How the Brain Grasps Tools: fMRI & Motion-Capture Investigations

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A thesis submitted in partial fulfilment of the requirements of the University of East Anglia for the degree of Doctor of Philosophy.

Research undertaken in the School of Psychology, University of East Anglia.

14/10/2019

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Abstract

Humans' ability to learn about and use tools is considered a defining feature of our species, with most related neuroimaging investigations involving proxy 2D picture viewing tasks. Using a novel tool grasping paradigm across three experiments, participants grasped 3D-printed tools (e.g., a knife) in ways that were considered to be typical (i.e., by the handle) or atypical (i.e., by the blade) for subsequent use. As a control, participants also performed grasps in corresponding directions on a series of 3D-printed non-tool objects, matched for properties including elongation and object size. Project 1 paired a powerful fMRI block-design with visual localiser Region of Interest (ROI) and searchlight Multivoxel Pattern Analysis (MVPA) approaches. Most remarkably, ROI MVPA revealed that hand-selective, but not anatomically overlapping tool-selective, areas of the left Lateral Occipital Temporal Cortex and Intraparietal Sulcus represented the typicality of tool grasping. Searchlight MVPA found similar evidence within left anterior temporal cortex as well as right parietal and temporal areas. Project 2 measured hand kinematics using motion-capture during a highly similar procedure, finding hallmark grip scaling effects despite the unnatural task demands. Further, slower movements were observed when grasping tools, relative to non-tools, with grip scaling also being poorer for atypical tool, compared to non-tool, grasping. Project 3 used a slow-event related fMRI design to investigate whether representations of typicality were detectable during motor planning, but MVPA was largely unsuccessful, presumably due to a lack of statistical power. Taken together, the representations of typicality identified within areas of the ventral and dorsal, but not ventro-dorsal, pathways have implications for specific predictions made by leading theories about the neural regions supporting human tool-use, including dual visual stream theory and the two-action systems model.

Table of Contents

List of Figures

List of Tables

Acknowledgements

First and foremost, I extend my sincere gratitude to my supervisor **Dr. Stephanie Rossit**. Since 2013, Stephanie has acted as an outstanding mentor, steering my progression throughout my entire research career - spanning from the first undergraduate research projects to those during my PhD. Her enthusiasm for research alongside her supportive nature has continued to push me forward, even at times where my confidence in myself has wavered. I hope that we continue our collaborations and friendship for many years to come.

Second, I wish to thank **Dr. Fraser Smith** for his invaluable help throughout my PhD. Without Fraser's willingness to share his practical knowledge and to provide me with his insights during many useful discussions, my journey would have been much more arduous, and for that I am grateful. I would also like to thank **Prof. John Spencer**, my secondary supervisor, for his encouragement and support, particularly during research group meetings.

Past and present Rossit Lab peers have supported me over the years, and I am thankful of this. In particular I wish to thank **Courtney Mansfield, Holly Weaver, Nedislav Petrunov, Emmeline Mottram** and **Iwona Szymura** for their assistance and good-will during our many visits to the Norfolk & Norwich University Hospital MR unit. Last, but certainty not least, I thank **Dr. Diana Tonin** for the great work we have done together and for always lending an ear.

I thank **Dr. Gavin Buckingham** for his continued support since our earlier collaboration, particularly when providing a friendly face during conference presentations. For their technical assistance I am also thankful to **Andre Bester, Malcolm Rae** and **Richard Knight.** Similarly, I wish to thank the radiography team at the NNUH for their extensive support and cooperation during the fMRI projects;

all of whom have been hugely accommodating though I wish to specifically acknowledge **Jenna Green** for her efforts.

Outside of these research projects, I want to give a special thank-you to all of my peers whose friendships have greatly enhanced this experience for me. In particular I cherish the memories shared with **Kerri Bailey,** from our meticulously planned sightseeing itineraries to evenings spent talking about nothing at all. Nor will I forget strolling around the UEA lake with **Megan Rudrum** and the many hours ticked away spent with **Dr. Vicky Adams** in the analysis laboratory.

My family, including my partner **Jenny Lewis**, have always given me unconditional love & support. Without them it would have been far more difficult to accomplish my goals. I am privileged to have these special people in my life and for that I am forever grateful - I owe you all dearly.

Finally, I recognise that this thesis would not have been possible without the financial and practical support provided by the staff comprising the **UEA School of Psychology**, of which I am appreciative. I also thank **Dr. Kenneth Valyear** and **Dr. Sara Bengtsson** for taking the time to read and assess this thesis, as well as **Dr. Natalie Wyer** for agreeing to act as the independent chair for my viva.

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.

