tasks, the tools were moved to the same final position. GTM and GTU tasks were performed in separate blocks of 54 trials each (45 experimental trials, 15 repetitions for each tool identity in each block) with task order counterbalanced across participants. Figure 4.2 shows the sequence and timing of events within a given trial.

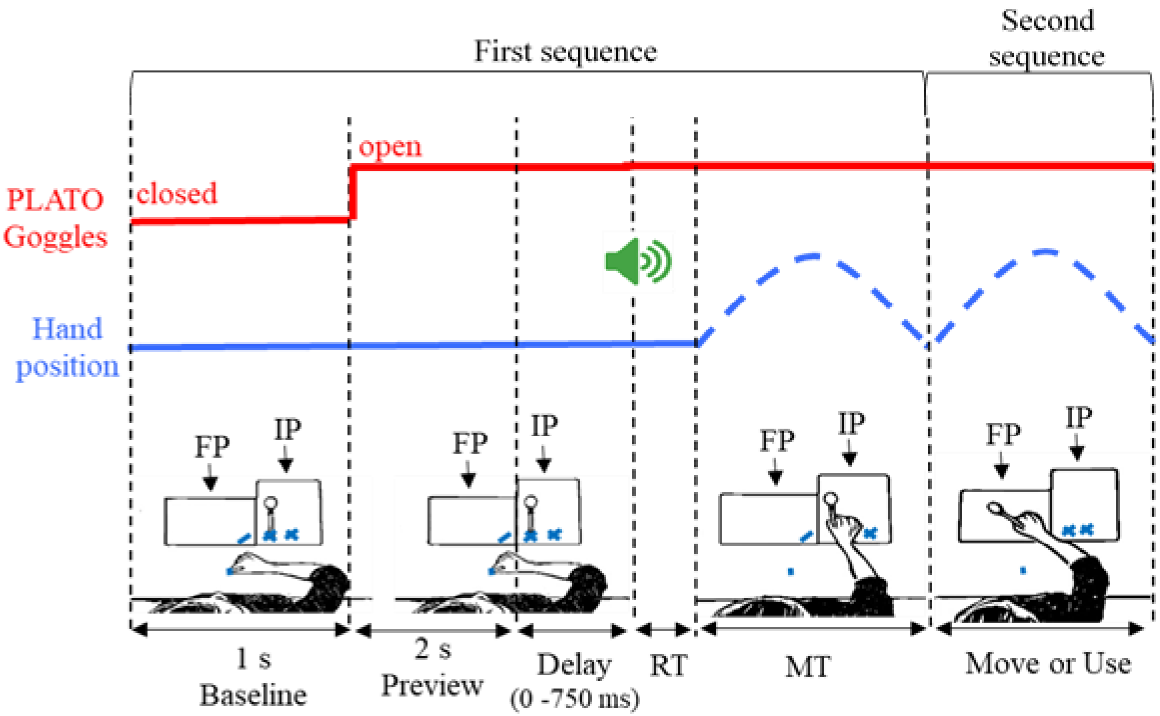


Figure 4.2 Example Trial timing for GTM and GTU. The top red line represents the state of the PLATO goggles and whether or not vision was available to the participants. The blue line indicates hand position: full line indicates no movement, whereas dashed line indicates that participants are performing hand actions. Light green sound symbol indicates the beep used to cue participants to start the action. RT = Reaction Times, MT = Movement Time, IP: initial platform, FP: final platform.

4.2.4 Tools Questionnaire

At the end of the behavioural experiment, all participants had to answer a questionnaire, checking their knowledge about the tools and how familiar they are with the usage of the tools presented in the experiment. Completing the questionnaire took approximately 10 minutes. Although pictures of the tools used during the experiment were presented, participants were reminded to think about the type of object depicted rather than the exact exemplar shown in the image when rating.

For each item, we computed the median of the group answers (Brandi et al., 2014). Table 4.2 reports questions, scale rating and the median score for each question.

The results of the questionnaire show that all the participants were familiar with the tools and how to use them. Moreover, the median shows that participants rated the tools easy to pantomime and with few actions associated with them.

Table 4.2 Tools Questionnaire. This table includes the items in the questionnaire, the response range and the median score for each question for each tool. We used a seven-level Likert-type scale in which participants had to indicate their answers for each item of the questionnaire. Items in the questionnaire were adapted from relevant studies in the field from Kellenbach, Brett, & Patterson (2003) and Lagace, Downing-Doucet & Guerard (2013).

Question	Answer's Range	Whisk median (range)	Scoop median (range)	Knife median (range)
Before you took part in this study, in your daily life how familiar were you with this object?	1 = no idea to 7 = very familiar	7 (3-7)	7 (3-7)	7 (7)
Before you took part in this study, did you know the function of this object?	1 = no idea to 7 = perfect idea	7 (6-7)	7 (6-7)	7 (7)
How often do you use this object?	1 = less often to 7 = every day	4 (1-7)	4 (1-7)	7 (1-7)
Please determine the number of actions that you can perform with each object.	1 to 7 +	1 (1-6)	2 (1-4)	2 (1-5)
How easily can you grasp this object?	1 = not at all to 7 = very easy	7 (4-7)	7 (5-7)	7 (4-7)
How easy can you pantomime the use of the object?	1 = not at all to 7 = very easy	7 (4-7)	7 (4-7)	6 (3-7)
How similar is the shape of your hand when you grasp the object to move it compared to when you grasp it to use it?	1 = not similar at all to 7 = very similar	4.5 (1-7)	4.5 (1-7)	6 (2-7)
		Whisk - Scoop	Scoop - Knife	Knife-Whisk
In this task you have to rate how similar is the function of the two objects in the picture	1 = very different to 7 = very similar	2 (1-6)	2 (1-4)	1 (1-4)
In this task you have to rate how similar is the shape of your hand when grasping the two objects in the picture	1 = very different to 7 = very similar	5 (3-6)	5.5 (1-7)	4 (1-7)
In this task you have to rate the similarity of the movement performed when using the two objects in the picture	1 = very different to 7 = very similar	3 (1-6)	2 (1-4)	1 (1-5)

4.2.5 *Analysis*

Kinematic data were obtained by localising the x, y, z positions of markers attached to the index finger, thumb and wrist of the participants' right hand and were analysed off-line using a customised software written in Matlab (The MathWorks, USA). Raw data for each marker were filtered using a low-pass Butterworth filter (10 Hz-cut-off, 3rd order) for each trial. Each trial was visually inspected for any errors.

Reaction times were defined using the wrist marker and were calculated as the time between the auditory cue and the first frame in which the velocity exceeded 50 mm/s. Movement onset was defined as the time at which the velocity of the wrist marker exceeded 50 mm/s and the end of the movement was determined as the time at which the velocity of the wrist marker fell below 50 mm/s (e.g., Cohen et al., 2009). For a complete list of the dependent variables see table 4.3.

Trials were excluded from the analysis for the following reasons: data points were missing due to occlusion of the markers (5% of trials), participants moved before the auditory cue (0.43 % of trials) or multiple peaks of grip aperture were detected (1.42 % of trials). In addition, trials were visually inspected and when a failure to detect the end movement was observed, they were excluded (6.5 % of trials). Also, we performed an outlier analysis on MGA, removing trials that were more than two standard deviations of the mean (2.8 % of trials). This procedure resulted in 84.1% of trials being included in the analysis for GTM and 83.59% of trials being included in the analysis for GTU with around 12 repetitions per tool per condition. Table 4.4 shows the total number of trials included in the analysis for each object across participants and the mean number of trials included per condition.

Table 4.3 List of variables analysed.

Dependent Measures	Name	Unit	Marker(s)	Description
Reaction time	RT	ms	wrist	Time of the onset of the movement
Movement duration	MT	ms	wrist	Time from movement onset to movement offset
Time to Peak Velocity	tPV	ms	wrist	Time interval between PV and movement onset
Time to Maximum Grip Aperture	tMGA	ms	index, thumb	Time interval between MGA and movement onset
Peak Velocity	PV	mm/s	wrist	Maximum resultant velocity of the wrist marker within MT
Maximum Grip Aperture	MGA	mm	index, thumb	Peak Euclidean distance between the thumb and index finger's positions

Table 4.4 Mean (standard deviation, SD) of trials within participants included in the analysis.

	GTM Mean of included trials (SD)	GTU Mean of included trials (SD)
Whisk	12.6 (1.9)	12.2 (2.2)
Scoop	12.8 (1.8)	12.5 (2.2)
Knife	12.7 (1.8)	12.4 (1.9)

All dependent variables were entered into a 2 x 3 repeated measure analysis of variance (RM-ANOVA), with factors task (GTM and GTU) and tools (whisk, scoop and knife). All comparisons in the RM-ANOVAs were analysed using the Greenhouse-Geisser correction when sphericity was not assumed and considered significant at α-level of 0.05 (two-tailed). Post hoc pairwise contrasts used the Bonferroni correction for multiple comparisons with a corrected $p < .05$. Moreover, partial eta squared (η_p^2) was calculated to determine effect size.

4.3 Results

4.3.1 Reaction Time

Analysis of reaction time (RT; figure 4.3) revealed that overall participants took the same time to begin the movement between the GTM (mean = 515.24 ms) and the GTU (mean = 540.23 ms) task ($F_{(1,\,17)} = 1.874$, $p = .189$, $\eta_p^2 = .099$) and across the three different tools ($F_{(2,\,34)} = .843$, $p = .439$, $\eta_p^2 = .047$). No significant interaction between task and tool identity was found ($F_{(2,\,34)} = .071$, $p = .931$, $\eta_p^2 = .004$).

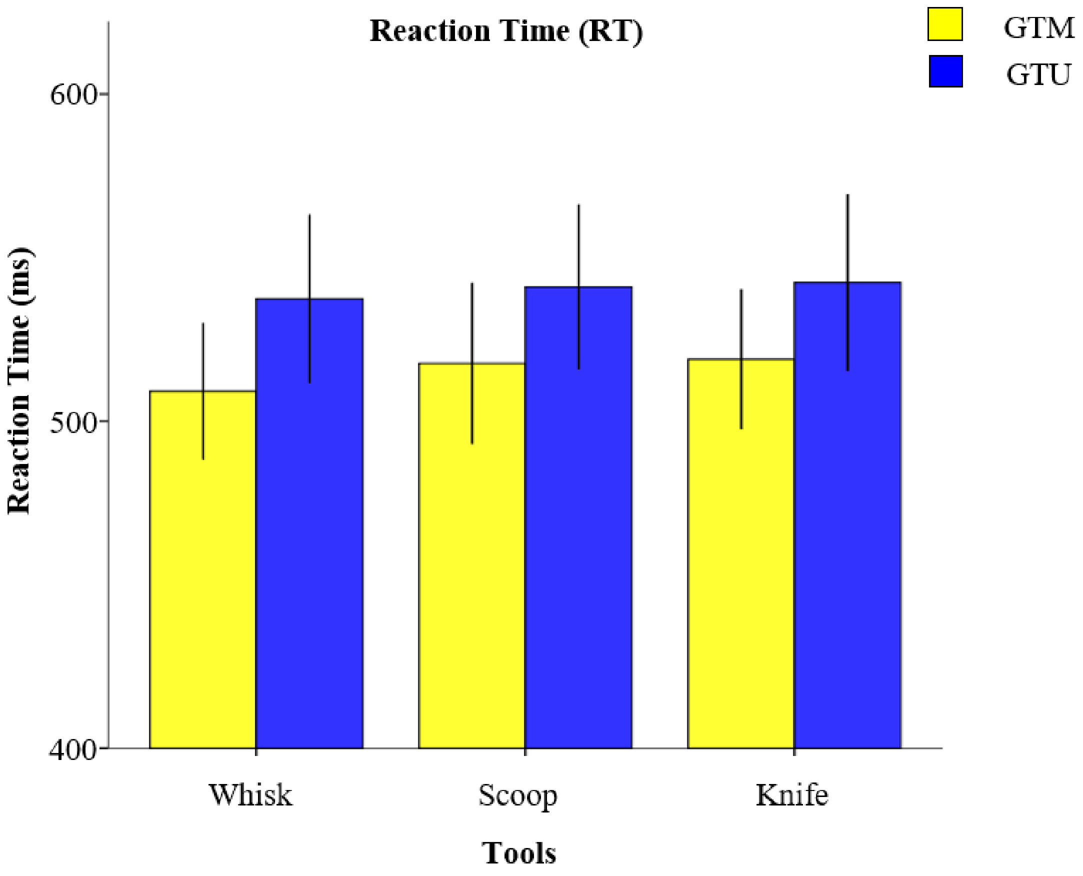


Figure 4.3 Graph depicts reaction time. Bars indicate means for each tool in GTM (yellow bars) and GTU (blue bars). Error bars represent standard error of the mean (SEM). No significant main effect or interactions were observed for RT.

4.3.2 Movement Time

We found a significant main effect of tool identity for MT ($F_{(2, 34)} = 3.739$, $p = .034$, $\eta_p^2 = .180$; figure 4.4). Participants were overall faster to perform movements when grasping the scoop (mean = 754.23 ms) than the knife (mean = 776.67 ms, $p = .033$). No significant main effect of task ($F_{(1, 15)} = .137$, $p = .716$, $\eta_p^2 = .008$) or interaction between task and tool identity ($F_{(2, 34)} = 269$, $p < .776$, $\eta_p^2 = .016$) were observed.

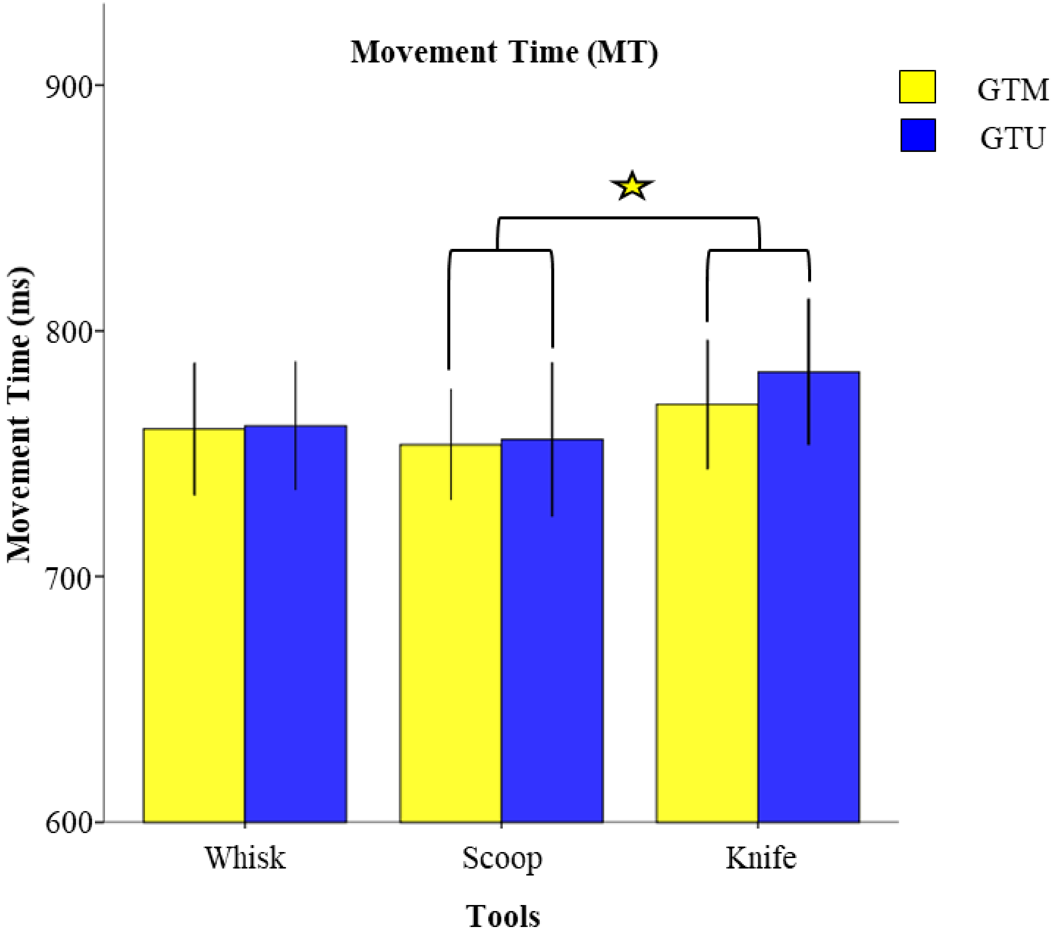


Figure 4.4 Graph depicts movement time. Bars indicate means for each tool in GTM (yellow bars) and GTU (blue bars). Error bars represent standard error of the mean (SEM). Yellow star denotes significant differences between conditions.

4.3.3 Peak velocity

No main effect of task ($F_{(1, 15)} = 2.390$, $p = .141$, $\eta_p^2 = .123$) or tool identity ($F_{(2, 34)} = .442$, $p = .646$, $\eta_p^2 = .025$) were observed (figure 4.5). However, we observed a significant interaction between task and tool identity for PV ($F_{(2, 34)} = 5.852$, $p = .007$, $\eta_p^2 = .256$). Within the GTM task, participants were faster when reaching to grasp the whisk (mean = 683.74) compared to the knife (mean = 664.86 mm/s, $p = .011$). When comparing GTM and GTU, participants were faster when reaching to grasp the knife in GTU (mean = 701.20 mm/s) compared to GTM (mean = 664.86 mm/s, $p = .034$).

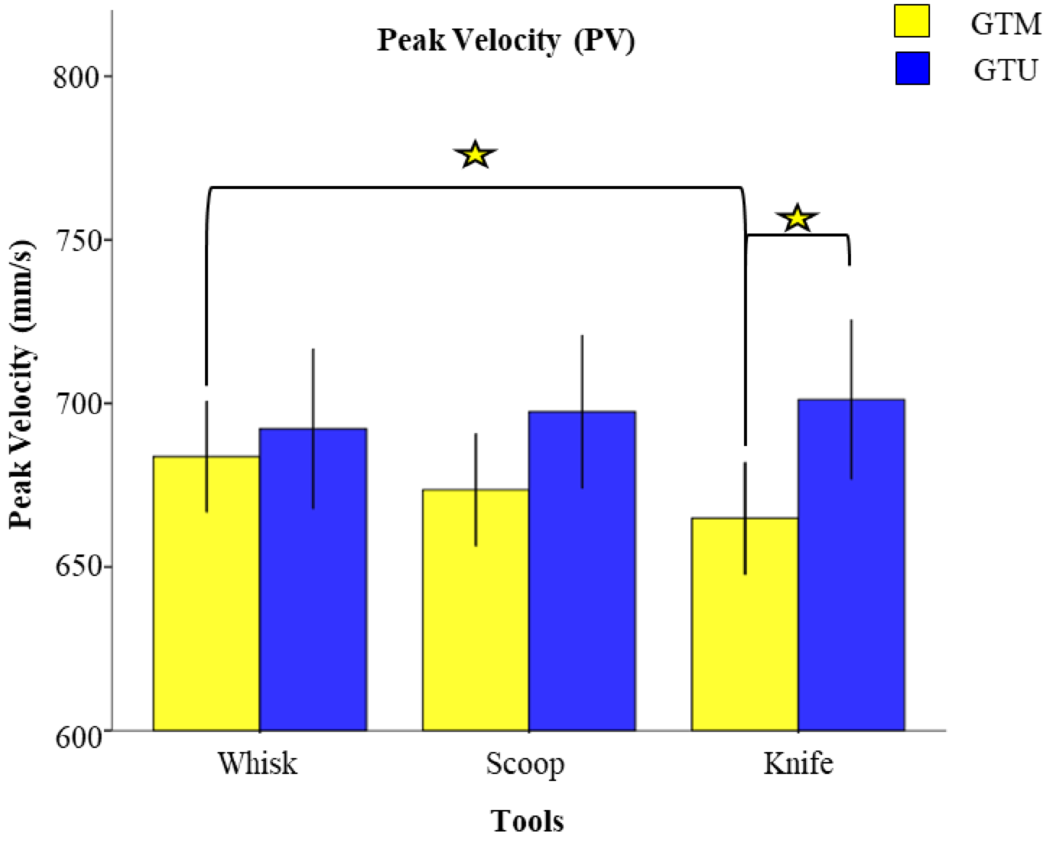


Figure 4.5 Graph depicts peak velocity (PV). Bars indicate means for each tool in GTM (yellow bars) and GTU (blue bars). Error bars represent standard error of the mean (SEM). Yellow stars denote significant differences between conditions.

4.3.4 Time to peak velocity

Regarding time to peak velocity (tPV), no significant main effects of task (F $_{(1, 17)}$ = .444, *p* = .514, η_p^2 = .025) or tool identity (F $_{(2, 34)}$ = 629, *p* = .629, η_p^2 = .027), nor significant interactions (F $_{(2, 34)}$ = 224.86, *p* = .366, η_p^2 = .057) were observed (figure 4.6).