The research presented in Chapter 2 has been previously presented in oral and poster formats:

Oral Presentations

Knights, E., Smith, F.W., Mansfield, C., Tonin, D., Weaver, H., Green, J., Saada, J., & Rossit, S. (2018). Hand-selective areas in the ventral and dorsal visual streams represent how to appropriately grasp 3D tools. **Society for Neuroscience Annual Meeting - CA, USA.**

Rossit, S., Smith, F.W., Mansfield, C., Tonin, D., Weaver, H., Green, J., Saada, J., & **Knights, E.** (2018). Hand-selective areas in the ventral and dorsal visual streams represent how to appropriately grasp 3D tools. **British Association of Cognitive Neuroscience annual meeting (BACN) - University of Glasgow, UK.**

Knights, E., Smith, F.W., Mansfield, C., Tonin, D., Weaver, H., Green, J., Saada, J., & Rossit, S. (2018). Decoding typicality with real tools from both dorsal and ventral visual streams. **The Multifaceted Body Workshop: Updates into body representation and embodiment - Heriot Watt University, UK.**

Knights, E., Smith, F.W., Mansfield, C., Tonin, D., Weaver, H., Green, J., Saada, J., & Rossit, S. (2018). Decoding typicality with real tools from both dorsal and ventral visual streams. **Vision Sciences Society Annual Meeting - FL, USA.**

Knights, E., Smith, F.W., Mansfield, C., Tonin, D., Weaver, H., Green, J., Saada, J., & Rossit, S. (2018). Decoding typicality with real tools from both dorsal and ventral visual streams. **Concepts, Actions & Objects Workshop - Rovereto, Italy.**

Poster Presentations

Knights, E., Smith, F.W., Mansfield, C., Tonin, D., Weaver, H., Green, J., Saada, J., & Rossit, S. (2018). Hand-selective areas in the ventral and dorsal visual streams represent how to appropriately grasp 3D tools. **Society for Neuroscience Annual Meeting - CA, USA.**

Knights, E., Smith, F.W., Mansfield, C., Tonin, D., Weaver, H., Green, J., Saada, J., & Rossit, S. (2018). Hand-selective areas in the ventral and dorsal visual streams represent how to appropriately grasp 3D tools. **British Psychological Society East of England Conference - University of East Anglia, UK.**

Knights, E., Smith, F.W., Mansfield, C., Tonin, D., Weaver, H., Green, J., Saada, J., & Rossit, S. (2017). Cortical representations of typical tool Actions. **BACN Annual Meeting - University of Plymouth, UK.**

Knights, E., Smith, F.W., Mansfield, C., Tonin, D., Weaver, H., Green, J., Saada, J., & Rossit, S. (2017). Cortical representations of typical tool actions. **Novelty, Repetition & the Brain Conference - University of East Anglia, UK.**

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.

Name: Ethan Knights

Signature: ………………………….

Date: 11/10/2019

Word count: 87,605

Chapter 1

General Introduction

1.1. Why study the neural basis of human tool-interactions?

Humans encounter and utilise many different tools throughout daily life; consider, for example, a morning routine involving the use of a toothbrush for cleansing teeth, a spoon for scooping cereal, a key for unlocking the front-door and so forth. The emergence of these objects in human culture dates back to around 2.5 million years ago (De Heinzelin et al., 1999; Semaw, 2000), marking the beginning of a major cognitive discontinuity between us and our closest relatives (Ambrose, 2001; Vaesen, 2012). Humans' unique ability to invent, manufacture, think about and use tools is unsurpassed across the animal kingdom and these skills are considered a defining feature of our species (Corballis, 1989; Paillard, 1993; Mithen, 1996; Noble & Davidson, 1997). These behaviours hold clues to our evolutionary history (Darwin, 2016/1871; Dawkins & Wong, 2005; Prothero, 2017) and continue to captivate scientists across disciplines (e.g., anthropology, neuroscience, psychology; Arbib, 2011).

Certain animal sub-species display rudimentary uses of tools (for review see Bentley-Condit & Smith, 2010) where some chimpanzee tribes, for example, modify stones and use them as makeshift anvils to crack nuts (McGrew, Ham, White, Tutin & Fernandez, 1997). In fact, seminal evidence showing that a reach-extending tool can rapidly increase the brain's representation of limb length are based on neural recordings from the monkey (Iriki, Tanaka & Iwamura, 1996; see Martel, Cardinali, Roy & Farne, 2016 for a recent review in the human brain). But, ultimately, these skills in animals are largely linked to extractive foraging (van Schaik et al., 1999) and pale in comparison to humans' vast repertoire of tool-using behaviours

(Davidson & McGrew, 2005; Iriki & Sakura, 2008). Humans are unique in that we constantly use complex tools (e.g., compound artefacts where multiple parts are joined together) that transform limb movements into functionally distinct actions (e.g., cleansing teeth by moving a toothbrush with the hand; Johnson-Frey, 2003; 2007).