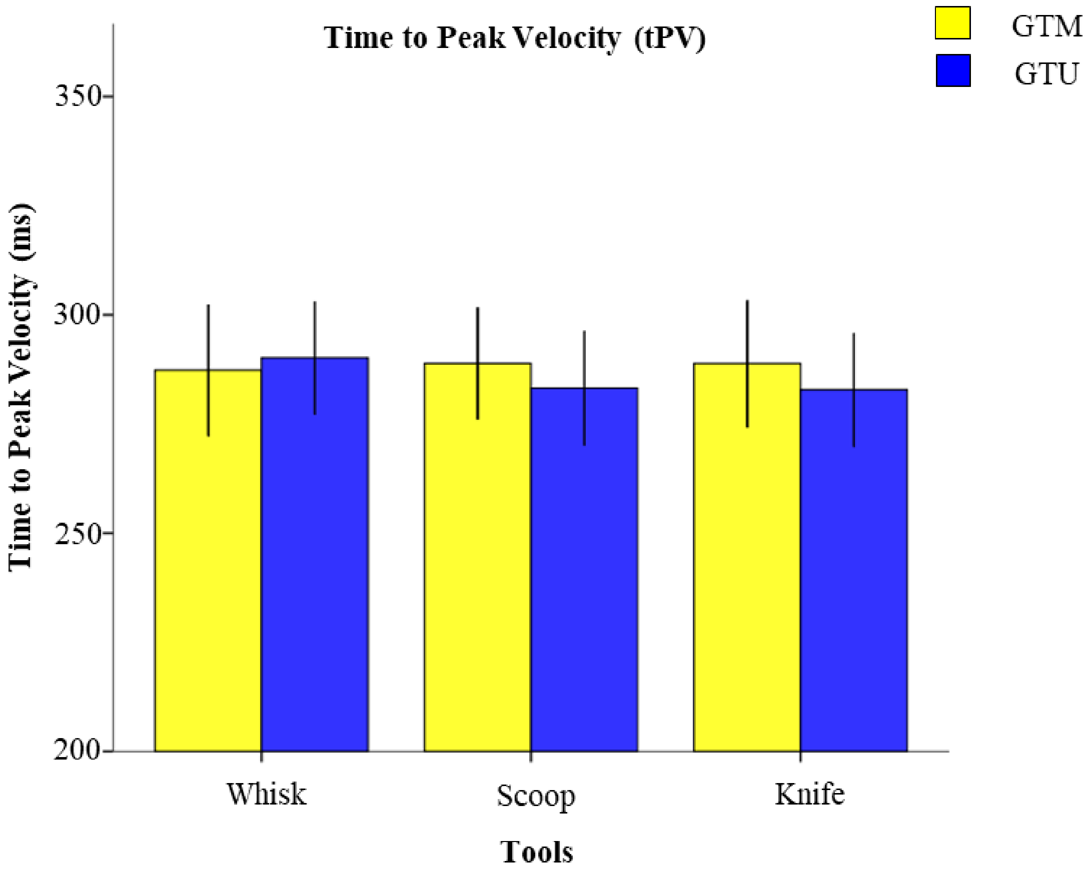


Figure 4.6 Graph depicts time to peak velocity (tPV). Bars indicate means for each tool in GTM (yellow bars) and GTU (blue bars). Error bars represent standard error of the mean (SEM). No significant main effect or interactions were observed for tPV.

4.3.5 Maximum grip aperture

For MGA, we observed significant main effects of task ($F_{(1, 17)} = 8.007$, $p = .012$, $\eta_p^2 = .320$) and of tool identity ($F_{(2, 34)} = 19.519$, $p < .001$, $\eta_p^2 = .534$). Participants opened their hand wider in the GTU (mean = 56.88 mm) compared to the GTM task (mean = 54.43 mm). Moreover, participants opened their hand wider for the whisk (mean = 56.62 mm) compared to the scoop (mean = 55.67 mm, $p = .019$) and the knife (mean = 54.67 mm, $p < .001$). In addition, participants opened their hand less wide for the knife (mean = 54.67 mm) compared to the scoop (mean = 55.67 mm, $p = .003$). No significant interactions were observed between task and tool identity ($F_{(2, 34)} = 1.394$, $p = .262$, $\eta_p^2 = .076$; figure 4.7).

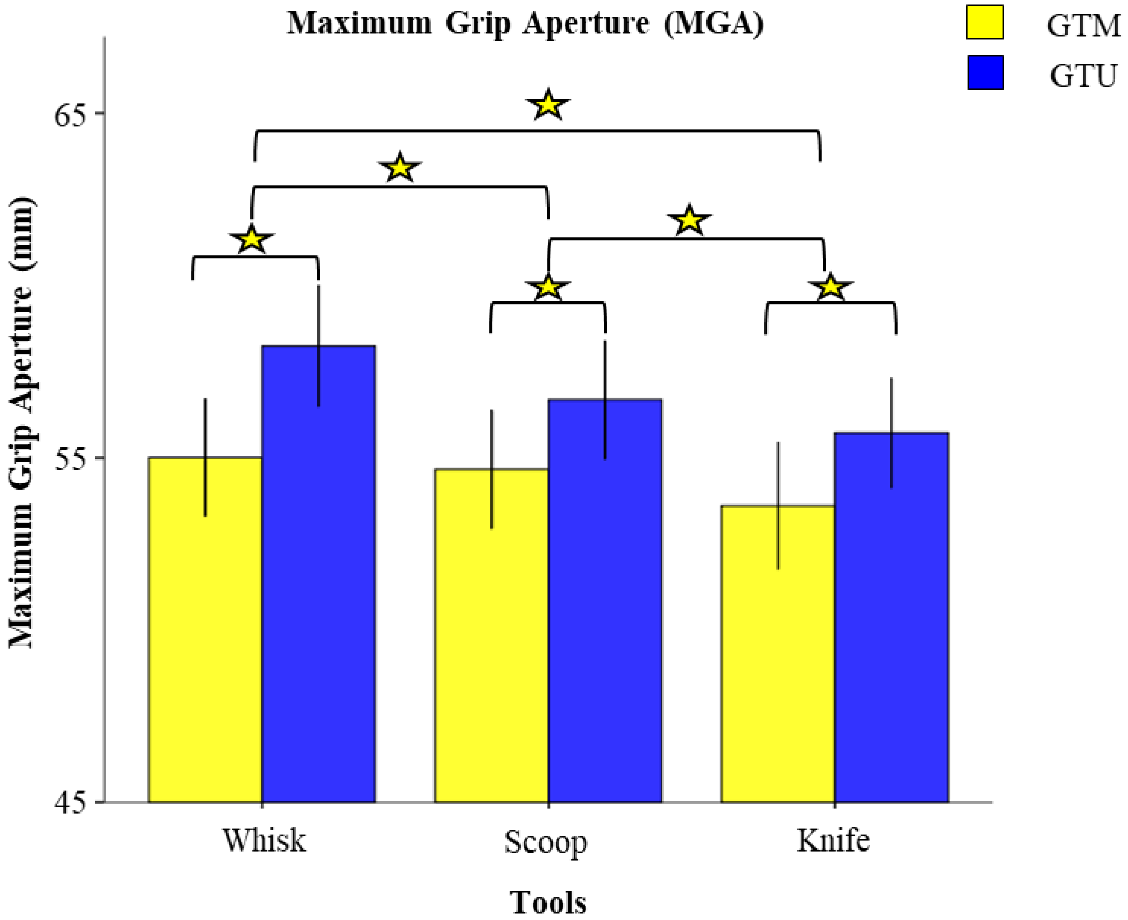


Figure 4.7 Graph depicts maximum grip aperture (MGA). Bars indicate means for each tool in GTM (yellow bars) and GTU (blue bars). Error bars represent standard error of the mean (SEM). Yellow stars denote significant differences between conditions.

4.3.6 Time to maximum grip aperture

We observed a significant main effect of tool identity for tMGA ($F_{(1.48, 25.22)} = 5.491$, $p < .017$, $\eta_p^2 = .244$). Participants reached earlier tMGA for the whisk (mean = 544.57 ms) compared to the knife (mean = 562.34 ms, $p = .028$). No main effect of task ($F_{(1, 17)} = 1.626$, $p = .219$, $\eta_p^2 = .087$) or interactions ($F_{(2, 34)} = 1.347$, $p = .273$, $\eta_p^2 = .073$) were observed (figure 4.8).

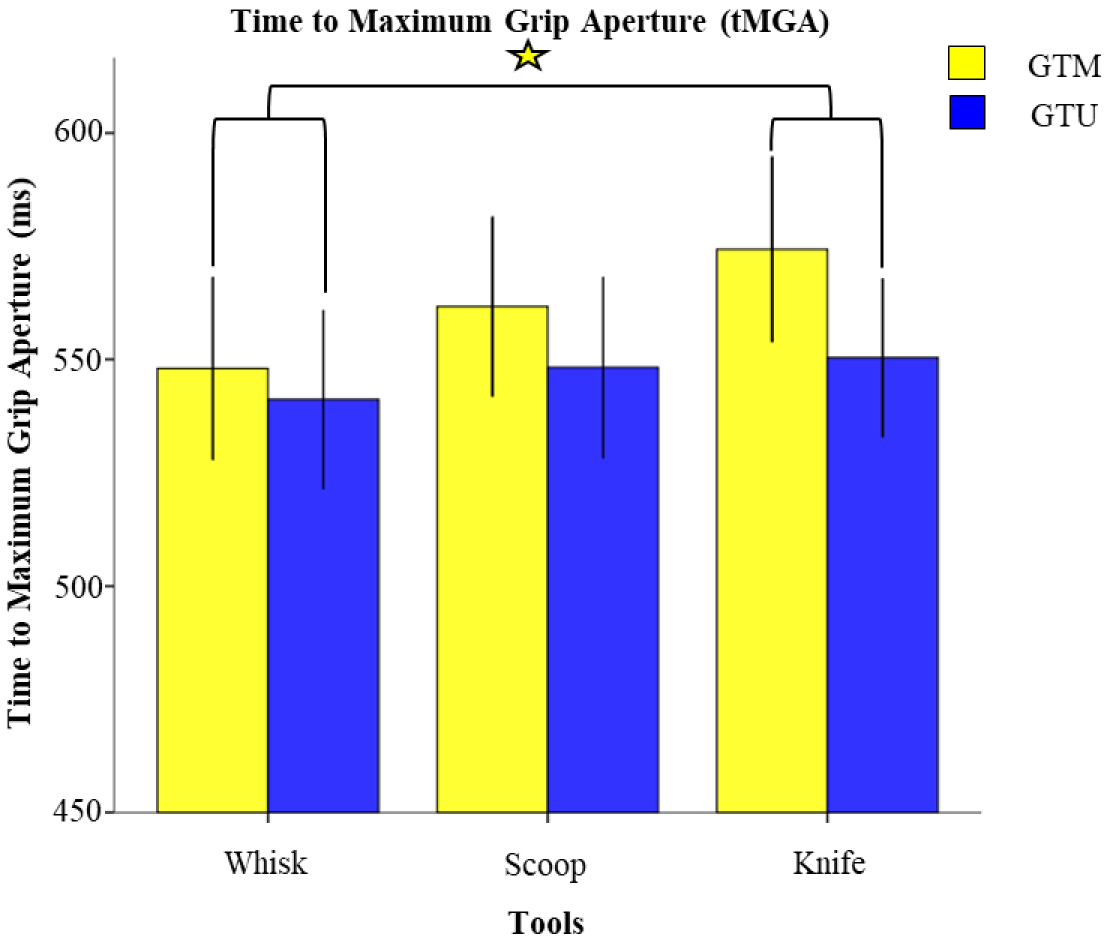


Figure 4.8 Graph depicts time to maximum grip aperture (tMGA). Bars indicate means for each tool in GTM (yellow bars) and GTU (blue bars). Error bars represent standard error of the mean (SEM). Yellow star denotes significant differences between conditions.

4.4 Discussion

To explore whether and how reach-to-grasp movements with familiar tools differ depending on whether they are grasped based on structural characteristic (e.g., size, shape) or the task end-goals, we implemented a GTM and a GTU task. Moreover, using different tools we were able to test whether tool identity influenced grasping kinematics of the reach-to-grasp movement in GTU and GTM. We show that the initial reach-to-grasp movement involved in tool-directed actions varies depending on the action following the initial movement and according to the identity of the tools.

First, our study confirmed that the end-goal of the action influences the initial reach-to-grasp movement when interacting with tools (see also Marteniuk, Leavitt, MacKenzie, & Athenes, 1990). In line with previous studies using shapes (Ansuini et al., 2008, 2006; Marteniuk et al., 1987) and more recently tools (Valyear et al., 2011; Cicerale et al., 2014), we observed distinct kinematics characteristics in the initial reach-to-grasp movements for GTU and GTM. We observed that in the GTU, where after the initial grasp participants had to functionally use the tools, participants opened their grip aperture wider compared to the GTM task. Consistent with previous findings, we suggest that MGA depends on the demands of the action following the grasp (Rosenbaum et al., 2009; Ansuini et al., 2008, 2006; Cohen & Rosenbaum, 2004; Marteniuk et al., 1987; Valyear et al., 2011). Thus, although all the tools had the same handle, the placement of the thumb and index finger at grasp closure might have been different between GTU and GTM to reflect a more comfortable position for the next steps of the action. This sensitivity toward comfortable and more controllable final goal postures is called end-state comfort effect. This effect was discovered by Rosenbaum while he was in a restaurant while having a meal. He spotted a waiter filling a glass with water (Rosenbaum et al., 1990). Each glass was inverted to begin with, so each glass had to be turned right-side up before he could pour water into it. Rosenbaum observed that the waiter grasped each glass with an awkward thumb-down grasp. However, as soon as the waiter turned the glass upright to fill it with water, the position of the hand was a less awkward thumb-up grasp, which was a comfortable, biomechanically controllable posture to fill the glass with water and place it back on the table. This suggested that the waiter was aware of the end-state of the action and was planning in advance his actions (Rosenbaum et al., 1990).

The end-state comfort effect was then tested by Rosenbaum et al. (1990) in the laboratory. They asked the participants to grasp a horizontally positioned bar and place either the left or the right end of the bar into a left or right target. The authors observed that regardless of the location of the target, participants, always used an overhand (e.g., palm facing down) grasp posture when the right end of the bar was to be placed into the target, while they always used an underhand (e.g., palm facing up), when the left end of the bar was to be placed in the target (Rosenbaum et al., 1990). The authors concluded that the initial grasp postures were selected so that the hand would end up in a more comfortable position at the end of the movement, when the bar was placed into the target (Rosenbaum et al., 1990) Subsequently, Cohen and Rosenbaum (2004) asked participants to take hold of a bathroom plunger and carry it from its initial position (at a fixed height) to a number of target shelves at varying height. They observed that participants grasped the plunger according to the final position: the higher the final position, the lower the grasp height. According to the authors, this indicates that participants planned their grasping posture based on the end-goal (Cohen & Rosenbaum, 2004).

Our results are in line with Valyear et al. (2011), which observed that grip apertures were wider in GTU versus GTM. The authors interpreted their results as evidence that the end positions of the index finger and thumb are different for GTU versus GTM. Valyear et al. (2011), plotted the relative 3-D position of the thumb and index marker at the end of the movement time separately for task and tool identity to look at the how the hand is positioned just prior to grasp completion (e.g., the hand position in space just prior to handle contact). They reported that for the GTM task, the thumb made contact with the surface of the tool nearer to the participant, while the index finger made contact with the top surface for all the different tools. While in the GTU task, although the orientation of the fingers was similar to the GTM task, the position of the finger along the handle were different and coincided with some of the kinetic features for the actions that follows. The authors concluded that for the GTM task, the index played a relatively passive role in both the reach-to-grasp movement and the movement following grasping, which is reflected into the smaller MGAs observed, while in the GTU task, the index finger was more actively involved (e.g., help maintain support).

To further explore this effect, we could analyse the position of the fingers when making contact with the objects. Moreover, to further test the hypothesis that MGA depends on the demands of the action following the grasp, we could ask participants to reach-out to grasp tools to lift them up. Only once they have started the movement (i.e., while they are reaching for the tool), a cue could instruct them to use or move the tool. As no information regarding the subsequent action is given during movement planning, if MGA depends on the action following the grasp, we would expect a similar MGA across tasks and tools, due to uncertainty of the task following grasp.

Perhaps surprisingly, we did not observe an effect of task on reaction times. We observed that participants consistently took longer to initiate GTU movements, which is consistent with the hypothesis that reaction times are thought to reflect the time taken to plan actions (e.g., Rosenbaum et al., 1992), this was not significant. Our findings are in contrast with Valyear et al. (2011), who observed that participants were much faster to initiate grasping for GTM versus GTM. However, there are differences between our task and Valyear et al. (2011), that might explain this. First, while they computed the RT as the time at which participants released the start button, we computed the reaction times based on motion tracking data. Specifically, we used the velocity marker and computed RT as the time at which the marker reached a velocity of 50 mm/s therefore our RTs rely on the velocity of the hand and might be less accurate than the RT obtained by button release. Second, due to the timing of the EMG, we had a longer preview than Valyear et al. (2011), which might have caused a ceiling effect in our data and explain why we did not find an effect of task on reaction times.

Moreover, we observed an interaction between task and tool identity for peak velocity. Specifically, we observed slower velocities for the knife in GTU versus GTM and faster velocities in GTM for the whisk versus the knife, which may be interpreted as in line with affordance suppression mechanisms (Ellis, Tucker, Symes, & Vainio, 2007; Tipper, Lortie, & Baylis, 1992; for a review see Thill, Caligiore, Borghi, Ziemke, & Baldassarre, 2013). Our results may be explained by the fact that different tools may afford a different number of actions, which could trigger different affordance suppression mechanisms. Specifically, the knife afforded more actions (median = 5 actions) than the whisk (median = 1 action), therefore participants were faster at grasping to move the whisk compared to the knife. Similar findings have been reported by Ellis et al. (2007), who investigated the effects of distractor affordances by adding a distractor next to the target. The distractor suggested a type of grasp that was either compatible or incompatible with the requested task response. They showed that the presence of a distractor led to faster reaction times when the distractor depicted incompatible affordances. In contrast, when the distractor depicted compatible affordances with the requested task response (e.g., type of grasp) it led to slower reaction times. The authors suggested that the inhibitory mechanisms that suppress the affordance elicited by the distractor interfered with the execution of the task actions (Ellis et al., 2007).

Here, we selected tools that triggered only few post-grasp actions, however, based on our observations, further investigations are needed. For example, in future experiments we should explore the affordance suppression mechanisms further by investigating grasping kinematics when participants are grasping to use tools to perform different actions associated with them. For example, to use the knife to cut and to use the knife to spread butter. If peak velocities between use the knife to cut and use the knife to spread were different, this might suggest that some actions might have stronger functional associations with a tool compared to other actions. To continue the example, if the peak velocity in use-to-cut was faster than in use-to-spread condition, this may suggest that when using the knife to spread, the cut action needs to be suppressed. According to the affordance suppression effect it may be related to the fact that the knife may be more strongly linked to the “cut” action, compared to the “spread” action.

A possible explanation is that when a tool is not grasped to be functionally used, affordances suppression mechanisms might be in place, to suppress the functional use in order to accomplish the task. This is in line with neurophysiological studies in monkeys, showed that two areas that are reciprocally connected (Rizzolatti et al., 1998), the anterior part of the intraparietal sulcus (AIP; Murata et al., 2000; Sakata et al., 1995) and F5 premotor areas (Murata et al., 1997; Rizzolatti et al., 1988), are involved in the control of grasping. Specifically, area AIP is supposed to send visual signals of object properties to area F5 for selecting the type of grip and the appropriate hand movements, and area F5 sends information of the selected motor command to area AIP (Sakata et al., 1995). Therefore, the exchange of information between these interconnected areas plays a role in the control of movement execution, such as matching the hand shape with the characteristics of the object and with the corresponding affordances (Gentilucci, 2002). Gentilucci (2002) proposed that the AIP-F5 circuit concurrently extracts all the possible affordances when an object is presented. Specifically, he proposed that within the AIP-F5 circuit, the motor representation of the whole object is coded, and that information is exchanged between the two areas until the grasp is accomplished. To further test this affordance suppression mechanism hypothesis, future experiments should look at differences when using the same tool for different functional end-goals (i.e., use a knife to spread butter and use a knife to cut) as well as for non-common use (e.g., use the knife to stir coffee) and atypical use (e.g., new learned movement). According to the affordance suppression account, higher velocities should be observed for common actions compared to atypical uses.

We observed a main effect of tool identity for movement time, grip aperture and time to grip aperture. The observation that tool identity affects the initial reaching and grasping movement is a novel finding. This suggests that regardless of task, the identity of the tools affects the kinematics of the movement even when all graspable parts (i.e., the handles) are the same size. Although effects on grasping kinematics between different objects in GTU and GTM tasks have been previously observed by Cicerale et al. (2014), they used tools with different size handles, therefore differences in grasping kinematics such as maximum grip aperture and time to peak velocity are interesting, but perhaps expected.

For grip aperture, we observed that participants opened their hand wider for the whisk, compared to the scoop and the knife and less wide for the knife compared to the scoop. As the MGA seems to increase when the tool head size increases, our results may be in line with previous suggestions that object affordances are not only affected by the portion of the object which the hand interact with (e.g., the handle), but by the whole object (e.g., business head; Gentilucci, 2002).

For movement time, participants took less time to complete the movement towards the scoop versus the knife, but no difference was observed between the whisk and the knife, nor between the whisk and the scoop. Previous investigations using wooden blocks have shown that grasping kinematics were strictly correlated to the width of the object being grasped (e.g., Goodale et al., 1994). As such, increases in object width led to an increase in movement duration, maximum grip aperture and the time at which this is achieved. However, the pattern observed in our data is different. Specifically, for maximum grip aperture we observed that participants opened their hands wider for tools with larger heads (e.g., whisk), compared to tools with smaller heads (e.g., knife) even if the handles they grasped were identical across all tools. This is a novel observation and could be interpreted in the view that the head end of the tool drives attentional orientation (Skiba & Snow, 2016).

For example, Skiba and Snow (2016), using a modified version of the Posner cueing task (Green & Woldorff, 2012), investigated whether attention is oriented towards the head or the handle of images of familiar elongated tools that have a strong action association versus control stimuli that are not associated with a specific function or motor routine, such as images of fruits and vegetables with a shape similar to the tools (e.g., knife – asparagus; peeler -chili pepper). In their task, participants were instructed to detect a target grey dot that appeared briefly near the handle/stem or head/tip of the target (either a tool or vegetable/fruit). They observed a lateralised bias in detection performance for the tool cues compared to the control stimuli (e.g., targets were detected more rapidly when they appeared near the head versus the handle of the tools). No attentional bias in favour of either end of the control stimuli was observed. Moreover, in a separate experiment, to provide evidence that tools are strongly associated with specific action routines compared to elongated fruits and vegetables, they took pictures of participants grasping the same tool and control stimuli used in the previous experiment. They then asked a separate sample of participants to judge the similarity of grasps performed with each object and results confirmed that grasps for the tools were significantly more similar than those for control stimuli. The authors concluded that attentional bias is toward the region of a tool that carry information about the identity and functional use (e.g., tool heads versus handles), and that the attention is drawn rapidly to the head of the tool to facilitate activation of specific motor routines that are linked to tool identity (Skiba & Snow, 2016).

A possible explanation for the observation that the tool identity affects grasping kinematics in our data is that affordances that are related to tool features, other than the handle, such as the business head, influence grasping kinematics. For example, in a series of experiments Gentilucci (2002) presented participants with two plastic fruits with a different shape, volume and weight (an apple and a strawberry) but with the same size and shape stalk. In one of the experiments, participants were instructed to grasp the stalk of the fruit and lift the fruit up. Although the stalks were the same size and shape, the author observed that the movement kinematics differed between object. Specifically, he observed an increase in peak velocity and acceleration as well as a decrease in reaction times when reaching the strawberry stalk compared to the apple stalk. On the other hand, he observed faster peak velocity of finger aperture and faster peak grip aperture when participants were grasping the apple stalk. The author suggested that hand shaping is wider and reach is faster when grasping larger wooden shape objects (Goodale et al., 1994; Jakobson & Goodale, 1991). The same results were observed when the fruit was larger despite the stalk being grasped was the same across fruits. Our results seem in line with this interpretation, as we observed that grip aperture decreased from the whisk to the scoop and the knife. In particular, participants automatically activated a reach-to-grasp motor program directed to the tool handle, however their grip was influenced by the shape and the size of the head of the tool. This observation might be linked to an attentional bias effect toward the region of the tool that indicates its identity and function as discussed above. To explore this hypothesis further, we could ask participants to grasp-to-use and grsp-to-move tool handles without the business head and cue participants by using either tool sounds or words. If the hypothesis of the attentional bias toward business head is true, then we would expect no effect of tool identity in MGA when no business end is available. However, if differences in grip aperture between tools are observed even if the business head is removed, it might be that MGA is influenced by manipulation and function knowledge associated with tools. Thus, the differences in MGA might reflect differences in the end posture necessary to use the object.

Moreover, Ambrosini and Costantini (2017) recorded eye movements while participants were looking at pictures of tools, graspable and ungraspable objects while their hands were either resting on the table or tied behind their back. They observed that participants mostly fixated first the action-related functional part of the tools (e.g., business head) versus the manipulation part (e.g., the handle), however, when participants had their hands tied behind their backs, this effect was significantly reduced. The authors concluded that how we visually explore objects, is biased towards action-relevant information (Ambrosini & Costantini, 2017; Handy et al., 2003). Our results complement and extend this finding by showing that grasping kinematics may be influenced by the functional part of the tools. Importantly, in Ambrosini and Costantini (2017), no overt movement towards the object were performed. Future investigations should look at eye movements during GTU and GTM. If differences in gaze behaviour across tools are observed, this might suggest that it is the functional knowledge of the stimulus that affects gaze behaviour towards tools. On the other hand, if differences in gaze behaviour across tasks are observed, this might suggest that different actions affect gaze behaviour. Additionally, if an interaction between tool and task is observed, this may suggest that according to the task, the functional knowledge of a tool may influence the gaze behaviour differently.

We also observed that participants took longer to complete movements towards the knife compared to the scoop and reached MGA earlier for the whisk compared to the knife, which seems at odds with the hypothesis that the MGA follows the size of the business head. As such, time to MGA and movement time usually increase as the object size increases (e.g., Goodale et al., 1994). Additionally, the surface area of a tool may influence kinematics (e.g., Goodale et al., 2006). As we used everyday tools, these were not matched for surface area and luminance. Although in real life it is unlikely that we interact with objects that are matched for surface areas, to disentangle the possibility of the effects being driven by the overall surface area of the tools, we could design tools with the same surface area and then 3D-print them.

However, there are other factors that we need to consider and that might have implications for our results. First, our tools had different weight, which could have influenced reach-to-grasp movements since the weight of objects play a critical role due to the different grip force required to functionally hold different tools (e.g., Gentilucci, 2002, Jeannerod, 1988). Although our tools had different weights, we could not identify a pattern in our results. In particular, although we observed shorter movements towards the heavier scoop, compared to the lighter-knife, and faster time to maximum grip aperture for the mid-weight whisk versus the lighter-knife, it is unlikely that our results could be explained by differences in the weight of the tools. In fact, if weight played a critical role on movement time and time to MGA, we would have expected movement time and time to MGA to increase as the weight of the objects increased. However, this was not the case.

Second, we need to take into account, the position of the centre of mass (COM). Goodale et al. (1994), observed that when meaningless shapes are grasped, the final position of the fingers tend to be influenced by the centre of mass. As such they used lines to connect the points were the thumb and index finger first made contact with the object and observed that these lines tended to pass through the COMs of the objects (Goodale et al., 1994).

Moreover, de Grave, Hesse, Brouwer and Franz (2008) examined fixation locations during reaching and grasping tasks to objects (e.g., flat shapes) that were either fully visible or that had the grasp location of the index finger, thumb or both partially occluded. They found that the first and second eye fixations on the objects were above the COM of the fully visible objects. Similarly, in the case of partially occluded objects, their fixation was above the COM calculated based on the object’s visible surface area. The author suggested that gaze locations are sensitive to COM location. Recently, Desanghere and Marotta (2015) examined grasp and fixation locations when grasping objects with different shapes and therefore different COMs. They observed both fixation and grasp locations were influenced by COM location. Specifically, grasp and fixation location were directed towards the location of the COM (Desanghere & Marotta, 2015). The authors concluded that object features differentially influence both gaze and grasp location (Desanghere & Marotta, 2015).

These findings are in contrast with Gentilucci (2002), who reported that the maximum grip aperture was not affected when grasping the handle (i.e., the opposition space) of objects with different COMs. However, while the objects used by Goodale et al. (1994), de Grave et al. (2008) and Desanghere and Marotta (2015), were simple shapes, with no obvious handle, the objects used by Gentilucci's (2002) had an obvious handle. In fact, he used a graspable rod (e.g., handle) attached to a sphere (body of the object). By manipulating the position of the sphere on the rod, he manipulated the position of the COM of the whole object. However, the COM of the handle was constant between the two objects, as the handle used was exactly the same. According to Gentilucci (2002), the difference in object used may explain the difference observed between his and previous experiments. Specifically, he suggested that it is the COM of the part of the object that is grasped that influences the grasp, and not the whole object. Thus, based on Gentilucci's (2002) observation, it is unlikely that the position of the COM affected the grasping kinematics in our experiment as the size of the handles was the same across the different tools. In future analyses it would be interesting to compute the COM to understand if any of our effects of tool identity could be related to differences in the COM between tools.

To conclude the present findings suggest that grasp kinematics are influenced by the subsequent action (Cicerale et al., 2014; Rosenbaum et al., 2009; Tucker & Ellis, 2004; Valyear et al., 2011) and the identity of the tool that will be grasped. Although we did not manipulate attention, a possible interpretation is that some attentional orienting mechanisms to the business head, versus the handle, might be involved. In fact, the MGA did not follow the size of the handle but seemed to follow the size of the business head of the tools. We propose that it is the business head that carries information about identity and function and is relevant for action planning and that drives the possibility for actions. To confirm this hypothesis, future studies are needed to address for the confounds identified here, such as weight, COM, size, shape and number of actions associated with each tool.

Chapter 5

5. General Discussion

5.1 Summary of findings

Hand actions constitute a critical link between perceiving our surroundings and interacting with objects within it. The goals of my thesis were to gain new insights into the behavioural and neural mechanisms underlying hand actions in different contexts combining different techniques. My approach focused on how we interact with both meaningless shapes (project 1) and familiar tools (projects 2 and 3), and on different actions we perform in our everyday life, such as grasping (projects 1 and 3), pantomime (projects 1 and 2) and actual tool use (project 3). My studies were designed for three main purposes: (i) to gain an insight on the role of key regions within the dorsal and the ventral visual streams in grasping and pantomiming (projects 1 and 2); (ii) to understand what specific aspects of objects and movements associated with them are represented within key regions in the two streams (project 2) and (iii) whether grasping made towards the same tool is influenced by the end-goal of the subsequent action and whether tool identity was processed in both grasp-to-use and grasp-to-move or not (project 3).

In Project 1 (chapter 2), we used fMRI-guided offline cTBS to assess the causal role of left aIPS, a key region for grasping in the dorsal stream, and left LO, a key region for object recognition in the ventral stream, in the control of real and pantomimed grasping. We found that cTBS-to-aIPS versus cTBS-to-vertex overall, weakened the relationship between grip aperture and object size. Furthermore, participants were scaling less efficiently in the pantomimed versus real grasping after cTBS-to-LO. These findings were taken to indicate that aIPS is causally involved in hand pre-shaping regardless of grasping task (real or pantomimed), while LO in the ventral stream is additionally required for pantomimed grasping. From a methodological point of view, we used a novel technique to identify brain regions for TMS. In particular, we extracted activations from the NeuroSynth (http://neurosynth.org/) database of previous neuroimaging studies and superimposed the activations onto each participants' high-resolution anatomical MRI images. Our results could be taken as a proof-of-concept evidence that using coordinates derived from numerous participants from previous neuroimaging studies can be effective to localise regions for future neuromodulation studies.

In Project 2 (chapter 3), to examine how and where in the human brain tool identity, structural (i.e., select the appropriate grip such as power grasp for tongs versus precision grasp for key) and functional manipulation knowledge (i.e., squeeze for tongs versus rotation for key) are represented we used fMRI multi voxel pattern analysis (MVPA). Moreover, we used a view and a pantomime condition to explore whether activity patterns in tool processing regions are modulated by the task. We found that different regions within the dorsal and the ventral visual streams represent tool identity, structural and functional manipulation knowledge. Moreover, we found that the tool network is modulated by the task. Specifically, we observed that decoding within the ventral stream regions was stronger for viewing than pantomiming, while decoding within the frontoparietal regions was higher for pantomiming than viewing.

In Project 3 (chapter 4), to explore how grasping kinematics are modulated by the subsequent movement, we implemented a grasp-to-move (GTM) and grasp-to-use task (GTU). All the tools had the same handles, this was done so that the structure of where they were grasped was kept constant across the two tasks. We found that participants opened their hand wider for the GTU compared to the GTM task. Tools had identical handles, thus, larger grip apertures for GTU versus GTM indicated that the end-goal of the action influence the initial reach-to-grasp movement. Moreover, using different tools we were able to test whether tool identity influenced grasping kinematics of the reach-to-grasp movement in GTU and GTM. We observed that different tool identities affected grasp kinematics of the reach-to-grasp movements. Specifically, the tools with the larger business head led to larger grip apertures, while the tools with smaller business head led to smaller grip aperture.

Overall, my studies show that both real objects grasping and pantomiming actions without the objects in hand require the left dorsal stream and that the left aIPS plays a critical role in hand preshaping. In fact, aIPS represents structural manipulation knowledge (e.g., power versus precision) even when simply viewing images of tools.

Additionally, area aIPS also contains information linked to functional knowledge (e.g., rotation versus squeeze) not only when overt movements are performed, but also when simply viewing images. However, when executing pantomime actions, my findings show that the ventral stream is additionally required, thus demonstrating that pantomime actions require both the dorsal and the ventral visual streams. Similarly, during tool use pantomiming, regions in the ventral stream represent tool identity, structural and functional manipulation properties. These findings are consistent with the idea that semantic knowledge (e.g., naming tools and retrieve experience of previous interactions with tools) need to be retrieved from the ventral stream to select the appropriate manipulation and functional properties (e.g., Frey, 2007). Although the aIPS performs visual analyses of objects for grasps, regions within the ventral stream could additionally provide the aIPS with additional resources (e.g., allocentric computations, conceptual and semantic knowledge) for its visuomotor computations. These findings provide further confirmation that although the dorsal and the ventral streams are two separate circuits, the anatomical separation between the two streams is not absolute. Connection between the two streams have, in fact, been reported between V4 and areas MT and lateral intraparietal, as well as between the anterior inferotemporal cortex and area AIP in monkeys (Borra et al., 2008). Similarly, in humans the dorsal stream is additionally divided into two subdivisions: a dorso-dorsal stream involved in reaching and grasping and a ventro-dorsal stream, which appears to underlie the processing of long-term object sensorimotor representations (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010). Our findings seem to fit well with the account that the dorso-dorsal stream is involved in grasping and is dissociated by the ventro-dorsal stream, which instead seems to be involved in actions that require knowledge of object use, such as tool pantomime and tool use. Moreover, both dorsal and ventral regions seem to contain information about tool identity (as shown in project 2), which also seems to be reflected at a behavioural level (as shown in project 3).

My general discussion is divided into sections. First, I will consider my findings with respect to the dorsal and ventral streams contributions to real and pantomimed grasping and in our everyday interactions with tools. Second, I will outline a few methodological and theoretical issues that should be taken into consideration when interpreting the findings of the current projects and I will offer some suggestions for future avenues based on the findings provided here. Third, I will discuss the impact and implications of my findings. Lastly, I will offer concluding remarks and highlight the new contributions offered by this thesis.

5.2 The role of the dorsal and the ventral stream in real and pantomimed grasping

In a seminal paper, Goodale et al. (1994) observed that in healthy controls, spatially displaced pantomimed grasping movements had lower peak velocities, lasted longer and had significantly smaller maximum grip aperture compared to real grasping. Moreover, they highlighted that pantomimed grasping performed by healthy participants resembled memory-guided grasping. The authors suggested that in contrast to object-directed grasping, spatially displaced pantomimed grasping requires participants to rely on the perceptual representation of the objects (Goodale et al., 1994). Additionally, compared to healthy controls, visual form agnosic patient DF performed poorly in the pantomimed task, but was unimpaired in real object-directed grasping. Based on these findings, Goodale et al. (1994) suggested that the transformations underlying spatially displaced pantomimed grasping are mediated by the ventral visual stream, while real grasping is mediated by the dorsal stream.

Subsequently, Cohen et al. (2009) applied TMS to either left LO or left aIPS. They found that TMS to left LO impaired delayed grasping, but TMS to aIPS impaired both immediate and delayed grasping. Specifically, they concluded that while LO was causally involved in delayed grasping, aIPS was causally involved in both real and delayed grasping. Our results seem in line with Cohen et al.'s (2009) observations, however, we concluded that area aIPS is necessary in both real and pantomimed grasping in hand preshaping, even when the pantomimed action is executed in real time (without a delay). In contrast, LO is involved in hand preshaping only for pantomimed grasping. Importantly, in our task, no retrieval of information from memory was necessary, as the object was in front of the participants. Therefore, LO seems to be additionally involved in grasping alongside the aIPS, not only when information about the object is retrieved from memory (e.g., delayed pantomimed grasping), but also when the action is performed in real time and no memory is required. Moreover, based on our results we demonstrate for the first time that aIPS is causally involved in hand preshaping to object size specifically. In fact, previous TMS studies in aIPS only report effects on timing and velocity variables (Cohen et al., 2009; Rice et al., 2006; Rice et al., 2007; Tunik et al., 2005).

Although we provide some support to Milner and Goodale's account of the two visual streams (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006, 2008) as we show that the dorsal visual stream is necessary to real grasping, our data indicate that for successful pantomiming, even in real time, both visual streams are required. We suggest that some refinement of the model is necessary to account for these new findings in grasping simple shapes. Milner and Goodale (1995; 2006; 2008) proposed that there may be particular action contexts in which the ventral and the dorsal streams must interact, such as when grasping tools. As such, when DF was observed selecting the comfortable wrist orientation and end-position when grasping objects (Dijkerman, McIntosh, Schindler, Nijboer, & Milner, 2009) or grasping and using tools (Carey et al., 1996), DF's grasping behaviour was impaired. Based on these observations, in a critical review, van Polanen and Davare (2015) suggested that increased functional interactions are needed for tasks that require more complex processing of the object conceptual knowledge. Based on our results from project 1, we could speculate that the two streams are interacting, not only when conceptual knowledge is critical to complete the task, but also when perceptual information (e.g., allocentric coordinates) about the object is required. Indeed, our decoding results from project 2 seem to be in line with the van Polanen and Davare (2015) account: representations for both tool identity, tool structural and functional manipulation knowledge of how grasp and use tools were found in regions within both the ventral and dorsal stream for viewing tools and for pantomime movements.

5.3 The role of the dorsal stream in tool processing

The findings from projects 1 and 2 fit rather well with previous neuroimaging results. Specifically, Lewis (2006) in a meta-analysis of tool related neuroimaging results from 35 studies involving 64 different paradigms, distinguished between a motor skill network and a tool conceptual semantic network. Lewis (2006) identified a motor skill frontoparietal network bilaterally, but with a strong left-hemisphere lateralization and includes regions such as the SPL and the IPL, the PMd and PMv. The motor skill network is involved in the retrieval and production of tool-use motor skills, such as reaching, grasping and manipulating tools (e.g., using a precision grasp to pick-up a key or using a power grasp to pick-up a corkscrew). On the other hand, the conceptual semantic networks, includes the left inferior frontal gyrus (IFG), the left pMTG and the bilateral fusiform cortex and is involved in processing inputs and semantic representations (e.g., tool identity and tool function) and associated motor output representations, such as how tools should be used (e.g., the key is for opening a door, the corkscrew is for opening a bottle). More recently, Valyear, Fitzpatrick and McManus (2017) performed a meta-analysis of 16 published studies of grasping and 11 published studies of pantomime and/or actual tool use with the right hand by right-handed individuals. The authors observed that there are both shared and separate neural representations underlying grasping and tool use. They observed that the aIPS and the PMd were both involved in grasping and tool use. Conversely, SMG, fusiform gyrus and pMTG were associated solely with tool use. The fact that aIPS is involved in both grasping and tool use fits well with our results from projects 1 and 2. Also, we could decode tool identity, tool manipulation and function knowledge in the pantomime tool use task, in the regions identified by Valyear et al. (2017) – excluding the fusiform gyrus which was not included in our ROIs.

Moreover, project 2 involved passive viewing of tool images. Comparing the pantomime task and the viewing task, we observed that regions in the motor skill network showed higher decoding accuracy for the pantomime task, while regions within the conceptual semantic network, showed higher decoding accuracy for the view task. This is in line with the account that tool use pantomimes are expected to involve dorsal stream areas more strongly, while passive viewing is expected to involve perceptual areas in the conceptual semantic network more. However, as shown in project 1, pantomimes require both streams to cooperate, and so does tools use, as it requires the integration of both motor (e.g., how tool is grasped), semantic (e.g., naming tools and experience of previous interactions with tools) and conceptual (what it is and what it is used for) knowledge (e.g., Frey, 2007; Orban & Caruana, 2014). This is also reflected in decoding accuracy in project 2. In fact, we could decode tool identity and functional manipulation knowledge in most of the ventral stream regions and posterior parietal cortex regions for tool pantomimes, which is in line with the idea that tool use requires ventral stream inputs as well as that these inputs reach the dorsal stream through the ventro-dorsal stream (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010). Additionally, for tool structural manipulation knowledge, we observed decoding, mainly in frontal and parietal regions. This observation fit well with the account of a subdivision in the dorsal stream between a grasp and a use system (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010) . As such, the dorso-dorsal stream is specialised for responding to physical and structural (e.g., shape, size, location) object's properties rather than semantic and conceptual information (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010; Pisella et al., 2006). The fact that we observed decoding for tool structural manipulation knowledge, mainly in the frontoparietal network versus the occipitotemporal network, is consistent with its specialisation for prehensile actions, such as grasping, with tools. Additionally, we observed patterns of activity that represented functional manipulation knowledge in the dorsal stream which is consistent with the account that the ventro-dorsal stream, is considered a function system and relies more on long-term representations of interactions with tools (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010; Pisella et al., 2006).