The intelligent use of tools is generally agreed to have neurocognitive origins (Gibson, 1993; Wynn, 2002; Reynaud, Lesourd, Navarro & Osiurak, 2016) with changes in brain structure (e.g., encephalisation, functional organisation; Navarrete & Laland, 2015; Boire, Nicolakakis & Lefebvre, 2002; Reader & Laland, 2002; Barton & Harvey, 2000) and cognitive capacities (e.g., exploratory routines, sensorimotor learning; Lockman & Kahrs, 2017) being cited as strong predictors of how prevalent tool-use is in a species (Seed & Byrne, 2010; Fragaszy & Mangalam, 2018). Indeed, cognitive tool-use abilities can precede manual dexterity (Osiurak, Lesourd, Delporte & Rossetti, 2018), indicating that the human hand likely evolved as an adaptation to tool-making and -use (e.g., opposable thumbs and a shorter distance between finger and thumb tips; Napier, 1962, Marzke & Marzke, 2000), rather than it being the underlying cause of these skills' emergence. As elegantly put by Rosenbaum (2017, p. 29) 'the cognitive capacities expressed by tool use, which only humans can engage in, are *supported* by human hands, but aren't *due* to human hands'.

Yet the fundamental question about which brain mechanisms support human displays of complex tool-use is unresolved. Based on the complex and multifaceted nature of human tool-use, its related neuroscience is at the intersection of popular research topics including those related to object recognition (e.g., identifying a spoon), visuomotor control (e.g., reaching and grasping the spoon) and higher-level goal processing (e.g., using the spoon to scoop sugar into a mug before stirring the contents). Yet, few experiments in cognitive neuroscience have directly investigated the neural mechanisms that enable us to interact with these special objects and, instead, frequently rely on 'proxy' tasks where tools are presented as 2D pictures (Lewis, 2006; also see Snow, Pettypiece, McAdam, McLean, Stroman, Goodale & Culham, 2011 for a similar point). This is a major issue because we would never intend to reach out and manipulate a picture of an object (though see Ferretti, 2016a), nor is their manipulation even possible. Therefore, the novel neuroimaging and motion-capture experiments presented in my thesis involve real grasping of 3D tools in order to overcome this limitation.

First, this chapter considers the definition of what makes an object a tool. Next, across four main sections, key findings are reviewed from a range of behavioural, neuropsychological and neuroimaging approaches, focusing particularly on those drawable from functional Magnetic Resonance Imaging (fMRI), Positron Emission Tomography (PET) and Transcranial Magnetic Stimulation (TMS) techniques. In these main sections, two leading models are introduced in turn (i.e., the *dual visual stream theory* and *two-action systems model*) because of their claims about how different neural pathways are related to tool-use. After this the concept of *affordances* is introduced, before turning to the *tool processing network* that has been revealed by neuroimaging research. Crucially, each of these four sections includes a separate sub-section evaluating relevant points that, together, motivated important research questions for the current projects.

1.2. What is a tool?

A classic definition considers tools to be 'any handheld physical implement that is used to make changes to other objects in the environment' (Osiurak, Jarry &

Le Gall, 2010 p.5). This enables the distinction that a hammer is a tool, but a nail is not, in the case that the hammer is used to alter the state of the nail. Following this tradition, my thesis focuses on physical tools, as opposed to those that Osiurak, Navarro & Reynaud (2018) describe as sophisticated (e.g., a coffeemaker) or symbiotic (e.g., Brain-Computer Interface) and would consequently require a greater degree of cognitive abstraction (e.g., the hand's motion when button-pressing is a poor reflection of the tool's function; Goldenberg & Iriki, 2007).

In a comprehensive review, Osiurak, Jarry & Le Gall (2010) have highlighted three features common to tool (and tool use) definitions from ergonomics, primatology and psychology (Baber, 2003; van Lawick-Goodall, 1970; Gibson, 1970): tools are commonly described to be (1) discrete and detached objects in the environment that (2) amplify the user's sensorimotor capabilities and are (3) restricted to what is manipulated by the user. This summary does not, however, emphasise the well learnt action routines (e.g., the oscillation of the elbow for swinging a hammer) and their interrelated functions (e.g., the pounding outcome associated with a hammer) that others have considered to be critical to tools (e.g., Mahon, Milleville, Negri, Rumiati, Caramazza & Martin, 2007; Mruczek, von Loga & Kastner, 2013). The ability to attach certain functions and action routines to particular objects may be what sets humans apart from other primates; unlike chimps that may achieve associative object-action learning after laborious training (McGrew, 2013), humans quickly make these links, even exhibiting functional fixedness (i.e., a hesitancy to use a tool for its non-designated purpose; Munoz-Rubke, Olson, Will, James, 2018) after being informed of a tool's function only once (Defeyter & German, 2003).