Moreover, results from project 2 are in line with the view that action plans and the motor system can be activated by the mere presence of visual stimuli, as proposed by the theory of motor affordances (Gibson, 1979). In fact, we have shown significant decoding of tool identity even in the motor cortex even simply viewing tool images. Evidence from monkey neurophysiology has shown that visual object properties such as size, shape and orientation, activate the corresponding motor representation in frontoparietal neurons that code for these properties to control the grasping movement (Murata et al., 2000; Rizzolatti et al., 1988; Taira et al., 1990). However, when we grasp tools in our surroundings, these can be grasped based on their structural properties (e.g., size, shape, orientation) to be moved from one place to another (e.g., grasp-to-mover, GTM) or they can be grasped based on their function (e.g., a knife is for cutting; grasp-to-use, GTU).

Additionally, in project 3 we tested whether grasps made towards the same tool are influenced by the end-goal of the subsequent action and whether tool identity is processed in both GTU and GTM or not. At a behavioural level, we observed that grasping kinematics are influenced by tool identity for both GTU and GTM. Similarly, we could decode tool identity in both ventral and dorsal stream regions when people viewed images of tools and pantomimed tool use in project 2. Taken together, these results seem to suggest that actions with tools depend on inputs from the ventral stream, important for the specification of tool identity and stored use knowledge. In other words, in contrast to simple meaningless shapes, efficient tool grasping requires recognition of what the tool is and its function. Tool identification is necessary to successfully use tools, and requires information regarding both what the tool is and what the tool is for, which are information processed in the ventral stream, including the MTG. As a result, cortical regions within both the dorsal and the ventral pathway are involved in processing tools.

How does our results fit with Milner and Goodale's model (1995, 2006, 2008)? Evidence for the involvement of the dorsal stream in vision-for-action came mainly from inferences based on the behaviour observed in patient DF. However, in the last decade it has become clearer that patient DF's lesions extend beyond her ventral stream (e.g., Bridge et al., 2013; James et al., 2003; Rossit et al., 2017). Moreover, the role of the dorsal stream as a visuomotor network has been challenged, with growing evidence of the existence of object perceptual representations in the posterior parietal cortex (e.g., Bracci & Op de Beeck, 2016; Freud et al., 2017; Konen & Kastner, 2008; Van Dromme et al., 2016; for a review see Freud, Plaut, & Behrmann, 2016). For instance, Konen and Kastner (2008), investigated the neural representations related to different types of object images (i.e., images of 2D and 3D objects, line drawing and images of tools) which were presented under different viewing condition (e.g., from a range of 0° to 75° rotation to recreate different viewpoint) and with different sizes. The authors implemented fMRI adaptation, in which repeated presentations of the same stimuli lead to gradual response reductions as a function of the frequency of repetition. The authors found object-selective responses in areas within the ventral and dorsal visual pathway, which seemed to generalise across the type of stimuli. Specifically, while object-, size- and viewpoint-selective responses were observed in intermediate processing stages areas in the ventral stream (e.g., V3A, MT and V7), high-order areas in the lateral occipital (LO) and the posterior parietal cortex (posterior IPS), responded selectively to objects independently of the size or the viewpoint, however, no object-selective responses were observed in the anterior part of the IPS. The authors suggested that objects are represented in the dorsal stream and that these representations seemed to mirror the responses in LO. Thus, the authors concluded that, contrary to the two visual system model, object information may be processed similarly in the dorsal and ventral visual pathways.

Further evidence that object-selective responses are observed in dorsal stream regions, even for tasks that do not require overt movements came from a study with patient suffering visual object agnosia, after ventral occipitotemporal cortex lesions (Freud et al., 2017). To explore whether object representations in the dorsal stream are independent from ventral steam representations, Freud et al. (2017), presented patients and healthy controls with greyscale 3D line-drawing possible and impossible objects (e.g., objects that could exist in 3D space, versus objects that could not exist in 3D space). The authors found that despite a reduction in the sensitivity to object structure in the ventral stream, regions in the dorsal stream showed differential activations to the two classes of objects. In a behavioural examination, although the patients were impaired in object perception, they showed sensitivity to object-based structural information (e.g., showed faster reaction times for possible versus impossible objects). The authors concluded that the dorsal stream mediates visual information to generate object representations that are independent from the ventral stream. Although the dorsal stream was differentially activated by the two object categories, but the patients were still profoundly impaired in perceptual tasks, the authors concluded that the object representations in the dorsal stream are not sufficient for object perception and that these representations may support the processing of object-related structural information. Thus, it has been proposed that while the dorsal stream is critical in visuomotor control and the ventral stream in visual perception, both processing streams contribute to the representation of what we perceive in the surroundings (Freud et al., 2016). According to Freud et al. (2016), this account fits well with the evidence that the dorsal stream is sub-divided in two sub-networks, of which the ventro-dorsal plays a role in visual perception.

The results in this thesis seem to support the view that visual perception is not only a characteristic of the ventral stream, but that also the dorsal stream plays a role in visual perception. In fact, results from project 2 show that tool identity is processed in dorsal stream regions even when no overt movement is required. Additionally, our results from project 3 show that tool identity affects grasping kinematics, even if the structural properties of the handle were the same across tools. Thus, we suggest that vision-for-perception may not be a characteristic of the ventral stream alone, but of both streams.

5.4 The role of the ventral stream in tool processing

The results from project 2 showed several regions within the ventral visual pathway that represent tool identity, structural and functional manipulation knowledge. Thus, perceptual areas in the ventral visual streams may process not only semantic information related to the identity of tools, but also manipulation information in both the view and the pantomime task. In fact, in our view task, participants were instructed to simply view the images, and yet, it was possible to reliably decode different patterns of activity related to how tools were grasped (e.g., power versus precision) and even used (e.g., rotation for opening a door versus squeeze tongs to pick up salad leaves). Additionally, in project 3, even when structural differences between tools were controlled for, tool identity had a significant impact on grasping. These results seems to be in line with the account that the ventral stream and the dorsal stream exchange information, and that the ventro-dorsal stream is likely to act as an interface between both visual streams (Binkofski & Buxbaum, 2013).

However, how is this consistent with the model of tool use and the two visual streams hypothesis proposed by Milner and Goodale (Goodale, 2014; Milner & Goodale, 1995, 2006, 2008)? Milner and Goodale proposed that tool use involves the cooperation of both the dorsal and the ventral stream and described this cooperation using an analogy with the model of tele-assistance for the remote control of robots. In this view, they hypothesised that the ventral stream plays a role in identifying objects in the scene using a rich perceptual representation system, that is however not metrically precise. Specifically, it has been postulated that the perceptual mechanisms in the ventral stream participate in the identification of specific goals in the surroundings and then flag the relevant tool in the scene to the visuomotor mechanisms in the dorsal stream (Goodale, 2014; Milner & Goodale, 2006). Then, dedicated visuomotor networks in the dorsal stream with their precise egocentric coding of size, shape, location and orientation process information to perform the expected motor act. Milner and Goodale (Goodale, 2014; Milner & Goodale, 2006), postulated that tools are processed in parallel by both streams for different purposes. Specifically, while the ventral stream selects the goal object from the scene, the dorsal stream processed the metrical computations for the goal-directed actions. However, they did not make clear predictions regarding the role of the dorsal and the ventral stream in tool processing.

In the context of the perception and action model (Milner & Goodale, 1995, 2006), our finding that action-related information are represented in the ventral stream, would be rather surprising. Traditionally vision-for-action has been described as a characteristic of the dorsal stream, while areas in the ventral stream are traditionally assumed to serve perceptual roles (e.g., object identification, shape recognition; Grill-Spector et al., 2001; Grill-Spector & Malach, 2004; Malach et al., 1995). However, recent lines of research have shown that the LOTC also represents several aspects of action, including representing overt actions, perceiving tools and hands and use-related gestures (e.g., Bracci et al., 2016; Gallivan et al., 2013; Oosterhof et al., 2012; Perini et al., 2014; Valyear & Culham, 2010; for a review see Lingnau & Downing, 2015). In the monkey brain it has been shown that LOTC shares direct reciprocal anatomical connections with the aIPS in the dorsal stream (Borra et al., 2008; Borra, Ichinohe, Sato, Tanifuji, & Rockland, 2010). Similarly, in the human brain it has been consistently shown that viewing, pantomiming, and using tools induces activations in parietal and occipitotemporal areas (e.g., Lewis, 2006). Moreover, Bracci and colleagues (2011; 2016) have shown that also images of hands activate areas in parietal and occipitotemporal regions. Similar to these previous studies, we found a network of areas in parietal and occipitotemporal areas that were preferentially activated for tools and hands. However, while activity patterns in tool- and hand- selective occipitotemporal regions revealed significant decoding for tool identity, structural and functional manipulation knowledge in both tasks, only functional manipulation knowledge was significantly decoded above chance in tool- and hand-selective parietal areas in both tasks. Additionally, especially in tool-selective regions, decoding was modulated by task: while IPS-tools showed higher decoding accuracy for tool identity, structural and functional manipulation in the pantomime task, LOTC-tools showed higher decoding accuracy for tool identity and functional manipulation knowledge (but not structural manipulation knowledge) in the viewing task only. In contrast only IPS-hands showed higher decoding accuracies in the pantomime task for tool identity and functional manipulation knowledge, while LOTC-hands showed similar decoding accuracy in the two tasks. Thus, our results suggest that both streams represent properties of the tools that are linked to perceiving tools and motor information and that these are modulated by the task. Although there are similarities between the representational content in LOTC and IPS, there are also differences: specifically, while occipitotemporal areas seems to decode motor and functional related properties of tools from view and pantomime (e.g., tool identity, structural and manipulation knowledge), parietal regions seem to decode motor properties linked to the structure of the tools (e.g., structural manipulation knowledge) preferentially form the pantomime task. The observation that these regions are modulated by task suggests that although both IPS and LOTC represent functional and motor related properties, the posterior parietal cortex shows a preference for motor properties while the ventral stream shows a preference for functional properties.

One could however argue that the action-related representations may be linked to semantic representation in the LOTC associated with the meaning of tools. Although we cannot exclude this based on our results, this is quite unlikely. In line with our proposal, Gallivan, Chapman, Mclean, Flanagan and Culham (2013) reported decoding of action planning in the occipitotemporal cortex while participants were reaching and grasping 3D blocks. Moreover, Valyear and Culham (2010) suggested that prior to tool actual use, the ventral stream needs to provide information to parietal areas about tool semantic knowledge, identity, function and how to move or use it (Creem & Proffitt, 2001; Milner & Goodale, 1995, 2006, 2008). In this view, it is likely that the ventral stream identifies the part of the tool relevant for grasping and the subsequent action to then end the information to the dorsal stream. Our results from project 3 seems to fit with this view. As such, we observed that grasping tools (based on structural and functional properties) requires the computation of anticipatory kinematics parameters that need to take into account the subsequent movement typically associated with the tools being grasped. As Milner and Goodale (Goodale, 2014; Milner & Goodale, 1995, 2006, 2008) pointed out, acting with tools requires both streams to interact to mediate the final motor output.

A region that is likely to play a critical role in processing tools in the occipitotemporal cortex is the pMTG. In project 2 we observed that pMTG coded for tool identity, functional and structural manipulation knowledge in the pantomime task, whereas only tool identity and functional manipulation knowledge were decoded within this region in the view task. Moreover, selectivity for tools in pMTG has been shown in different tasks and contrast (Lewis, 2006) and may represent the region in which multiple information form separate modalities are integrated (e.g., Beauchamp, Lee et al., 2004). For example, motion is also an important attribute of tools and Beauchamp et al. (2002), observed that pMTG showed preferential responses to tool versus body motion and proposed that tool selective pMTG may play a specialized role in processing the typical motions of tool in action (Beauchamp & Martin, 2007). Evidence from monkey neurophysiology suggests possible correspondence between activity in the monkey superior temporal sulcus (STS) and tool selectivity in the human pMTG. For example, STS neurons in monkeys are responsible for the multimodal integration of sight and sound of actions (Barraclough et al., 2005) and similarly, the human pMTG shows similarity for both viewing and hearing tools in action (Beauchamp, Lee et al., 2004). Moreover, both neurons in the monkey STS (Barraclough et al., 2009; Perrett et al., 1989; Perrett et al., 1990) and in human pMTG (Valyear & Culham, 2010) show sensitivity to action intentions. Thus, human pMTG is likely to be the homologous of the monkey STS (Jastorff, Popivanov, Vogels, Vanduffel, & Orban, 2012; Orban & Caruana, 2014; Orban et al., 2004). According to the subdivision of the dorsal stream into a dorso-dorsal and a ventro-dorsal stream, it is thought that regions within the ventro-dorsal stream, such as pMTG and SMG, represent an interface between the ventral and the dorsal stream for the visual processing of information (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010; Pisella et al., 2006). The SMG is involved in recognition, naming and actions performed with tools and is thought to represent tool information, including semantic representation for tools and functional manipulation knowledge (Buxbaum, 2001; Ishibashi, Pobric, Saito, & Lambon Ralph, 2016; Johnson-Frey et al., 2005). Anatomical connectivity studies have shown that regions involved in tool processing and use in the left hemisphere are interconnected: specifically, it has been shown that SMG is connected to pMTG and PMv (Ramayya, Glasser, & Rilling, 2010). Based on the fact that the connections between SMG and pMTG were strongly left-lateralised, Ramayya et al. (2010), suggested that the SMG integrates spatial (e.g., position of the hand and fingers) and semantic information to generate actions plans. This account is consistent with our data from project 2 in which we observed that SMG represents tool identity, functional and structural manipulation knowledge in the pantomime task and also with previous studies that show that the IPL is involved in integrating information from the dorsal and the ventral stream (e.g., Buxbaum, Kyle, Grossman, & Coslett, 2007).

In sum, results from projects 2 and 3 suggest that ventral stream processing is important for everyday interactions with objects, specifically tools. Results from project 2 clearly show that regions within the ventral stream code both tool identity and action-related properties (e.g., grip and functional movements). Based on the results observed in the two tasks, we can speculate that these findings can be extended to real tool use. Specifically, we propose that the ventral stream provides information related to structural and functional manipulation knowledge based on previous interactions.

5.5 Limitations and future directions

In project 1 we showed that both aIPS and LO are causally involved in pantomimed grasping, whereas LO is causally involved in pantomimed grasping only. Although it is established that using TMS combined with behavioural experiments allows to conclude that the relationship between brain activity and behaviour causal (e.g., Pascual-Leone, Walsh, & Rothwell, 2000), there are limitations associated with the technique. In fact, transient disruption of a given cortical region provides us information not only about the causal role of that specific region but also about the capacity of the rest of the brain to adjust to it (Lomber & Payne, 1996; Pascual-Leone et al., 2000). For example, Mottaghy et al. (2000), combined PET and TMS to investigate the role of the prefrontal cortex in working memory and observed that the performance in the task was equally disrupted by TMS to the left or the right dorsolateral prefrontal cortex. However, PET analysis revealed differences in the brain activity associated with performance in the task between TMS applied to left and right dorsolateral prefrontal cortex. These examples confirm that TMS produces temporary functional lesions and that these are associated with different behaviours. However, it also highlights that disrupting cortical activity in a given region may have effects on a network of regions that are not directly targeted by TMS but are involved in the task. In our experiment, based on our results and previous neuropsychological and fMRI evidence, we concluded that aIPS is involved in grasping under real and pantomimed grasping. However, it might have been the case that by disrupting the aIPS we were actually disrupting its connections to other regions within the network, such as PMv, resulting in the observed impaired behaviour. For example, Davare et al. (2006) used TMS to dissociate the role of PMv and PMd in grip-to-lift movement and reported that a virtual lesion to the left PMv resulted in a more variable position of the fingers on the object versus TMS to PMd and the control condition (e.g., M1). In contrast, a virtual lesion to PMd resulted in a longer delay between the contact of the second finger with the object and the subsequent lifting movement. Thus, the authors concluded that the PMv played a role in the visuomotor transformation required for hand posture configuration. A similar account could be applied to LOC. Future investigations could combine TMS, neuroimaging and behavioural investigations to track the changes of activity over a widely distributed network linked to an observed behaviour. Moreover, by using TMS to transiently modulate different regions within a specific network, it would be possible to evaluate the different involvement of the regions that constitute the network throughout. To further complement our TMS findings, it might be necessary to implement fMRI, EEG or MEG. For example, whilst examining the role of different regions in grasping, it would be interesting to compare the effects of TMS in the dorso-dorsal grasping subnetwork which includes aIPS and PMv. Moreover, as during pantomimed grasping, LO in the ventral stream is additionally required, it could be beneficial to investigate whether the effect may be related to the fact that we disrupted connections with the ventro-dorsal stream. In fact, future studies could explore connectivity between the ventral and the ventro-dorsal stream for the tasks we used here.

Another limitation of our study was that the object was not visible during grasping (e.g., movements were performed in open-loop), therefore online visual feedback of the approaching hand was not available. Since the two visual systems hypothesis (Goodale, 2014; Milner & Goodale, 2008, 1995, 2006) states that the dorsal stream controls movements through online visual control in an egocentric frame of references, it remains unclear from our results whether the same results would be found under full vision. However, Westwood and Goodale (2003) instructed participants to grasp a rectangular object that was presented beside a smaller, larger or same size object in front of them and initiate their grasping movement in response to an auditory tone which was given either at the end of the preview (no-delay group) or after a delay (delay group). In both groups, two visual conditions were interleaved. In the no-delay group in the vision trials, vision was available from the cue to movement onset, whereas in the no-vision trials vision was occluded coincidentally with the cue. In the delay group, vision was occluded during the delay following the preview in the vision and no vision condition. However, in the vision trials, vision was restored at the cue, while in the no vision trials, vision was not restored. The authors showed that the presence of a second object did not affect peak grip apertures on the vision trials for either the no-delay or the delay group, but it did affect peak grip aperture in the no-vision condition. Specifically, in the no-vision trials, grip aperture was larger when the target object was accompanied by a second smaller object and was smaller when the target object was accompanied by a larger object. In addition, they showed that this effect was larger in the delay group compared to the no-delay group. As the differences between the vision and the no-vision condition was that in the vision condition vision was occluded at the movement onset, thus allowing participants to use vision to plan the movement, whereas in the no-vision condition, vision was occluded at the time the cue was given, thus forced participants to rely on perceptual information of the target. Based on these results, the authors suggested that the dorsal stream operated in real time, transforming the visual information from the target into motor programs at the moment the action was required. However, if the target object was not visible when the action was required, the dorsal stream required additional perceptual information stored in the ventral stream. In other words, as long as the object is available during the planning phase, the movement should be performed with information from the dorsal stream only. It would be interesting to explore the role of the ventral stream in planning and executing pantomimed grasping movements. In fact, from our results it is unclear whether the ventral stream is involved in the planning or in the control of pantomimed grasping. Further studies implementing TMS to LO at different stages during the planning and the execution of the movement in pantomimed grasping may be informative about the role played by the ventral stream.

Here we show that aIPS contributes to both real and pantomimed grasping. Perhaps this happens as perceptual information from the ventral stream reaches the dorsal stream, and here merges with action information to control online grasping (as suggested by Cohen et al., for real and delayed grasping). This observation presents a new question: how are LO and aIPS interconnected during grasping? Important insights as to how the two streams interact come from connectivity studies in monkeys which describe how the ventral inferior temporal area projects to both the inferior parietal lobe (Zhong & Rockland, 2003) and the prefrontal cortex (Borra et al., 2010; Gerbella, Belmalih, Borra, Rozzi, & Luppino, 2011) but also how area AIP projects to the temporal gyrus (Borra et al., 2008). fMRI studies in humans reported that the dorsal and the ventral stream showed strong functional connectivity during object recognition between the SPL in the dorsal stream and the temporal pole in the ventral stream (Sim, Helbig, Graf, & Kiefer, 2015) and between the left medial fusiform gyrus and the left IPL (Mahon, Kumar, & Almeida, 2013), but also between hand/tool LOTC with left parietal and premotor cortex in response to hands and tools images (Bracci et al., 2011). Additionally, it has been shown that regions that are preferentially activated by a specific category (e.g., tools) in the ventral stream seem to be connected to regions outside the ventral stream that exhibit the same category-preferences (Chen, Garcea, Almeida, & Mahon, 2017). For example, ventral stream regions that show a preference for tools show functional connectivity to left IPL, which represents object-directed actions (Almeida et al., 2013; Garcea & Mahon, 2014; Mahon et al., 2013). With the data available from our experiment, we cannot provide an answer for this question, however, this does open up avenues for future studies which could be implemented via a dual coil TMS paradigm (De Gennaro et al., 2003) to explore how LO and aIPS are interconnected during real and pantomimed grasping.

Furthermore, a highly challenging but important next step in moving forward would be to investigate the causal role of aIPS and LO in hand shaping during grasping (whether real or pantomimed) in more natural and ecologically relevant behaviours. In fact, in our everyday life, target-directed reach to grasp movements rarely constitute on their own the completion of a planned action. Often the end-goal is further object manipulation (e.g., move the object, use the object), thus the grasping movement is only the first step of a more complex manipulation. Thus, future studies should implement TMS-to-LO and TMS-to-aIPS to explore grasping within more ecological settings, such as sequence of planned actions with meaningful shapes as well as sequence of planned action with tools (this is further discussed below).

In project 2, we did not observe cross-decoding between the view and the pantomime task (although we observed a trend in PMd). When interpreting these findings, we should consider that while the view task did not require any overt movement, during the pantomimed task, participants were performing actions with their hand and arm. Thus, in the latter, although we tried to minimise head motion (e.g., using a strap around the upper arm to keep the shoulder still), motion artifacts are introduced into the data when the movement of the limb perturbs the magnetic field within the scanner (Culham, 2006). While these motion artifacts did not appear to affect the fMRI signal (e.g., no motion artifacts were identified), whether these might have affected the spatial patterns of the signal being measured is unclear. Future investigations should look at comparing videos of hands performing actions versus participants performing actions with tools in hand or compare pantomime versus real actions. Additionally, looking at viewing pictures of tools and imagining tool use to overcome the potential perturbations of the magnetic field related to limb movements.

It is worth noting that, while accurate decoding strongly argues for different underlying neural representations with respect to different conditions (Norman, Polyn, Detre, & Haxby, 2006), a lack of decoding could have different meanings. Firstly, it might indicate that neural pattern differences between the two condition exist, but these are not picked up by the vector pattern classifier, thus they may reflect limitations of the methodology rather than the data (Pereira & Botvinick, 2011); secondly, that the two conditions engage the area in a similar or indistinguishable manner; and thirdly, the area is not recruited for either of the conditions. Based on our results, it is likely that regions that do not show decoding for a particular condition might play a similar functional role that particular condition. For example, while patterns of activity within the IPS tools discriminate between power and precision grip in the pantomime task, they do not discriminate in the same condition in the view task. This is likely to suggest that power and precision grip engage the IPS tools in a similar way in the view condition. Although we cannot exclude the possibility that the differences are not picked up by the vector machine, this is less likely, as the same differences are picked up in the pantomime condition. Moreover, if two conditions (i.e., functional and structural manipulation knowledge) engaged an area in a similar manner across tasks, this may have been evidenced in the cross-decoding.

While we could decode above chance within-task, we could not cross-decode between tasks (other than in PMd, which however did not survive FDR correction). However, this does not mean that the representations do not differ. In our MVPA cross-task analysis we extracted the average decoding from both training on view and test on pantomime and training on pantomime and test on view. However, when training a classifier on one stimulus set and testing on another, there might be an issue associated with training direction or ordering (Kaplan, Man, & Greening, 2015). In the analysis reported in this thesis, we reported classification results averaged across both directions of training. However, there are alternatives, such as report the direction separately (e.g. report train on view and test on pantomime averages separately from train on pantomime and test on view; Akama, Murphy, Na, Shimizu, & Poesio, 2012; Quadflieg et al., 2011). As mentioned above, data from the pantomime runs might be noisier than data from the view task, and this approach might help pattern classification.

Moreover, in our lab, we have recently set-up searchlight MVPA (Kriegeskorte et al., 2006) and are in the process of running searchlight on present data. It might be the case that regions not included in our ROI analysis may represent our conditions across the two tasks. Additionally, we could implement representational similarity analysis (RSA), in which data samples are converted into self-referential distant space and therefore help with comparison across domains (Kriegeskorte, 2008; Kriegeskorte & Kievit, 2013). RSA is a widely used approach to characterise the correspondence between brain activity patterns and behavioural measurement (Kriegeskorte, 2008). It consists in constructing representational dissimilarity matrices (RDMs) for both measures and calculating the correlation between them.

Moreover, to further explore how the dorsal and the ventral stream interact, the next step could be to use EEG and event related potentials (ERPs) to map the temporal dynamics of these interactions. Both the tasks implemented in project 2 and 3 could be easily adapted to be combined with EEG. Using ERP to track the neural events when viewing, pantomiming and using tools could offer an insight of the involvement of ventral and dorsal stream regions in tool interactions.

In project 3, we used familiar tools while participants were performing GTU and GTM actions to examine actions with tools in a more ecological environment. Although the setting was more natural, it posed some limitations linked to the fact we used everyday objects. Although we used tools with the exact same handles, the tools did have different surfaces, weights and sizes, which might have affected the observed differences in kinematics, as discussed in chapter 4. In the future we could design and print 3D familiar tools and match the size, weight and surface area, to exclude the possibility that differences in kinematics are linked to these differences across tools.

Moreover, due to the nature of our experiment, whether the observed difference in grasping kinematics were linked to tool identity or to semantic knowledge and knowledge of previous interactions remains unclear. Thus, future experiments should investigate

GTU and GTM and implement both real tools as well as control objects, such as non-tools with no semantic knowledge/knowledge of previous use. The non-tools should have different sizes business heads (e.g., made by overlapping multiple tools) but with the same handles. If differences in grasping kinematics are observed between different tool identities but not between the non-tools, this may suggest that is not the shape and size of the tools that guides grasping, but it might be the semantic knowledge associated with it. However, if differences are observed between control bars, these may be linked to physical properties of the objects, instead.

TMS may also be particularly informative to understand the neural correlates underlying tool identity, GTU and GTM actions and how information is exchanged between ventral and the ventro-dorsal and dorso-dorsal stream areas. For instance, TMS delivered over SMG, but not aIPS, after cue onset has been shown to delay the onset of the movement during both grasp-to-move and grasp-to-use a cup (e.g., grasp a cup to pour liquid in it), but not in the control condition (e.g., lift the hand; Tunik, Lo, & Adamovich, 2008). Based on these results, the authors suggested that SMG may be involved in planning movements. Recently, McDowell, Holmes, Sunderland and Schürmann (2018) instructed participants to grasp-to-use tools placed in front of them that was rotated from the initial start position while participants were reaching the tools. Double-pulse TMS was delivered over the SMG at the onset of tool rotation (and 100 ms afterwards). The authors found that TMS over SMG led to an increase in the percentage of trials in which participants grasped the tool in the incorrect orientation (versus no-TMS), as well as longer movement times and deceleration times. The authors concluded that SMG is important for the selection of appropriate orientation of the hand in grasp-to-use tools and suggested that this effect may be related to the role of the SMG in transforming tool use conceptual knowledge into the motor plan for action. These findings are consistent with the proposal that the ventro-dorsal stream is involved in grasp-to-use (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010). Based on our behavioural results and these previous TMS studies, it would be interesting to use TMS over SMG during planning and execution of GTU and GTM to further explore the role of this region. Based on the account of the dorsal stream divided (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010), TMS to SMG should disrupt grasping kinematics in GTU, but not GTM. Moreover, Perini et al. (2014), used TMS over tool-/hand-selective LOTC (versus sham TMS) during a hand-action (e.g., knowing that a screwdriver involves a rotation movement) or location discrimination task. This resulted in significantly slower responses during hand-action discrimination compared to a location discrimination task. Based on these results and our results it would be interesting to explore the causal role of LOTC in GTU and GTM to understand whether LOTC is causally involved in processing semantics but also action-related properties of tools. Moreover, the GTU and GTM paradigm could be paired with dual coil TMS to investigate how and what information (e.g., functional or structural manipulation) is exchanged between LOTC and regions in the IPL during GTU and GTM.

5.6 Implications and applications

Our results have important implications for Milner and Goodale’s model of the two visual streams. Specifically, the results in project 1 (chapter 2) in this thesis show that area aIPS in the dorsal stream is necessary for fine hand preshaping to object’s size under real or pantomimed grasping movements, however, for pantomimed actions, information regarding object size processed in LO is additionally required to grasp efficiently. While our results provide some support for Milner and Goodale’s model, we suggest that some refinement of the model is necessary to account for this new evidence. In particular, we propose that in the real grasping condition, the dorsal stream acts independently from the ventral stream to control the grasping movement by computing information in an egocentric frame of reference. However, under the pantomimed grasping condition, in addition to the computations performed by the dorsal stream, the ventral stream is additionally required, as the distance between the index finger and thumb need to be computed in relation to the size of the object in an allocentric frame of reference.

Additionally, our results that LO is causally involved in hand preshaping in pantomimed grasping, seem in line with the hypothesis that regions in the ventral stream (e.g., LOTC) are also involved in the representation of actions (Lingnau & Dowing, 2015). The finding from project 2 (Chapter 3) seems to support the view that visual perception is not only a characteristic of the ventral stream, but that also the dorsal stream plays a role in visual perception. In fact, results from project 2 show that tool identity is processed in dorsal stream regions even when no overt movement is required. Additionally, our results from project 3 show that tool identity affects grasping kinematics, even if the structural properties of the handle were the same across tools. Thus, we suggest that vision-for-perception may not be a characteristic of the ventral stream alone, but of both streams. Overall, our results highlight that some refinements of the model are needed to take these new findings about the role played by both streams in tool processing into account and also offer manifold future research opportunities.

The knowledge resulting from grasping and tool use research might ultimately find applications in different fields: it could (i) help develop rehabilitation programs for functional recovery after hand surgery (e.g., Jones, 2002; Valero-Cuevas & Hentz, 2002); (ii) provide a better understanding and help develop and improve new rehabilitation programs for patients with motor impairment after brain damage such as stroke (e.g., Grosse-Wentrup, Mattia, & Oweiss, 2011; Marchal-Crespo & Reinkensmeyer, 2009; Lewis & Perreault, 2009; Lang, 2003; Li, Latash, Yue, Siemionow, & Sahgal, 2003; Murase, Duque, Mazzocchio, & Cohen, 2004; Haaland & Delaney, 1981); (iii) offer new insights in the field of biomechanical engineering to aid the development of robotic hands; (iv) help inform the design and improvement of brain-controlled prostheses to assist movement-impaired patients, such as spinal cord injury patients (e.g., Bensmaia & Miller, 2014; Jackson & Zimmermann, 2012).

Several diseases of the nervous system (e.g., Parkinson’s disease, amyotrophic lateral sclerosis), brain lesions (e.g., stroke, tumours) and injuries (e.g., spinal cord injury, limb amputation) result in the loss of the ability to make skilful and purposeful actions, affecting the ability of the patients to interact with the surroundings and their quality of life. Thus, developing therapeutic interventions to support the rehabilitation of these patients is a major field of research.

Over the last years, scientists have been working to design and improve technologies to develop human-controlled effectors that do not require physical movement, but instead use a brain-machine interface (BMI). BMIs are systems that are built to measure the patient’s intention-related brain signals, for example using electrocorticography, and use these signals to decode the planned movement. This information is then converted into out commands capable of controlling external devices bypassing the conventional neuromuscular pathways to interact with the environment (Beurze, de Lange, Toni, & Medendorp, 2007; Hochberg et al., 2006; Kim et al., 2015; Schalk & Leuthardt, 2011). Gallivan et al. (2011), highlighted that the knowledge about how movements and intentions are encoded in patterns of neural activity is at the basis of BMIs, thus it is important to gain a deeper understanding of how the brain controls hand actions to continue to develop even more sophisticated, precise and effective neural prostheses. The findings provided in this thesis pinpoint several possible brain regions that can be further explores to aid the development and efficiency of BMI devices. In particular, this thesis offers new insights on regions in the brain that are critical for real and pantomimed grasping and on how tool properties and motor information are represented in the brain, which are critical for the development of sophisticated, precise and effective neural prostheses. Thus, understanding where tool properties and motor information and represented in the brain is key in supporting optimal positioning for electrode arrays to capture appropriate intention-related signals.

5.7 Concluding remarks

Together, the set of findings from the three projects highlight systems in the brain important for grasping both meaningless shapes (Project 1) and tools (Projects 2 and 3) and the neural systems important for tool processing (Project 2). Moreover, these findings shed new light on different but interacting systems in the human brain important for grasping and tool use. Project 1 used a real and pantomimed grasping tasks and showed the additional involvement of the ventral stream in pantomimed, but not real grasping. Findings from Project 2 further showed that different systems in the brain are task-sensitive and highlights that patterns of decoding in the tool network are modulated by the task, with higher decoding patterns in the occipitotemporal network for viewing tools and higher decoding patterns in the frontoparietal network for pantomime. Project 3 also indicated the importance of the end-goal of an action as well as tool identity in our everyday interactions with tools.

The projects in this thesis have given us a new insight into the role played by the dorsal and the ventral streams and how information processed in both streams is necessary for adaptive behaviour. Milner and Goodale (Goodale & Milner, 1992; Milner & Goodale, 1995, 2006, 2008) proposed a model that made clear predictions about the role of the dorsal stream in grasping and the role of the ventral stream in perceptual tasks (e.g., memory-guided grasping). However, it is important to highlight that Milner and Goodale's observations were mainly coming from sessions in the lab using meaningless objects, such as wooden blocks (e.g., have no semantic knowledge associated with them). Instead, in our everyday life we interact with tools, that have a meaning associated with them, have handles and are man-made while it is unlikely that we interact with simple blocks with no semantic meaning or handles. Milner and Goodale (Goodale, 2014; Milner & Goodale, 1995, 2006, 2008) postulated that the two streams must interact in everyday life and suggested that while the perceptual mechanisms in the ventral stream are involved in identifying tools to enable the selection of the functional posture to use tools, the visuomotor mechanisms in the dorsal stream processes metrical information to grasp the object based on structure. However, they did not make clear whether the two streams interact during object-directed movements towards tools only, or also when processing tools (e.g., viewing pictures of tools). These existing distinctions have recently been challenged. For instance, it has been shown that actions are actually represented not only in dorsal stream, but also in the ventral stream (e.g., Lingnau & Downing, 2015) as well as growing evidence of the existence of perceptual representations in the dorsal pathway (e.g., Bracci & Op de Beeck, 2016; Freud, Plaut, & Behrmann, 2016; Van Dromme et al., 2016). Our results in project 2 are in line with this account as we found that functional and structural manipulation knowledge was decoded not only in dorsal, but also in ventral stream areas. Moreover, our results from project 3 seem to suggest that tool processing influenced visuomotor mechanisms in the dorsal stream. Overall, our results highlight that some refinements of the model are needed to take these new findings about the role played by both streams in tool processing into account.

To conclude this line of research is important as it provides insights for neuro-rehabilitation of patients who have suffered from brain damage as well as amputee patients as it can support the development of neural prosthetics to assist movement-impaired patients. However, beyond the therapeutic applications, the benefits of basic research exploring how the brain controls hand actions are manifold, from refining and building theoretical models to technological advances in various related fields, such as robotics.

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Appendix A

NeuroSynth list of studies for “anterior intraparietal” (N=70)

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Appendix B

NeuroSynth list of studies for "Lateral Occipital" (N=180)

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Appendix C

C.1 – List of studies (N = 18) from which we extracted aIPS coordinates (N = 20)

Binkofski, F., Buccino, G., Posse, S., Seitz, R. J., Rizzolatti, G., & Freund, H. (1999). A fronto-parietal circuit for object manipulation in man: evidence from an fMRI-study. *Eur J Neurosci, 11*(9), 3276-3286.

Binkofski, F., Buccino, G., Stephan, K. M., Rizzolatti, G., Seitz, R. J., & Freund, H. J. (1999). A parieto-premotor network for object manipulation: evidence from neuroimaging. *Exp Brain Res, 128*(1-2), 210-213.

Cavina-Pratesi, C., Goodale, M. A., & Culham, J. C. (2007). FMRI reveals a dissociation between grasping and perceiving the size of real 3D objects. *PLoS One, 2*(5), e424. doi:10.1371/journal.pone.0000424

Chao, L. L., & Martin, A. (2000). Representation of manipulable man-made objects in the dorsal stream. *Neuroimage, 12*(4), 478-484. doi:10.1006/nimg.2000.0635

Culham, J. C., Danckert, S. L., DeSouza, J. F., Gati, J. S., Menon, R. S., & Goodale, M. A. (2003). Visually guided grasping produces fMRI activation in dorsal but not ventral stream brain areas. *Exp Brain Res, 153*(2), 180-189. doi:10.1007/s00221-003-1591-5

Davare, M., Andres, M., Clerget, E., Thonnard, J. L., & Olivier, E. (2007). Temporal dissociation between hand shaping and grip force scaling in the anterior intraparietal area. *J Neurosci, 27*(15), 3974-3980. doi:10.1523/JNEUROSCI.0426-07.2007

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Jäncke, L., Kleinschmidt, A., Mirzazade, S., Shah, N. J., & Freund, H. J. (2001). The role of the inferior parietal cortex in linking the tactile perception and manual construction of object shapes. *Cereb Cortex, 11*(2), 114-121.

Kadmon Harpaz, N., Flash, T., & Dinstein, I. (2014). Scale-invariant movement encoding in the human motor system. *Neuron, 81*(2), 452-462. doi:10.1016/j.neuron.2013.10.058

Króliczak, G., Cavina-Pratesi, C., Goodman, D. A., & Culham, J. C. (2007). What does the brain do when you fake it? An FMRI study of pantomimed and real grasping. *J Neurophysiol, 97*(3), 2410-2422. doi:10.1152/jn.00778.2006

Monaco, S., Sedda, A., Cavina-Pratesi, C., & Culham, J. C. (2015). Neural correlates of object size and object location during grasping actions. *Eur J Neurosci, 41*(4), 454-465. doi:10.1111/ejn.12786

Shikata, E., Hamzei, F., Glauche, V., Knab, R., Dettmers, C., Weiller, C., & Büchel, C. (2001). Surface orientation discrimination activates caudal and anterior intraparietal sulcus in humans: an event-related fMRI study. *J Neurophysiol, 85*(3), 1309-1314. doi:10.1152/jn.2001.85.3.1309

Shikata, E., Hamzei, F., Glauche, V., Koch, M., Weiller, C., Binkofski, F., & Büchel, C. (2003). Functional properties and interaction of the anterior and posterior intraparietal areas in humans. *Eur J Neurosci, 17*(5), 1105-1110.

Shmuelof, L., & Zohary, E. (2005). Dissociation between ventral and dorsal fMRI activation during object and action recognition. *Neuron, 47*(3), 457-470. doi:10.1016/j.neuron.2005.06.034

Singhal, A., Monaco, S., Kaufman, L. D., & Culham, J. C. (2013). Human fMRI reveals that delayed action re-recruits visual perception. *PLoS One, 8*(9), e73629. doi:10.1371/journal.pone.0073629

C.2 - List of studies (N = 21) from which we extracted LO coordinates (N = 22)

Altmann, C. F., Deubelius, A., & Kourtzi, Z. (2004). Shape saliency modulates contextual processing in the human lateral occipital complex. *J Cogn Neurosci, 16*(5), 794-804. doi:10.1162/089892904970825

Bona, S., Cattaneo, Z., & Silvanto, J. (2015). The causal role of the occipital face area (OFA) and lateral occipital (LO) cortex in symmetry perception. *J Neurosci, 35*(2), 731-738. doi:10.1523/JNEUROSCI.3733-14.2015

Bracci, S., Cavina-Pratesi, C., Ietswaart, M., Caramazza, A., & Peelen, M. V. (2012). Closely overlapping responses to tools and hands in left lateral occipitotemporal cortex. *J Neurophysiol, 107*(5), 1443-1456. doi:10.1152/jn.00619.2011

Cant, J. S., & Goodale, M. A. (2011). Scratching beneath the surface: new insights into the functional properties of the lateral occipital area and parahippocampal place area. *J Neurosci, 31*(22), 8248-8258. doi:10.1523/JNEUROSCI.6113-10.2011

Cavina-Pratesi, C., Goodale, M. A., & Culham, J. C. (2007). FMRI reveals a dissociation between grasping and perceiving the size of real 3D objects. *PLoS One, 2*(5), e424. doi:10.1371/journal.pone.0000424

Chouinard, P. A., Whitwell, R. L., & Goodale, M. A. (2009). The lateral-occipital and the inferior-frontal cortex play different roles during the naming of visually presented objects. *Hum Brain Mapp, 30*(12), 3851-3864. doi:10.1002/hbm.20812

Cohen, N. R., Cross, E. S., Tunik, E., Grafton, S. T., & Culham, J. C. (2009). Ventral and dorsal stream contributions to the online control of immediate and delayed grasping: a TMS approach. *Neuropsychologia, 47*(6), 1553-1562. doi:10.1016/j.neuropsychologia.2008.12.034

Culham, J. C., Danckert, S. L., DeSouza, J. F., Gati, J. S., Menon, R. S., & Goodale, M. A. (2003). Visually guided grasping produces fMRI activation in dorsal but not ventral stream brain areas. *Exp Brain Res, 153*(2), 180-189. doi:10.1007/s00221-003-1591-5

Freud, E., Rosenthal, G., Ganel, T., & Avidan, G. (2015). Sensitivity to object impossibility in the human visual cortex: evidence from functional connectivity. *J Cogn Neurosci, 27*(5), 1029-1043. doi:10.1162/jocn_a_00753

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Karanian, J. M., & Slotnick, S. D. (2015). Memory for shape reactivates the lateral occipital complex. *Brain Res, 1603*, 124-132. doi:10.1016/j.brainres.2015.01.024

Kourtzi, Z., Erb, M., Grodd, W., & Bülthoff, H. H. (2003). Representation of the perceived 3-D object shape in the human lateral occipital complex. *Cereb Cortex, 13*(9), 911-920.