Here, I consider tools as ‘manipulable objects that are used to transform an actor’s motor output into predictable mechanical actions for the purposes of attaining specific goals’ (Johnson-Frey, 2007, p.1.). This definition highlights the relationship between tools and stored knowledge in the sense that tools are manipulated in a predictable manner (e.g., the mechanics of the actions only predictable because they match learnt expectations of how to manipulate a given object) and for a specific goal (e.g., the goal of the action is only specific because a tool has been learnt to serve a particular function). With this important definition in place, I now review over four sections major findings related to the neural bases of tool-use.

1.3. Dual visual stream theory

Vision is the dominant sense in humans, often guiding our interactions with tools, ranging from their recognition to their dexterous manipulation. The Dual Visual Stream Theory (DVST; Milner & Goodale, 1995; 2006) has been highly influential (though see de Haan & Cowey, 2011) with its argument that the ventral and dorsal visual pathways are specialised for object perception (i.e., perceiving what an object is) and visuomotor control (i.e., transforming visual coordinates into motor commands), respectively (also see Milner & Goodale, 2008). The anatomically distinguishable cortical pathways can be seen in Fig. 1.1. (blue and red lines) where they both originate in the early visual cortex, but the ventral visual stream connects to the Inferior Temporal Cortex (ITC) and the dorsal visual stream to the Posterior Parietal Cortex (PPC; also see Ungerleider & Mishkin, 1982).