Large, M. E., Aldcroft, A., & Vilis, T. (2007). Task-related laterality effects in the lateral occipital complex. *Brain Res, 1128*(1), 130-138. doi:10.1016/j.brainres.2006.10.023

Lerner, Y., Hendler, T., & Malach, R. (2002). Object-completion effects in the human lateral occipital complex. *Cereb Cortex, 12*(2), 163-177.

Makuuchi, M., Someya, Y., Ogawa, S., & Takayama, Y. (2012). Hand shape selection in pantomimed grasping: interaction between the dorsal and the ventral visual streams and convergence on the ventral premotor area. *Hum Brain Mapp, 33*(8), 1821-1833. doi:10.1002/hbm.21323

Monaco, S., Sedda, A., Cavina-Pratesi, C., & Culham, J. C. (2015). Neural correlates of object size and object location during grasping actions. *Eur J Neurosci, 41*(4), 454-465. doi:10.1111/ejn.12786

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Park, S., Brady, T. F., Greene, M. R., & Oliva, A. (2011). Disentangling scene content from spatial boundary: complementary roles for the parahippocampal place area and lateral occipital complex in representing real-world scenes. *J Neurosci, 31*(4), 1333-1340. doi:10.1523/JNEUROSCI.3885-10.2011

Singhal, A., Monaco, S., Kaufman, L. D., & Culham, J. C. (2013). Human fMRI reveals that delayed action re-recruits visual perception. *PLoS One, 8*(9), e73629. doi:10.1371/journal.pone.0073629

Spiridon, M., Fischl, B., & Kanwisher, N. (2006). Location and spatial profile of category-specific regions in human extrastriate cortex. *Hum Brain Mapp, 27*(1), 77-89. doi:10.1002/hbm.20169

Appendix D

Part one – Instructions and example of trials

Instructions:

In the first part of this study you will see a picture of an object, for example a hammer, on the screen and you will be required to complete different tasks. Please read the instructions carefully and raise your hand if you have any question.

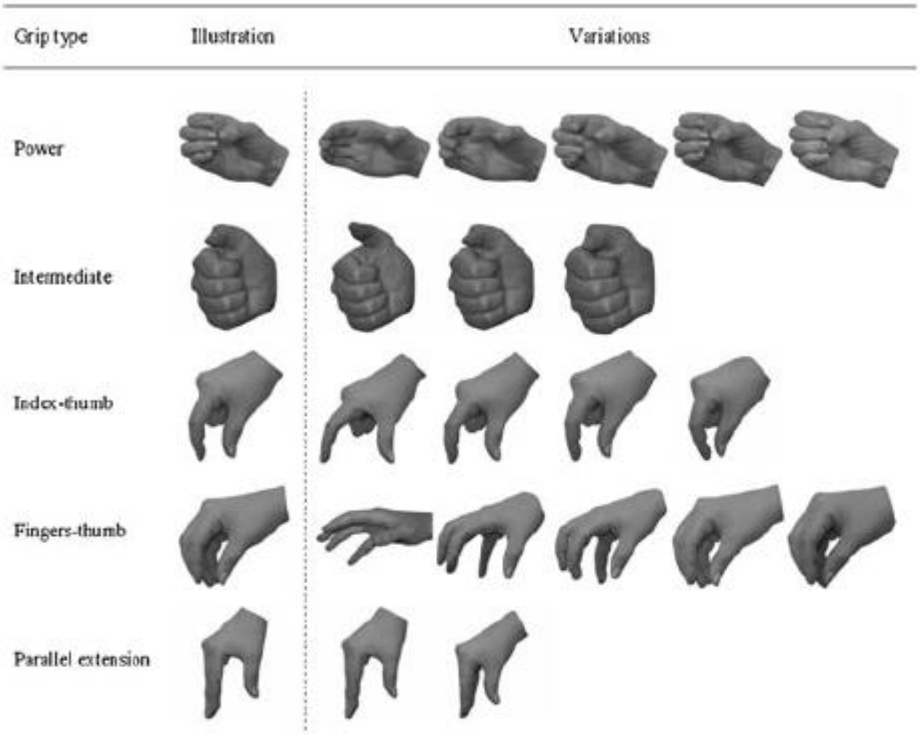
OBJECT NAMING TASK: please type the name of the object in the picture in the box. Please avoid the use of determinants (e.g., the, a) and adjectives (e.g., colour, size). If you don't know the name of the object, please write unknown or your best guess.

FAMILIARITY TASK: please rate how familiar you are with the object in the picture and how many times you use the object. Any object you are familiar with should be given a high rating. Any object you are not familiar with should be given a low rating. Your ratings will be made on a 1 to 7 scale, a value of 1 indicating that the object is very unfamiliar and a value of 7 indicating that the object is very familiar. Values of 2 to 6 indicate intermediate ratings. Click on the most appropriate value for each object. When rating an object, try to be as accurate as possible, but do not spend too much time on it.

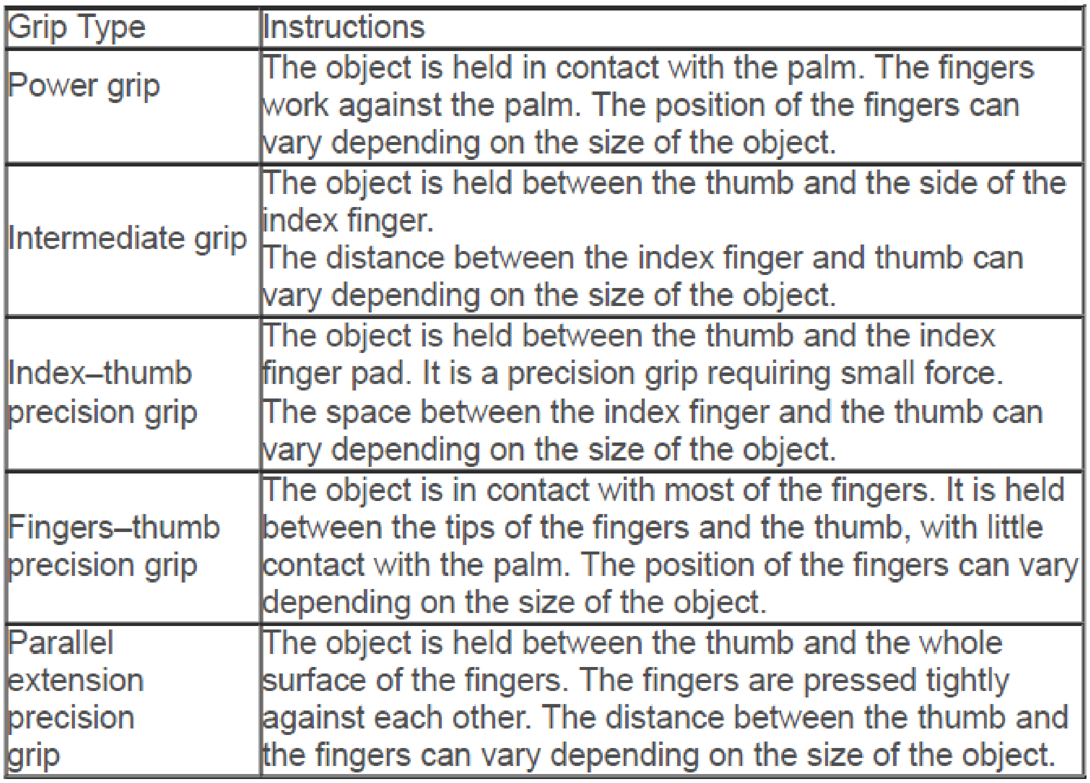
PANTOMIME RATING TASK: Objects differ in the extent to which a person can think of an action involving that object. For some objects it is easier to think of an action than for others. The purpose of this part is to rate objects regarding the ease with which a person can pantomime their use. For example, a hammer is associated with an action that is easy to pantomime (hammering). It is also possible to pantomime the use of a chair (you can sit on it). It is more difficult to pantomime the action than can be performed using a ceiling. Any object that is easy to pantomime should be given a high rating. Any object that is difficult to pantomime should be given a low rating. Your ratings will be made on a 1 to 7 scale, a value of 1 indicating that the object is very difficult to pantomime and a value of 7 indicating that the object is very easy to pantomime. Values of 2 to 6 indicate intermediate ratings. Click on the most appropriate value for each object. When rating an object, try to be as accurate as possible, but do not spend too much time on it.

NUMBER OF ACTIONS TASK: Please determine the number of actions that you can perform with the object. For example, with a hammer you can hammer (=1 action), with a spoon you can stir the soup, but you can also use the spoon to eat the soup (=2 actions). Click on the most appropriate value for each object. When rating an object, try to be as accurate as possible, but do not spend too much time on it.

GRIP RATING TASK: please select the grip type you would employ for grasping the object in the picture. When rating, please imagine that the object on the screen is life-sized. Please identify the posture in which you would place your hand if you are to grasp the object by clicking on the appropriate grip type. You will be required to rate between these 5 different grip types:



Adapted with permission from: Lagacé, S., Downing-Doucet, F., & Guérard, K. (2013). Norms for grip agreement for 296 photographs of objects. *Behavior research methods*, 45(3), 772-781.



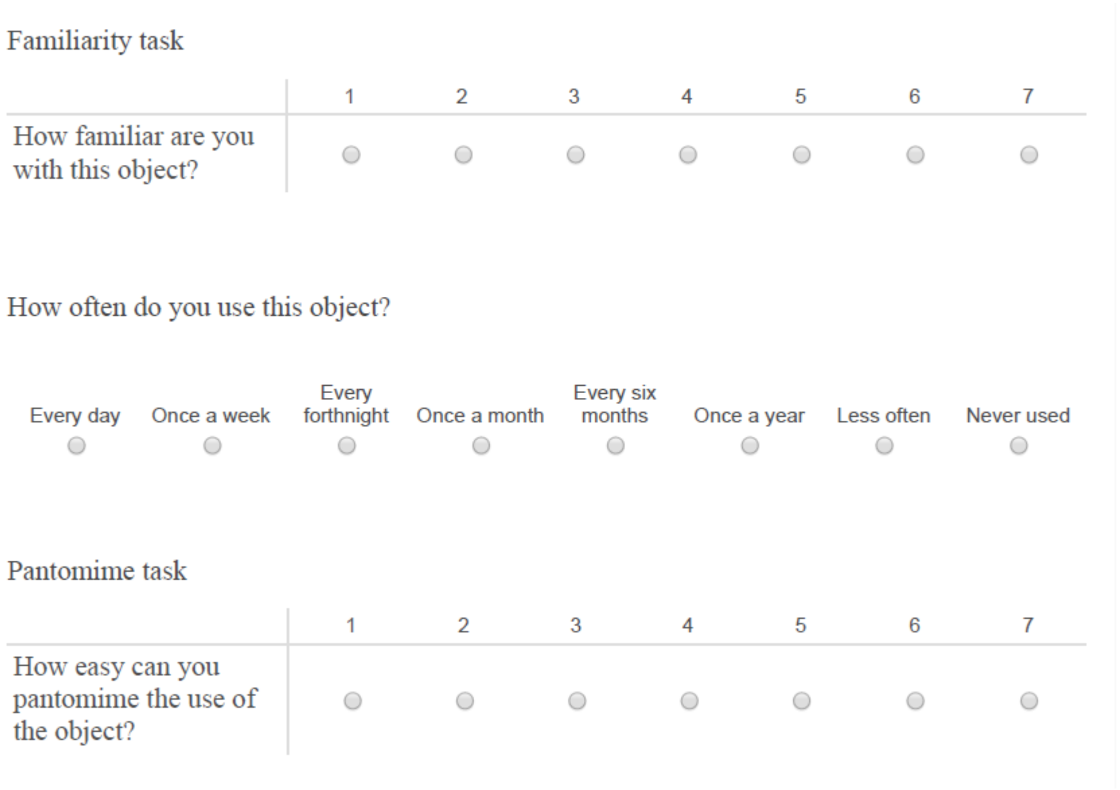
Grip Type	Instructions
Power grip	The object is held in contact with the palm. The fingers work against the palm. The position of the fingers can vary depending on the size of the object.
Intermediate grip	The object is held between the thumb and the side of the index finger. The distance between the index finger and thumb can vary depending on the size of the object.
Index–thumb precision grip	The object is held between the thumb and the index finger pad. It is a precision grip requiring small force. The space between the index finger and the thumb can vary depending on the size of the object.
Fingers–thumb precision grip	The object is in contact with most of the fingers. It is held between the tips of the fingers and the thumb, with little contact with the palm. The position of the fingers can vary depending on the size of the object.
Parallel extension precision grip	The object is held between the thumb and the whole surface of the fingers. The fingers are pressed tightly against each other. The distance between the thumb and the fingers can vary depending on the size of the object.

Adapted with permission from: Lagacé, S., Downing-Doucet, F., & Guérard, K. (2013). Norms for grip agreement for 296 photographs of objects. *Behavior research methods*, 45(3), 772-781.

MOVE VS USE SIMILARITY TASK: Objects differ in the extent to which a person can grasp them to use or to move them. The purpose of the present task is to rate objects regarding how similar the shape of your hand is when you grasp an object to move compare when you grasp it to use. Any object that is grasped in the same way to use it or to move it should be given a high rating; any object that is grasped in a different way to use it or to move it should be given a low rating. Your ratings will be made on a 1 to 7 scale, a value of 1 indicating that the grip is very different when you grasp it to move compare to when you grasp it to use and a value of 7 indicate that grip is very similar when you grasp it to move compare to when you grasp it to use. Values of 2 to 6 indicate intermediate ratings. Click on the most appropriate value for each object. Respond as spontaneously as possible. The instructions have been provided to you to keep on your desk.

Trial example:

[1]



Familiarity task

	1	2	3	4	5	6	7
How familiar are you with this object?	○	○	○	○	○	○	○

How often do you use this object?

Every day	Once a week	Every fortnight	Once a month	Every six months	Once a year	Less often	Never used
○	○	○	○	○	○	○	○

Pantomime task

	1	2	3	4	5	6	7
How easy can you pantomime the use of the object?	○	○	○	○	○	○	○

---

[1] Image taken from the BOSS database of visual stimuli. Brodeur, M. B., Guérard, K., & Bouras, M. (2014). Bank of standardized stimuli (BOSS) phase II: 930 new normative photos. *PLoS One*, 9(9), e106953.

Number of actions:

○ 1

○ 2

○ 3

○ 4

○ 5

○ 6

○ 7+

GRIP RATING TASK

Please select the grip type you would employ for grasping the object in the picture. When rating you should consider the variations provided to you (see instruction sheet).

[2]

MOVE VS USE SIMILARITY

	1	2	3	4	5	6	7	N/A
How similar is the shape of your hand when you grasp the object to move it compare when you grasp it to use it?	○	○	○	○	○	○	○	○

---

[2] Adapted with permission from Lagacé, S., Downing-Doucet, F., & Guérard, K. (2013). Norms for grip agreement for 296 photographs of objects. *Behavior research methods*, 45(3), 772-781

Appendix E

Part two – Instructions and one trial extracted from the questionnaire

Instructions:

In the second part of this study you will see two objects on the screen, for example a hammer and a wrench, on the screen and you will be required to complete different tasks. Please read the instruction carefully and raise your hand if you have any question.

FUNCTION SIMILARITY TASK

In this task you have to rate how similar is the function of each object (on the left) compared to the target object on the right. For example, a blow drier and a towel are both for drying. Any pair of objects for which function is similar to the target one (i.e. both objects are for drying) should be given a high rating. Any pair for which the function is different (e.g., the object on the left is for cutting and the object on the right is for hammering) should be given a low rating. Your ratings will be made on a 1 to 7 scale, a value of 1 indicating that the function is very different and a value of 7 indicate that the function is very similar. Values of 2 to 6 indicate intermediate ratings. Highlight the most appropriate value for each object. Respond as spontaneously as possible.

GRASP SIMILARITY RATING TASK

Objects differ in the extent to which a person can grasp them. In this task you have to rate how similar is the shape of your hand when grasping each object (on the left) compared to the target one (on the right). For example, when grasping a pin, only index finger and thumb are used, when grasping a tennis ball, the whole hand is used. Please ignore the particular action associated with the use of each object for this task. Any pair of objects that is grasped in the same way should be given a high rating; any pair of objects that is grasped in a different way should be given a low rating. Your ratings will be made on a 1 to 7 scale, a value of 1 indicating that the shape of your hand is very different when you grasp one object compare to the other and a value of 7 indicate that shape of your hand is very similar. Values of 2 to 6 indicate intermediate ratings. Select the most appropriate value for each object. Respond as spontaneously as possible.

MOVEMENT SIMILARITY RATING TASK

In this task you have to rate the similarity of the movement performed when using each object (on the left) to the target one (on the right). For example, when using a squeegee and a razor you perform the same action (i.e., up & down movement). Any object that has a similar action compared to the target one, should be given a high rating. Your ratings will be made on a 1 to 7 scale, a value of 1 indicating that the action is very different and a value of 7 indicate that the action is very similar. Values of 2 to 6 indicate intermediate ratings. Select the most appropriate value for each object. Respond as spontaneously as possible.

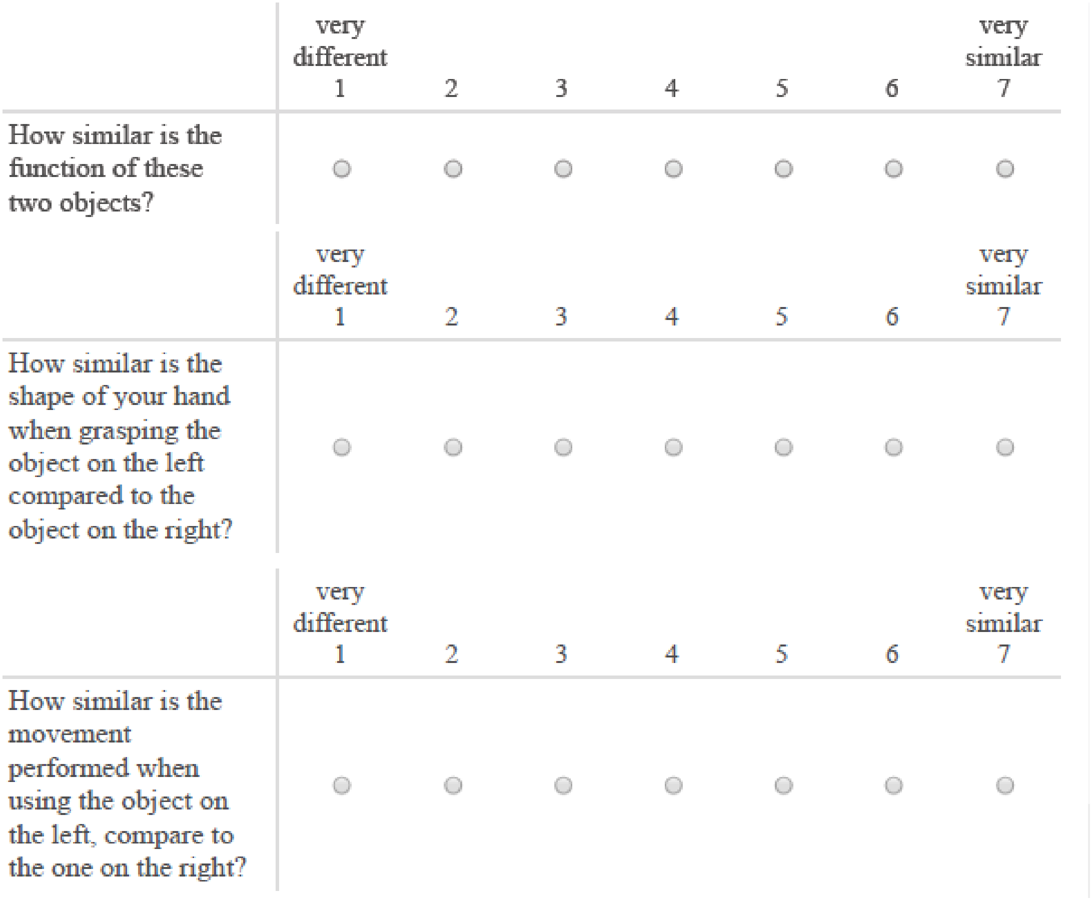
The instructions have been provided to you to keep on your desk.

The first two trials are for you to practice. Please contact the experimenter if anything is not clear.

Trials example:

[3]

Please rate:



	very different 1	2	3	4	5	6	very similar 7
How similar is the function of these two objects?	○	○	○	○	○	○	○
	very different 1	2	3	4	5	6	very similar 7
How similar is the shape of your hand when grasping the object on the left compared to the object on the right?	○	○	○	○	○	○	○
	very different 1	2	3	4	5	6	very similar 7
How similar is the movement performed when using the object on the left, compare to the one on the right?	○	○	○	○	○	○	○

---

[3] Images taken from the BOSS database of visual stimuli. Brodeur, M. B., Guérard, K., & Bouras, M. (2014). Bank of standardized stimuli (BOSS) phase II: 930 new normative photos. *PLoS One*, 9(9), e106953.

Appendix F

Descriptive ratings for part 1

F.1 – Naming task. Percentage of agreement with tool name. Only native English speakers (N = 9) were asked to complete this task.

	Naming Task
Corkscrew	88%
Key	100%
Nutcracker	100%
Peg	100%
Screwdriver	100%
Screw	100%
Tongs	88%
Tweezers	100%
Pliers	100%
Clippers	88%
Bolt	66%
Measuring Spoon	22%

F.2 – Grip Rating Task. Percentage of each grip selected for grasping.

	Grip rating					
	Power	Intermediate	Index-thumb	Fingers-thumb	Parallel Extension	Other
Corkscrew	33.3%	20.0%	0.0%	26.6%	13.3%	6.6%
Key	0.0%	6.6%	93.3%	0.0%	0.0%	0.0%
Nutcracker	66.6%	6.6%	6.6%	0.0%	13.3%	6.6%
Peg	0.0%	0.0%	86.6%	13.3%	0.0%	0.0%
Screwdriver	46.6%	26.6%	0.0%	20.0%	6.6%	0.0%
Screw	0.0%	0.0%	80.0%	20.0%	0.0%	0.0%
Tongs	13.3%	20.0%	0.0%	26.6%	40.0%	0.0%
Tweezers	0.0%	0.0%	93.3%	6.6%	0.0%	0.0%
Pliers	53.3%	0.0%	0.0%	13.3%	26.6%	6.6%
Clippers	0.0%	0.0%	60.0%	33.3%	0.0%	6.6%
Bolt	0.0%	0.0%	73.3%	26.6%	0.0%	0.0%
Measuring spoon	53.3%	13.3%	13.3%	20.0%	0.0%	0.0%

F.3 – Task 1 – Median and range for each task.

	Familiarity Task	Use Task	Pantomime Rating Task	Number of Actions Task	Move versus Use Similarity Task
Answer's Range	1 = very unfamilair to 7 = very familiar	1 = every day to 8 = never used	1 = not at all to 7 = very easy	1 to 7 +	1 = very different to 7 = very similar
Corkscrew median (range)	7 (4-7)	4 (2-7)	6 (5-7)	1 (1-2)	4 (1-7)
Key median (range)	7 (7)	1 (1)	7 (5-7)	1 (1-2)	5 (1-7)
Nutcracker median (range)	6 (1-7)	6 (4-8)	6 (2-7)	1 (1-2)	5 (1-7)
Peg median (range)	7 (6-7)	2 (1-5)	7 (5-7)	1 (1-3)	6 (1-7)
Screwdriver median (range)	7 (5-7)	5 (3 -7)	7 (4-7)	1 (1-2)	6 (2-7)
Screw median (range)	7 (5-7)	5 (4-7)	5 (1-7)	1 (1-2)	6 (1-7)
Tongs median (range)	7 (4-7)	2 (1-5)	7 (1-7)	1 (1-3)	5 (1-7)
Tweezers median (range)	7 (4-7)	2 (1-7)	7 (2-7)	2 (1-5)	5 (1-7)
Pliers median (range)	6 (2-7)	6 (4-7)	6 (2-7)	1 (1-3)	5 (1-7)
Clippers median (range)	7 (4-7)	4 (2-7)	7 (2-7)	1 (1-2)	5 (1-7)
Bolt median (range)	7 (5-7)	5 (3-8)	6 (1-7)	1 (1-2)	7 (4-7)
Measuring Spoon median (range)	6 (4-7)	3 (1-7)	6 (4-7)	2 (1-2)	6 (1-7)

Appendix G

Descriptive ratings for part two.

	Function Similarity Task	Grasp Similarity Rating Task	Movement Similarity Rating Task
	1 = very different to 7 = very similar	1 = very different to 7 = very similar	1 = very different to 7 = very similar
Screwdriver - Corkscrew median (range)	4 (1-7)	3.5 (2-7)	6.5 (5-7)
Screwdriver - Key median (range)	1 (1-6)	1 (1-5)	5.5. (1-7)
Screwdriver - Screw median (range)	6 (1-7)	1 (1-2)	6.5 (1-7)
Screwdriver -Nutcracker median (range)	1 (1-4)	4.5 (1-3)	1 (1-3
Screwdriver - Tongs median (range)	1 (1)	4 (1-7)	1 (1-3)
Screwdriver - Tweezers median (range)	1 (1)	1.5 (1-3)	1 (1-2)
Screwdriver - Peg median (range)	1 (1)	1.5 (1-3)	1 (1-2)
Screwdriver - Pliers median (range)	2 (1-5)	3 (1-6)	3.5 (1-6)
Screwdriver -Clippers median (range)	1 (1-2)	1.5 (1-3)	1 (1-2)
Screwdriver -Measuring spoon median (range)	1 (1)	5.5 (2-7)	1 (1-4)
Screwdriver -Bolt median (range)	4 (1-7)	1 (1-3)	5 (1-7)

	Function Similarity Task	Grasp Similarity Rating Task	Movement Similarity Rating Task
	1 = very different to 7 = very similar	1 = very different to 7 = very similar	1 = very different to 7 = very similar
Key - Screwdriver median (range)	1 (1-6)	1 (1-5)	5.5. (1-7)
Key - Corkscrew median (range)	5 (1-7)	1 (1-3)	6.5 (4-7)
Key - Screw median (range)	1 (1-4)	5.5 (2-7)	6 (3-7)
Key -Nutcracker median (range)	1 (1-7)	1 (1-2)	1 (1-5)
Key - Tongs median (range)	1 (1-2)	2 (1-6)	1 (1-2)
Key - Tweezers median (range)	1 (1-2)	6 (1-7)	1 (1-3)
Key - Peg median (range)	1 (1)	6 (2-7)	1 (1-2)
Key - Pliers median (range)	1 (1-5)	1 (1-3)	2 (1-7)
Key -Clippers median (range)	1 (1)	6 (1-7)	1 (1-3)
Key -Measuring spoon median (range)	1 (1)	1.5 (1-5)	1 (1-4)
Key -Bolt median (range)	1 (1-7)	6 (2-7)	6 (4-7)

	Function Similarity Task	Grasp Similarity Rating Task	Movement Similarity Rating Task
	1 = very different to 7 = very similar	1 = very different to 7 = very similar	1 = very different to 7 = very similar
Screw - Screwdriver median (range)	6 (1-7)	1 (1-2)	6.5 (1-7)
Screw - Key median (range)	1 (1-4)	5.5 (2-7)	6 (3-7)
Screw - Corkscrew median (range)	3 (1-7)	1 (1-3)	6 (3-7)
Screw -Nutcracker median (range)	1 (1)	1(1-2)	1(1-2)
Screw - Tongs median (range)	1 (1-5)	1 (1-2)	1 (1-2)
Screw - Tweezers median (range)	1 (1-5)	5.5 (4-7)	1 (1-2)
Screw - Peg median (range)	1 (1-5)	6 (1-7)	1 (1-2)
Screw - Pliers median (range)	1.5 (1-7)	1 (1-2)	3.5 (1-7)
Screw -Clippers median (range)	1 (1-2)	6 (1-7)	1 (1-2)
Screw -Measuring spoon median (range)	1 (1)	1 (1-3)	1 (1-2)
Screw -Bolt median (range)	6 (2-7)	6.5 (1-7)	7 (4-7)

	Function Similarity Task	Grasp Similarity Rating Task	Movement Similarity Rating Task
	1 = very different to 7 = very similar	1 = very different to 7 = very similar	1 = very different to 7 = very similar
Nutcraker - Screwdriver median (range)	1 (1-4)	4.5 (1-3)	1 (1-3
Nutcraker - Key median (range)	1 (1-7)	1 (1-2)	1 (1-5)
Nutcraker - Screw median (range)	1 (1)	1(1-2)	1(1-2)
Nutcraker -Corkscrew median (range)	1 (1-7)	2 (1-5)	1 (1-5)
Nutcraker - Tongs median (range)	1 (1-7)	7 (5-7)	6 (1-7)
Nutcraker - Tweezers median (range)	1 (1-6)	1.5 (1-4)	5 (1-7)
Nutcraker - Peg median (range)	1 (1-6)	2 (1-3)	5.5 (1-7)
Nutcraker - Pliers median (range)	2.5 (1-6)	7 (6-7)	7 (5-7)
Nutcraker -Clippers median (range)	1 (1-6)	1 (1-5)	5 (1-7)
Nutcraker -Measuring spoon median (range)	1 (1-2)	2 (1-7)	1 (1-2)
Nutcracker -Bolt median (range)	1 (1-2)	1 (1-2)	1 (1-3)

	Function Similarity Task	Grasp Similarity Rating Task	Movement Similarity Rating Task
	1 = very different to 7 = very similar	1 = very different to 7 = very similar	1 = very different to 7 = very similar
Tongs - Screwdriver median (range)	1 (1)	4 (1-7)	1 (1-3)
Tongs - Key median (range)	1 (1-2)	2 (1-6)	1 (1-2)
Tongs - Screw median (range)	1 (1-5)	1 (1-2)	1 (1-2)
Tongs -Nutcracker median (range)	1 (1-7)	7 (5-7)	6 (1-7)
Tongs - Corkscrew median (range)	1 (1)	1.5 (1-5)	1 (1-2)
Tongs - Tweezers median (range)	5 (1-7)	2.5 (1-4)	6.5 (4-7)
Tongs - Peg median (range)	4 (1-7)	1 (1-4)	6 (1-7)
Tongs - Pliers median (range)	2.5 (1-7)	6 (1-7)	5 (1-7)
Tongs -Clippers median (range)	1 (1-6)	2 (1-6)	5.5 (1-7)
Tongs -Measuring spoon median (range)	2 (1-6)	5 (1-7)	1 (1-5)
Tongs -Bolt median (range)	1 (1-5)	1 (1-3)	1 (1)

	Function Similarity Task	Grasp Similarity Rating Task	Movement Similarity Rating Task
	1 = very different to 7 = very similar	1 = very different to 7 = very similar	1 = very different to 7 = very similar
Corkscrew - Screwdriver median (range)	4 (1-7)	3.5 (2-7)	6.5 (5-7)
Corkscrew - Key median (range)	5 (1-7)	1 (1-3)	6.5 (4-7)
Corkscrew - Screw median (range)	3 (1-7)	1 (1-3)	6 (3-7)
Corkscrew -Nutcracker median (range)	1 (1-7)	2 (1-5)	1 (1-5)
Corkscrew - Tongs median (range)	1 (1-6)	2.5 (1-5)	1 (1-2)
Corkscrew - Tweezers median (range)	1 (1)	1 (1-6)	1 (1-2)
Corkscrew - Peg median (range)	1 (1)	1 (1-3)	1 (1-2)
Corkscrew - Pliers median (range)	1 (1-3)	2.5 (1-5)	2 (1-5)
Corkscrew -Clippers median (range)	1 (1)	1 (1-5)	1 (1)
Corkscrew -Measuring spoon median (range)	1 (1-2)	2 (1-5)	1 (1-4)
Corkscrew -Bolt median (range)	1 (1-6)	1 (1-2)	5.5 (1-7)

	Function Similarity Task	Grasp Similarity Rating Task	Movement Similarity Rating Task
	1 = very different to 7 = very similar	1 = very different to 7 = very similar	1 = very different to 7 = very similar
Peg - Screwdriver median (range)	1 (1)	1.5 (1-3)	1 (1-2)
Peg - Key median (range)	1 (1)	6 (2-7)	1 (1-2)
Peg - Screw median (range)	1 (1-5)	6 (1-7)	1 (1-2)
Peg -Nutcracker median (range)	1 (1-6)	2 (1-3)	5.5 (1-7)
Peg - Tongs median (range)	4 (1-7)	1 (1-4)	6 (1-7)
Peg - Tweezers median (range)	1 (1-7)	7 (5-7)	7 (6-7)
Peg - Corkscrew median (range)	1 (1)	1 (1-3)	1 (1-2)
Peg - Pliers median (range)	2.5(1-7)	1 (1-3)	5.5 (1-7)
Peg -Clippers median (range)	1 (1-7)	7 (6-7)	7 (6-7)
Peg -Measuring spoon median (range)	1 (1-5)	1 (1-7)	1 (1)
Peg -Bolt median (range)	1 (1-3)	6.5 (1-7)	1.5 (1-5)

	Function Similarity Task	Grasp Similarity Rating Task	Movement Similarity Rating Task
	1 = very different to 7 = very similar	1 = very different to 7 = very similar	1 = very different to 7 = very similar
Tweezers - Screwdriver median (range)	1 (1)	1.5 (1-3)	1 (1-2)
Tweezers - Key median (range)	1 (1-2)	6 (1-7)	1 (1-3)
Tweezers - Screw median (range)	1 (1-5)	5.5 (4-7)	1 (1-2)
Tweezers -Nutcracker median (range)	1 (1-6)	1.5 (1-4)	5 (1-7)
Tweezers - Tongs median (range)	5 (1-7)	2.5 (1-4)	6.5 (4-7)
Tweezers - Corkscrew median (range)	1 (1)	1 (1-6)	1 (1-2)
Tweezers - Peg median (range)	1 (1-7)	7 (5-7)	7 (6-7)
Tweezers - Pliers median (range)	3.5 (1-7)	1.5 (1-5)	5 (1-7)
Tweezers -Clippers median (range)	4 (1-7)	7 (2-7)	6 (5-7)
Tweezers -Measuring spoon median (range)	1 (1-6)	1 (1-5)	1 (1-2)
Tweezers -Bolt median (range)	1 (1-2)	5.5. (1-7)	1 (1-3)

	Function Similarity Task	Grasp Similarity Rating Task	Movement Similarity Rating Task
	1 = very different to 7 = very similar	1 = very different to 7 = very similar	1 = very different to 7 = very similar
Pliers - Screwdriver median (range)	2 (1-5)	3 (1-6)	3.5 (1-6)
Pliers - Key median (range)	1 (1-5)	1 (1-3)	2 (1-7)
Pliers - Screw median (range)	1.5 (1-7)	1 (1-2)	3.5 (1-7)
Pliers -Nutcracker median (range)	2.5 (1-6)	7 (6-7)	7 (5-7)
Pliers - Tongs median (range)	2.5 (1-7)	6 (1-7)	5 (1-7)
Pliers - Tweezers median (range)	3.5 (1-7)	1.5 (1-5)	5 (1-7)
Pliers - Peg median (range)	2.5(1-7)	1 (1-3)	5.5 (1-7)
Pliers - Corkscrew median (range)	1 (1-3)	2.5 (1-5)	2 (1-5)
Pliers -Clippers median (range)	1 (1-7)	1 (1-3)	3 (1-7)
Pliers -Measuring spoon median (range)	1 (1-7)	4 (1-7)	1 (1-2)
Pliers -Bolt median (range)	4 (1-7)	1 (1-2)	3 (1-6)

	Function Similarity Task	Grasp Similarity Rating Task	Movement Similarity Rating Task
	1 = very different to 7 = very similar	1 = very different to 7 = very similar	1 = very different to 7 = very similar
Clippers - Screwdriver median (range)	1 (1-2)	1.5 (1-3)	1 (1-2)
Clippers - Key median (range)	1 (1)	6 (1-7)	1 (1-3)
Clippers - Screw median (range)	1 (1-2)	6 (1-7)	1 (1-2)
Clippers -Nutcracker median (range)	1 (1-6)	1 (1-5)	5 (1-7)
Clippers - Tongs median (range)	1 (1-6)	2 (1-6)	5.5 (1-7)
Clippers - Tweezers median (range)	4 (1-7)	7 (2-7)	6 (5-7)
Clippers - Peg median (range)	1 (1-7)	7 (6-7)	7 (6-7)
Clippers - Pliers median (range)	1 (1-7)	1 (1-3)	3 (1-7)
Clippers -Corkscrew median (range)	1 (1)	1 (1-5)	1 (1)
Clippers -Measuring spoon median (range)	1 (1)	1 (1-3)	1 (1)
Clippers -Bolt median (range)	1 (1)	4.5 (1-7)	1 (1-4)

	Function Similarity Task	Grasp Similarity Rating Task	Movement Similarity Rating Task
	1 = very different to 7 = very similar	1 = very different to 7 = very similar	1 = very different to 7 = very similar
Measuring spoon - Screwdriver median (range)	1 (1)	5.5 (2-7)	1 (1-4)
Measuring spoon - Key median (range)	1 (1)	1.5 (1-5)	1 (1-4)
Measuring spoon - Screw median (range)	1 (1)	1 (1-3)	1 (1-2)
Measuring spoon -Nutcracker median (range)	1 (1-2)	2 (1-7)	1 (1-2)
Measuring spoon - Tongs median (range)	2 (1-6)	5 (1-7)	1 (1-5)
Measuring spoon - Tweezers median (range)	1 (1-6)	1 (1-5)	1 (1-2)
Measuring spoon - Peg median (range)	1 (1-5)	1 (1-7)	1 (1)
Measuring spoon - Pliers median (range)	1 (1-7)	4 (1-7)	1 (1-2)
Measuring spoon -Clippers median (range)	1 (1)	1 (1-3)	1 (1)
Measuring spoon -Corkscrew median (range)	1 (1-2)	2 (1-5)	1 (1-4)
Measuring spoon -Bolt median (range)	1 (1-5)	1 (1-2)	1 (1-2)

	Function Similarity Task	Grasp Similarity Rating Task	Movement Similarity Rating Task
	1 = very different to 7 = very similar	1 = very different to 7 = very similar	1 = very different to 7 = very similar
Bolt - Screwdriver median (range)	4 (1-7)	1 (1-3)	5 (1-7)
Bolt - Key median (range)	1 (1-7)	6 (2-7)	6 (4-7)
Bolt - Screw median (range)	6 (2-7)	6.5 (1-7)	7 (4-7)
Bolt -Nutcracker median (range)	1 (1-2)	1 (1-2)	1 (1-3)
Bolt - Tongs median (range)	1 (1-5)	1 (1-3)	1 (1)
Bolt - Tweezers median (range)	1 (1-2)	5.5. (1-7)	1 (1-3)
Bolt - Peg median (range)	1 (1-3)	6.5 (1-7)	1.5 (1-5)
Bolt - Pliers median (range)	4 (1-7)	1 (1-2)	3 (1-6)
Bolt -Corkscrew median (range)	1 (1-6)	1 (1-2)	5.5 (1-7)
Bolt -Measuring spoon median (range)	1 (1-5)	1 (1-2)	1 (1-2)
Bolt -Clippers median (range)	1 (1)	4.5 (1-7)	1 (1-4)

Appendix H

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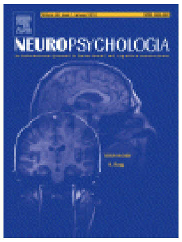