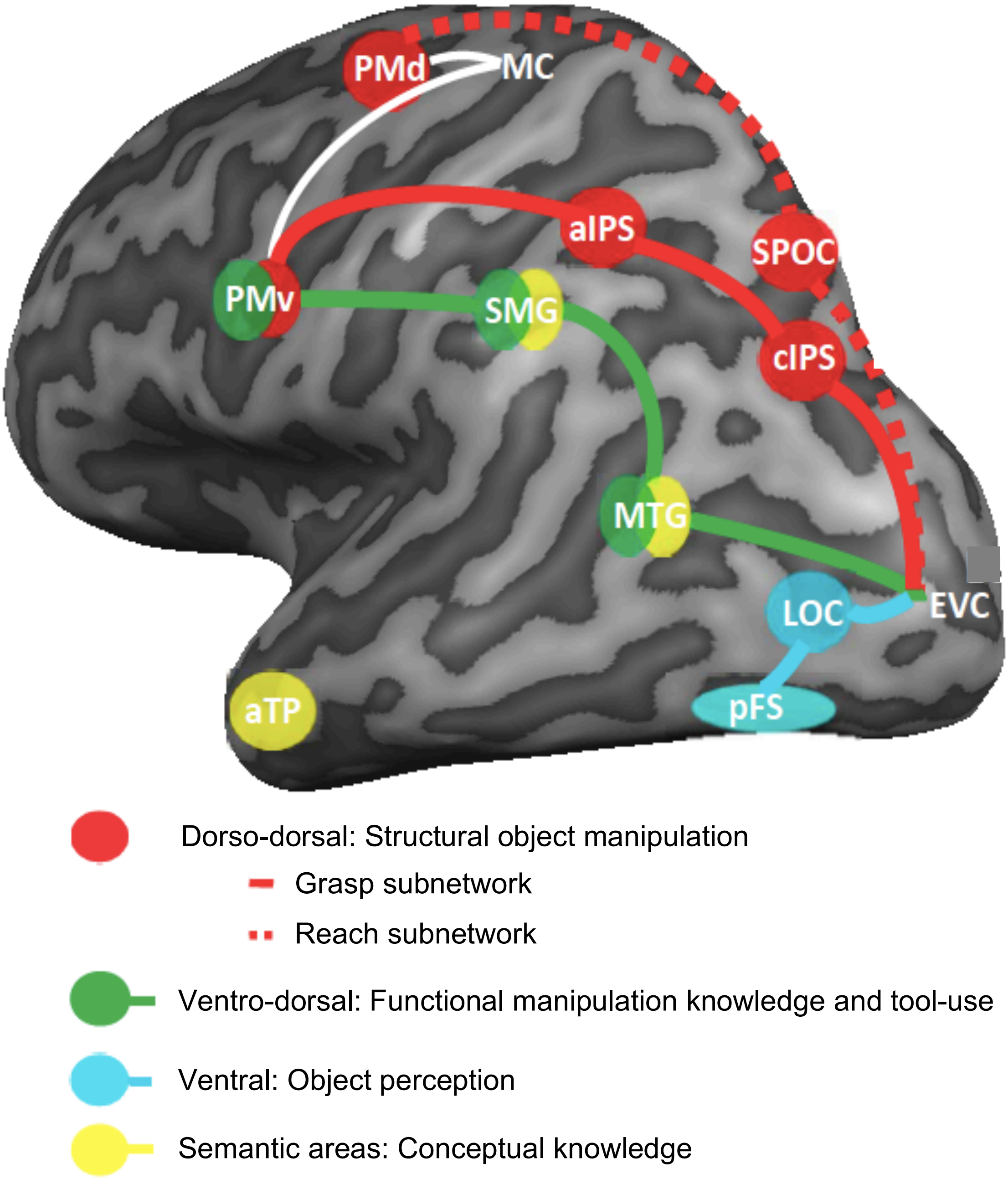

Fig. 1.1. Major functional areas of the neural pathways described in the DVST (red and blue) and the two-action systems model (green). According to the DVST, visual information travels from the EVC (see below for acronyms) to (1) the ventral visual stream for the process of object recognition which receives additional information about object concepts from areas known to process conceptual information about objects (yellow; see Binder et al., 2009) and (2) the dorsal visual stream for the

purpose of visuomotor control which can be separated into reaching and grasping subnetworks (see Gallivan & Culham, 2015; Perry, Amarasooriya & Fallah, 2016). According to the two-action systems model, a separate ventro-dorsal stream is critical for processing stored knowledge about the functions and manipulations associated with tools which can be translated into sensorimotor based motor plans by interacting with the dorso-dorsal stream, perhaps through the aIPS (Binkofski et al., 2013; Grefkes, & Fink, 2005; Sakreida, et al., 2016). Acronyms: PMd - Dorsal Premotor Cortex; PMv - Ventral Premotor Cortex; MC - Motor Cortex; SPOC - Superior parieto-Occipital Cortex; aIPS - anterior Intraparietal Sulcus; cIPS - caudal Intraparietal Sulcus; SMG - Supramarginal Gyrus; MTG - Middle Temporal Gyrus; aTP - anterior Temporal Cortex; LOTC - Lateral Occipital Temporal Cortex; pFs - posterior Fusiform Sulcus; EVC - Early Visual Cortex.

According to Milner & Goodale (1995; 2006) tool-use is a special form of visuomotor behaviour because it requires interactive processing between the ventral and dorsal visual pathways. Simple actions are thought to be achieved via dorsal visual stream computations based on currently available structural information about an object (e.g., its visual shape and size). To use a tool, however, depends on the retrieval of previously learnt object properties (e.g., its typical function and manipulation), via the ventral visual stream, to also be integrated into visually guided motor control (e.g., Goodale & Haffenden, 2003).

Twenty-five years since the conception of the DVST, many of its claims continue to be supported, atleast to some extent (for recent critical perspectives of neuropsychological evidence see Rossetti & Pisella, 2018; Rossit et al., 2018), by the behaviour of neuropsychological patients (see Ganel & Goodale, 2019 for a recent review). These patients tend to have damage predominantly to the ventral or dorsal visual stream such that they can no longer perceive (i.e., visual form agnosia; Culham, Witt, Valyear, Dutton & Goodale, 2008; Karnath, Ruter, Mandler & Himmelbach, 2009, Rennig, Karnath, Cornelsen, Wilhelm & Himmelbach, 2018) or act toward visually guided objects (i.e., optic ataxia; Jakobson, Archibald, Goodale & Carey, 1991; Jeannerod, 1986; Perenin & Vighetto, 1988, Jakobson et al., 1994; Goodale, Meenan, Bulthoff, Nicolle, Murphy & Racicot, 1994), respectively. These sources of evidence have provided grounds for the compelling argument that there is a double dissociation between the ventral stream's processing of perception and dorsal stream's processing of action (see Milner & Goodale, 1995; 2006) and, crucially here, have been used to argue that tool-use actions rely on the additional integrity of the ventral visual stream (see Young, 2006).

Visual form agnosia patient D.F. is well known for suffering severe damage to ventrolateral regions of the occipital lobe comprising the LOTC (James, Culham, Humphrey, Milner & Goodale, 2003) and suffering from profound object recognition deficits (e.g., D.F. cannot identify visually presented objects; Milner, et al., 1991). Interestingly, she is able to grasp everyday tools proficiently (i.e., with a well-formed hand posture) but has difficulty in visually selecting the correct part of the object to grasp for its subsequent use (e.g., the handle). Conversely, optic ataxia patient A.T. has been shown to grasp neutral objects (e.g., a cylinder) with the fingers widely spread and poorly calibrated to the size of the target (i.e., a grip scaling deficit; Jeannerod, 1986; Cavina-Pratesi, Ietswaart, Humphreys, Lestou & Milner, 2010), yet demonstrates less severe performance if grasping familiar objects such as a reel of thread (Jeannerod, Decety & Michel, 1994). The behaviour of patient D.F. therefore indicates that the ventral visual pathway may be critical for successful tool-use. Convergingly, the behaviour of patient A.T. highlights movements with familiar objects seem to be aided by a spared ventral visual stream.

Since the development of fMRI and virtual lesion (e.g., TMS) paradigms, a great deal of evidence from healthy participants also implicates the ventral and dorsal visual stream in their respective roles for perception and action. Yet, direct neuroimaging evidence that real functional tool actions requires processing within both visual streams is incredibly sparse because real tool manipulation has rarely been directly investigated (e.g., Gallivan et al., 2013; Imazu, Sugio, Tanaka & Inui, 2007).

Neural activity in the ventral stream is well known to contain information about visual object identity and stimulus categories (e.g., Larsson & Heeger, 2006; Kriegeskorte et al., 2008; Bell, Hadj-Bouziane, Frihauf, Tootell & Ungerlieder, 2009; for reviews see Reddy & Kanwisher, 2006; Weiner & Grill-Spector, 2012). Interference to the processing of areas in this pathway can also impair the ability to perceive object properties such as shape and form (e.g., Ellison & Cowey, 2006; Mullin & Steeves, 2011; Silson, McKeefry, Rodgers, Gouws, Hymers & Morland, 2013). Likewise, neural activity in the dorsal stream carries information about properties of shapes when required for motor control including their depth, orientation, size and location during reaching or grasping (e.g., Rice, Valyear, Goodale, Milner & Culham, 2007; Kroliczak, McAdam, Quinlan, & Culham, 2008; Di Bono, Begliomini, Castiello & Zorzi, 2015; Fabbri, Stubbs, Cusak & Culham, 2016; for reviews see Culham & Kanwisher, 2001; Grefkes & Fink, 2005; Culham & Valyear, 2006; Theys, Romero, van Loon & Janssen, 2015; Fattori, Breveglieri, Bosco, Gamberini & Galletti, 2015). Again, stimulation to various parts of the dorsal stream circuit has been causally related to visuomotor control (e.g., Vesia, Prime, Yan, Sergio & Crawford, 2010; Davare, Zenon, Pourtois, Desmurget & Olivier, 2012; Ciavarro, Ambrosini, Tosoni, Committeri, Fattori & Galletti, 2013). Nevertheless, to my knowledge, only two studies have systematically searched for the neural responses that are linked to performing well learnt tool manipulations (Valyear et al., 2012; Brandi et al., 2014) and, as will be discussed in Chapter 2, these experiments do not clearly implicate the ventral visual stream in this behaviour.

Thus, whether both streams are indeed recruited for tool use is as yet unclear. This is despite many advancements in the understanding of the organisation principles underlying the functional layout of these pathway more generally. For example, the ventral visual stream is thought to operate in a hierarchical fashion (e.g., Kim, Wohlwend, Leibo & Poggio, 2013; Kravitz, Saleem, Baker, Ungerleider & Mishkin, 2013) where signals travelling anteriorly from the early visual cortex come to represent categories of stimuli (e.g., tools, bodies, faces) invariantly (i.e., activity occurs regardless of different viewpoints retinal size or individual exemplars; e.g., Pitcher, Charles, Devlin, Walsh & Duchaine, 2009; for reviews see Martin, 2007) with access to increasingly abstract concepts (e.g., knowledge of an object's function, identity and other semantic associations such as where it tends to be found; Thomas, Avidan, Humphreys, Jung, Gao & Behrmann, 2009; Peelen & Caramazza, 2012; Clarke & Tyler, 2014; Chen, Garcea & Mahon, 2016; Hong, Yamins, Majaj & DiCarloe, 2016; Conway, 2018). This is possibly achieved due to connections with other temporal lobe areas (e.g., Ramayya, Glasser & Rilling, 2010) known to be critical for semantic cognition (see yellow regions in Fig. 1.1.) (e.g., Ishibashi et al., 2011; Pobric et al., 2010; Pelgrims et al., 2011; Whitney, Kirk, O'Sullivan, Lambon-Ralph & Jefferies, 2010; Davey, Thompson, Hallam et al., 2016). Equally, the dorsal visual stream is generally agreed to be separated into divisible dorsomedial and dorsolateral pathways (Rizzolatti & Matellii, 2003) and are thought to relate more strongly to the control of arm reaching and hand grasping, respectively (see separated red lines in Fig. 1.; for reviews see Turella & Lingnau, 2014; Gallivan & Culham, 2015; though also see Vesia et al., 2017).