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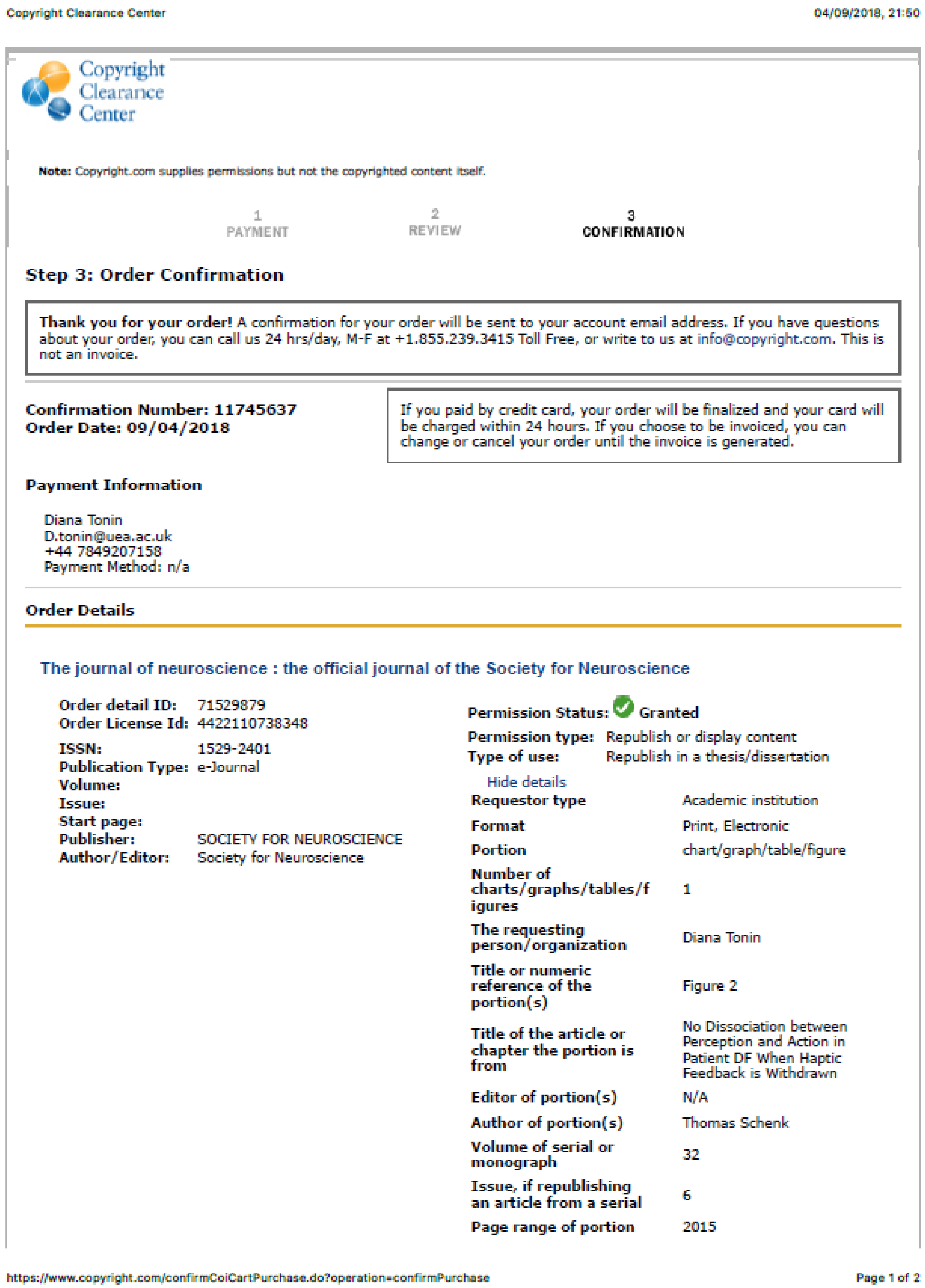

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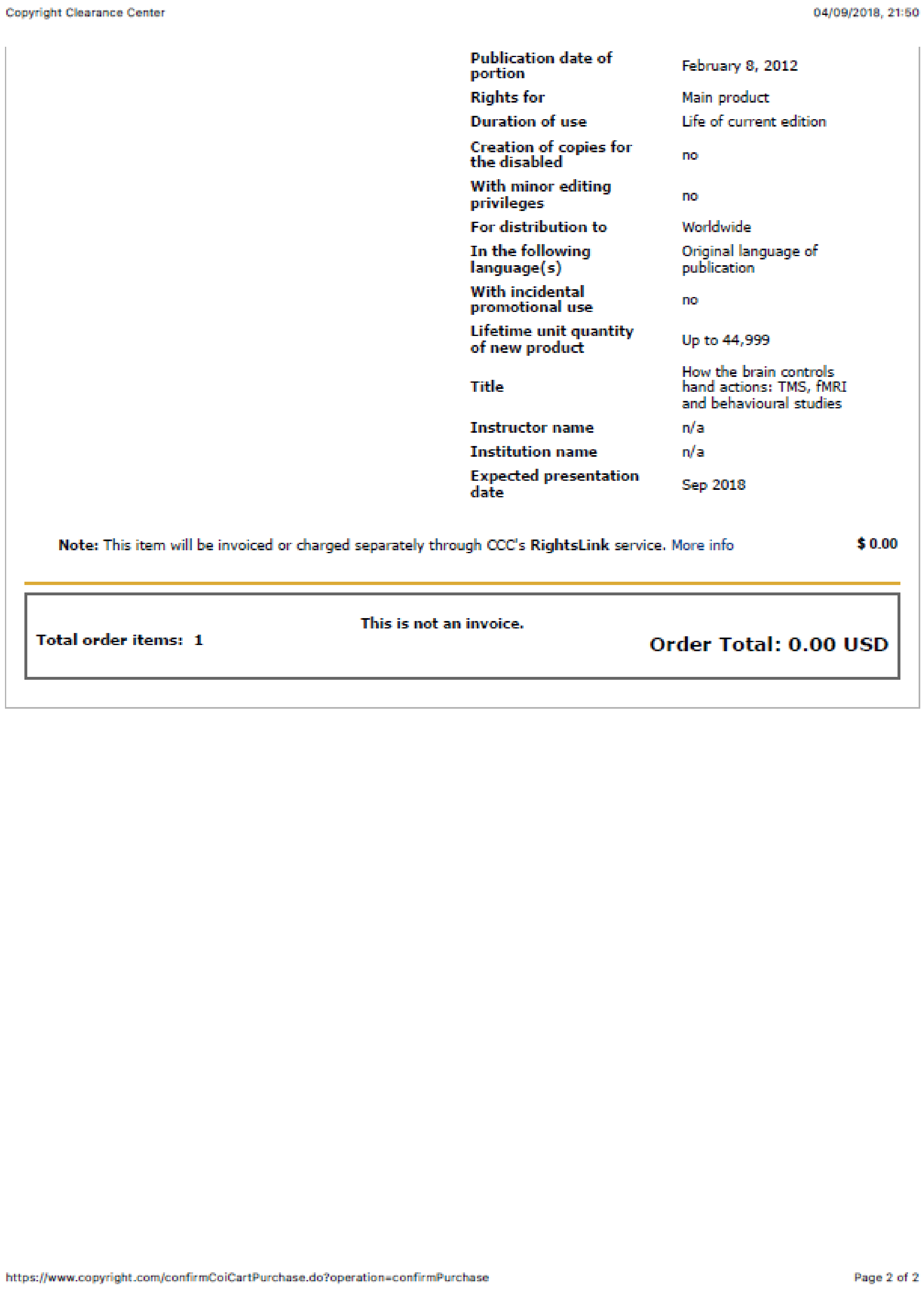

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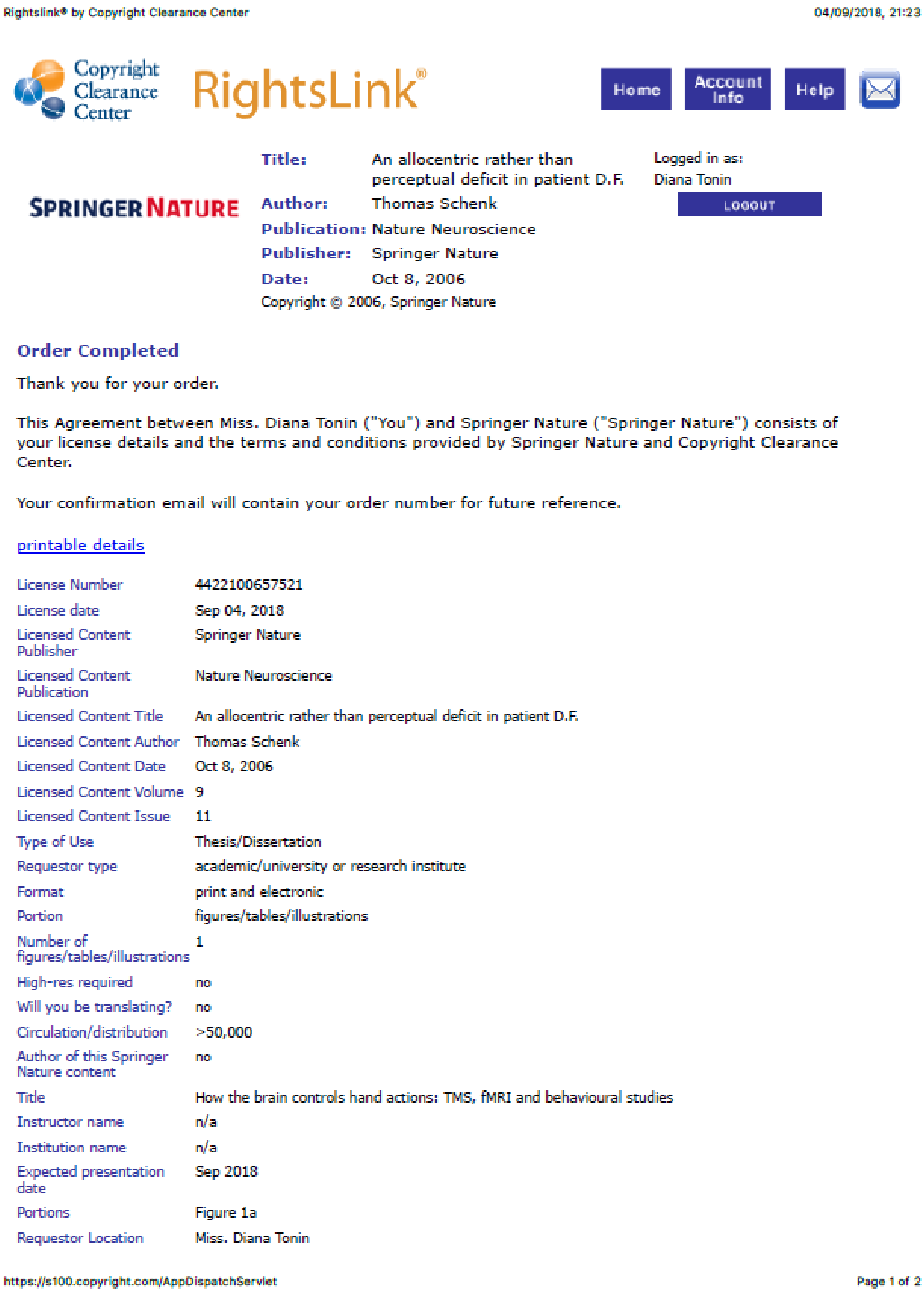

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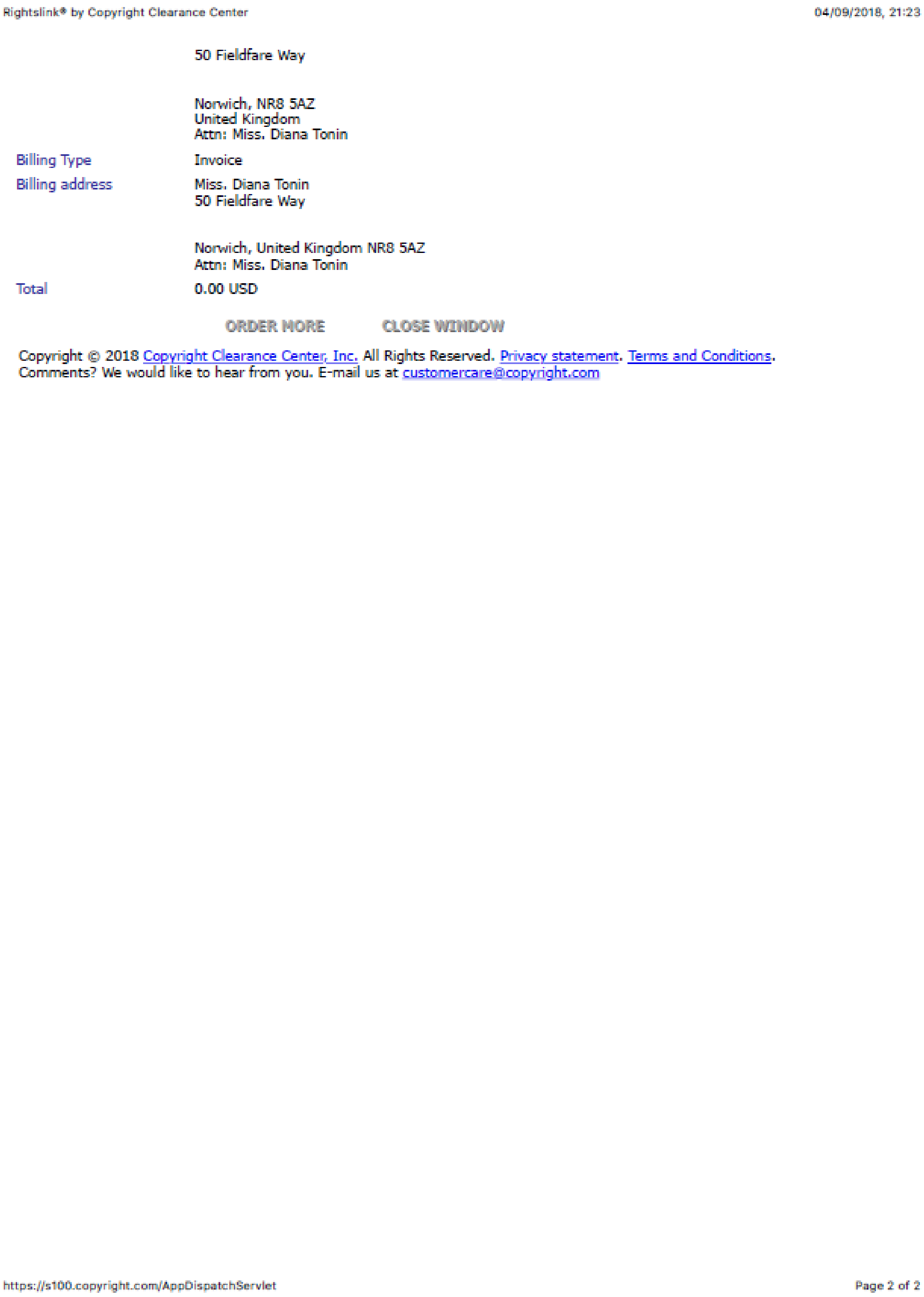
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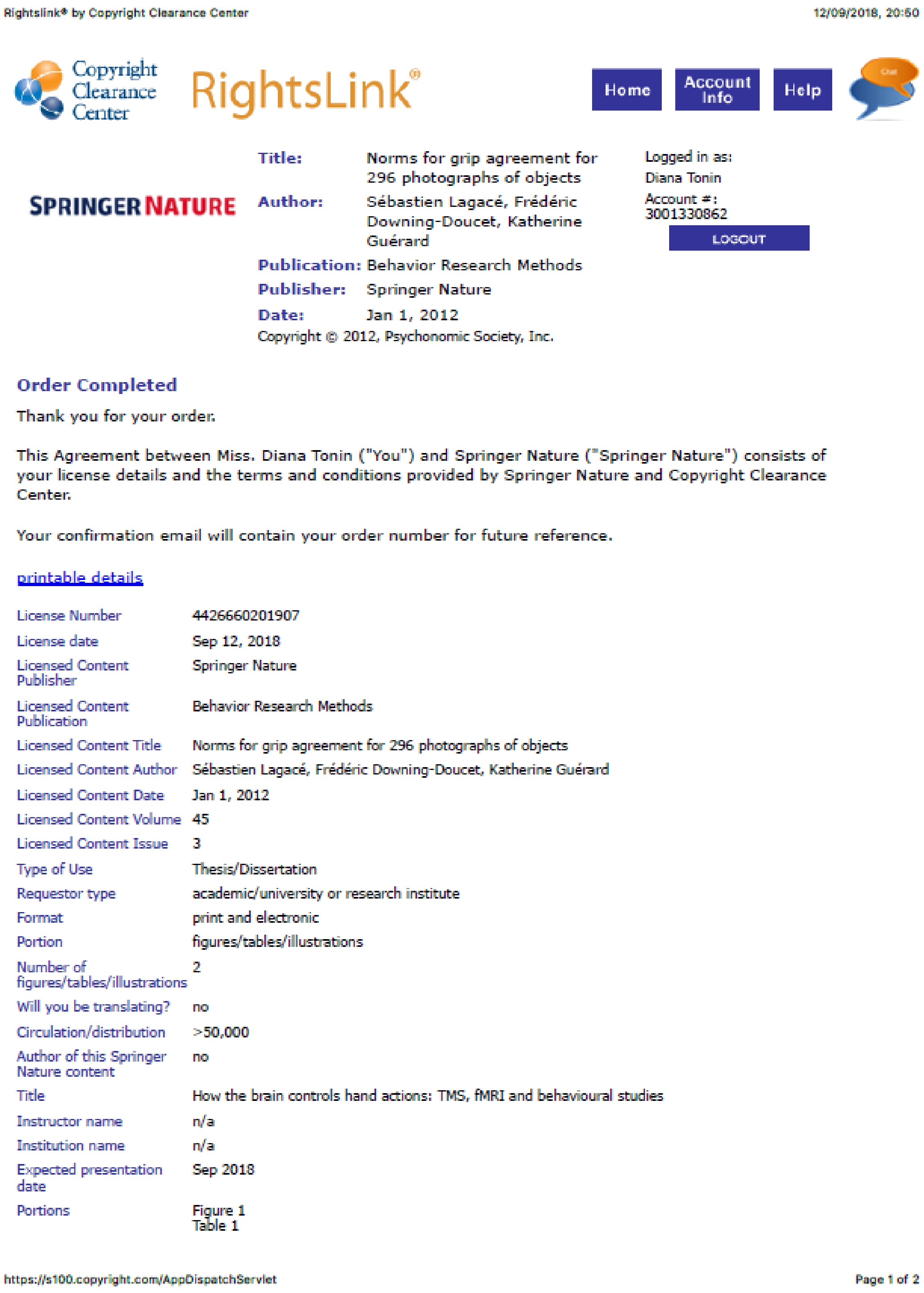

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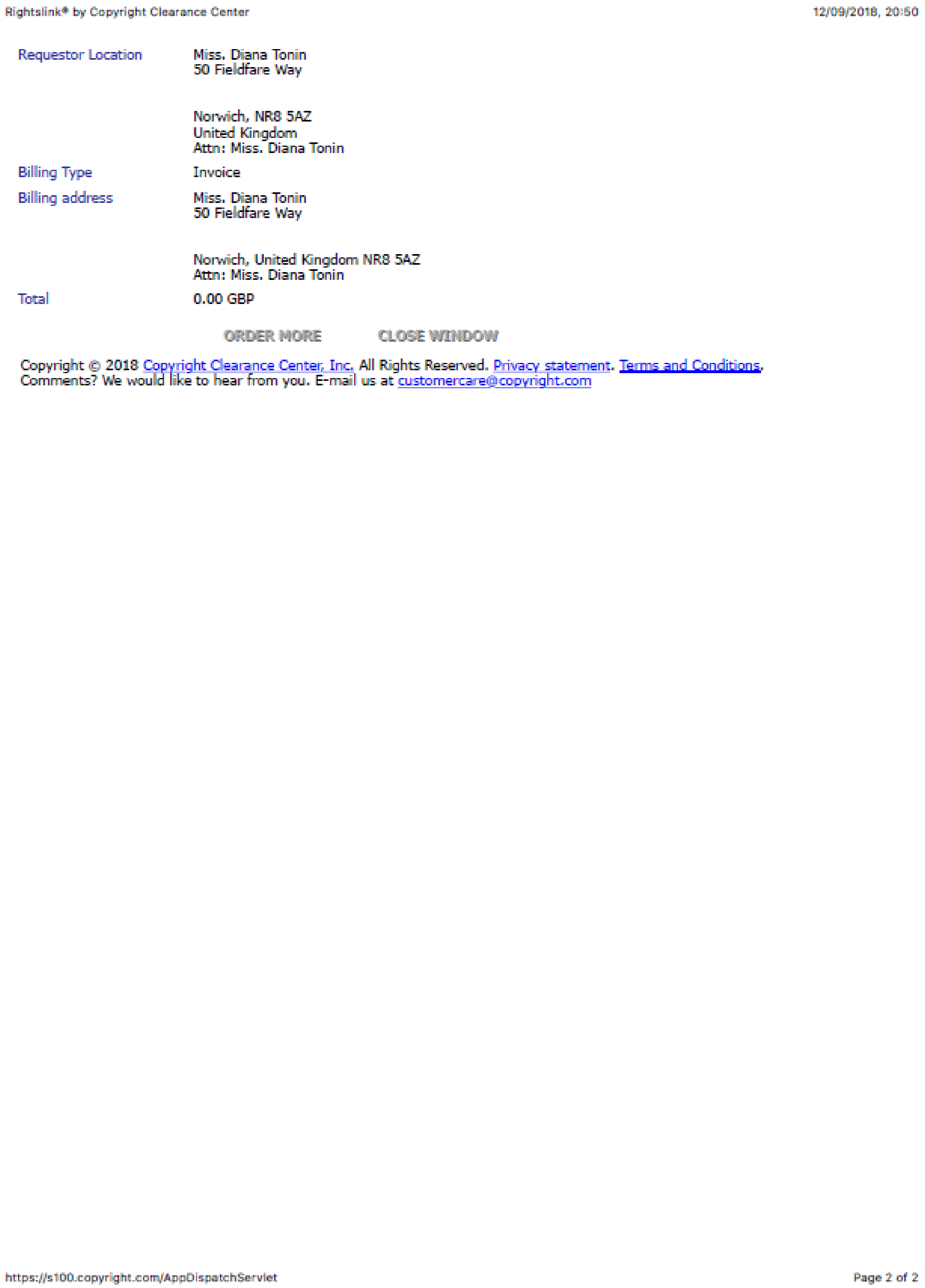

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