This said, a good deal of evidence from neuroimaging and TMS does indicate that other skilled actions, besides tool use, recruit and/or causally require both visual streams, such as when grasping-to-lift, reaching to a memorised location or pantomiming an action (e.g., Gallivan, Johnsrude & Flanagan, 2016; Tonin, Romei, Lambert, Bester, Saada & Rossit, 2017; see van Polanen & Davare, 2015 for a review). Consistently, anatomical pathways exist between the streams which could support such interplay (e.g., the vertical occipital fasciculus; Borra, Belmalih, Calzavara, Gerbella, Murata, Rozzi & Luppino, 2007; Takemura, Rokem, Winawer, Yeatman, Wandell & Pestilli, 2015) and functional connectivity techniques further evidence such interactions (e.g., Bracci, Cavina-Pratesi, Ietswaart, Caramazza & Peelen, 2012; Hutchison, Culham, Everling, Flanagan & Gallivan, 2014; Hutchison & Gallivan, 2018). Clearly, there is a possibility that object-related information is transferred between the dual visual pathways (also see Milner, 2017; Xu, 2018; Vaziri-Pashkam & Xu, 2018).

Therefore, a key question addressed in my thesis is whether the ventral and dorsal visual pathways are involved in the processing of real hand-tool interactions. Perhaps the best evidence so far showing that both visual streams are involved in tool-related processing can be drawn from experiments showing that neural responses across each pathway are sensitive to whether 2D pictures of familiar tools, as opposed to non-tools, are being passively viewed (e.g., Chao, Haxby & Martin, 1999; Chao & Martin, 2000). This evidence is introduced next and I highlight the intriguing question as to whether these visually defined regions would have a role in performing actions involving real 3D tools.

1.3.1. Seeing 2D tools to using 3D tools

Seminal neuroimaging studies had participants view, and sometimes name, 2D pictures of tools relative to images of stimuli from other semantically different object categories that were popularly studied at the time, including those of animals, faces or houses (for reviews see Joseph, 2001; Lewis, 2006; Martin, 2007; Chouinard & Goodale, 2010; Ishibashi et al., 2016; cf. Gerlach, 2007). Most, if not all, of these fMRI and PET studies find tool-specific activity in parts of the ventral visual stream such as the LOTC and fusiform cortex (e.g., Chao, Haxby & Martin, 1999; Chao & Martin, 2000; Whatmough, Cherktow, Murtha & Hanratty, 2002; Emmorey, Grabowski, McCullough, Damasio, Ponto, Hichwa & Bellugi, 2004; Okada et al., 2000). Similarly, tool-specific activity was also commonly reported in the dorsal visual pathway including the aIPS or the SPL (Chao & Martin, 2000; Buxbaum & Saffran, 2002; Boronat et al., 2005; Hermsdörfer et al., 2007; Peeters et al., 2009; Mruczek et al., 2013; Macdonald & Culham, 2015) as well as the premotor cortex (Chao & Martin 2000; Kellenbach et al., 2003; Creem-Regehr & Lee, 2005) that these areas are proposed to transmit to (Rizzolatti & Matelli, 2003; see Fig. 1.1). For both visual streams these effects tend to be largely left lateralised (Lewis, 2006).

Various other studies have since replicated these findings after contrasting neural activity associated with viewing tools to the viewing of other non-tool objects (e.g., musical instruments, graspable shapes) that are better matched for additional properties known to influence processing in the dorsal and/or visual pathways, including visual appearance (e.g., shape; Grill-Spector, Kourtzi & Kanwisher, 2001;

Malach, Levy & Hasson, 2002; Tanaka, 1996), animacy (Bell, Hadj-Bouziane, Frihauf, Tootell & Underleider, 2009; Kiani, Esteky, Mirpour & Tanaka, 2007; Kriegeskorte, Mur & Bandettini, 2008), real world size (Konkle & Olivia, 2012) or graspability (e.g., Handy, Tipper, Borg, Grafton & Gazzaniga, 2006). To illustrate the importance of this step, consider, for example, the point that vegetables which are of a similar elongated shape to tools, can induce tool-like priming effects (see Sakuraba, Sakai, Yamanaka, Yokosawa & Hirayama, 2012). Therefore, using similarly shaped non-tool control objects are needed to rule out the possibility that tool-specific activation in the dorsal visual stream is not simply driven by the high degree of elongation that characterises most tool exemplars (also see Almeida, Mahon, Nakayama & Caramazza, 2008; Almeida, Mahon, Zapater-Raverov, Dziuba, Cabaco, Marques & Caramazza, 2014; Fang & He, 2005).

The regions across each visual pathway that have been identified by these studies that use more suitable non-tool control stimuli (i.e., manipulable and elongated objects) have included the aIPS (Valyear et al., 2007; Mruczek, von Loga & Kastner, 2013), SPL (Vingerhoets et al., 2009; Mahon et al., 2010), premotor cortex (Creem-Regehr & Lee, 2005), fusiform gyrus (Mahon et al., 2007; Garcea & Mahon, 2014) and LOTC (Bracci et al., 2012; Perini et al., 2014) which often extends into the pMTG (Kellenbach et al., 2003; Boronat et al., 2005; Valyear, Culham, Sharif, Westwood & Goodale, 2006). In fact, similar tool-specific activations have been reported only once participants view novel objects that they have experience using (i.e., from a tool training intervention; Creem-Regehr, Dilda, Vicchrilli, Federer, & Lee, 2007; Weisberg, van Turennout, & Martin, 2007), thus, ruling out any low-level confounds because identical stimulus pictures are used.

Importantly, since these studies use 2D tool pictures as stimuli, tool-specific activation in the ventral visual stream could be accounted for by their roles in object recognition (see Grill-Spector & Weiner, 2014 for a review), but the role of same activation in the dorsal visual stream is less clear because no action is required. From cognitive embodiment perspectives, activation of these regions might enable our understanding of object concepts (i.e., the ability to retrieve knowledge from memory about a class of objects; Martin, 2007) because the ability to recall object concepts are supposed to involve simulations of its properties in the motor and perceptual systems (Allport, 1985; Barsalou, 1999; Martin, 1998; Hostetter & Alibali, 2008), such that we can experience the *full* representation of a tool (Mahon & Caramazza, 2008). An alternative and perhaps non-mutually exclusive view is that this activation signifies motor planning where parietal, as well as premotor activity, may reflect a prediction or prime for future action (Martin, 2009; Simmons & Martin, 2012; Martin, 2016; also see Ferretti, 2016 and *Theory of affordances:* section 1.5.). In both cases, these converge on the point that activation in sensorimotor cortex may relate to the retrieval information about the hand and finger movements associated with using familiar tools (e.g., Chao & Martin, 2000).

The views above elude to the possibility that these visually based 2D tool-selective regions are relevant for actual visuomotor control. Evidence of this point would have a notable implication for the study of tool-use because it would indicate that 2D tool viewing tasks are a suitable proxy for understanding real human tool-use. However, the relationship between brain activity when seeing 2D tools and performing real actions has rarely been explored.

Valyear et al., (2007) have shown that clusters in the left aIPS which are selective to the performance of grasping (versus reaching toward) shapes are not selective to naming 2D tool images, nor do they anatomically overlap with area in the aIPS that does show this pattern (i.e., a tool-selective cluster). One possibility for this distinction between tool- and grasp-selective clusters in the aIPS may relate to stimulus format: newer evidence shows that viewing 3D objects, relative to 2D planar representations of the same objects, lead to distinctive neural responses across the dorsal and ventral visual streams including the aIPS (Freud, Macdonald, Chen, Quinlan, Goodale & Culham, 2018; Snow et al., 2011). Thus, perhaps different parts of the aIPS are active based on information about, for example, the depth cues or the possibility of a genuine actions which is uniquely provided by 3D objects (Snow et al., 2011). Another possibility worth considering is whether grasping tools, rather than unfamiliar objects as were used to define grasp-selective aIPS, would have led to a functional and/or anatomical similarity between the grasp- and tool-selective aIPS areas.

Tellingly, Gallivan et al., (2013) have since used a sensitive Multivoxel Pattern Analysis (MVPA) approach for another fMRI dataset which, crucially, is well suited for addressing the question here. In this approach, patterns of voxel activity from a given Region Of Interest (ROI) can be extracted and passed to a classification-based machine learning algorithm in order to provide a test as to whether types of experimental condition (e.g., reaching versus grasping) can be successfully classified or, as often put, *decoded* (e.g., Mahmoudi, Takerkart, Regragui, Boussaourd & Brovelli, 2012) - if decodable, this suggests that an ROI store a neural *representation* (e.g.*,* Mur, Bandettini & Kriegeskorte, 2009) about the relevant information (e.g., a representation of action type).

In their study, Gallivan et al., (2013) had participants grasp versus reach (i.e., action type) an unfamiliar object with either their hand or a tool (i.e., a pair of tongs).

Crucially, decoding of action type from activity patterns within a left tool-selective aIPS ROI was successful regardless of which effector was being used. Rather interestingly, left hemisphere ROIs in the Supramarginal Gyrus (SMG) and posterior Middle Temporal Gyrus (pMTG) (note that the latter was also defined by visual 2D tool-selectivity) were unique in that their activity patterns could be used to decode action type when using the tool, not the hand.

These sensitive multivariate fMRI analyses paired with real tool interactions have, thus, been particularly revealing. First, these findings imply that 2D tool-selective visual areas (e.g., the aIPS and pMTG) may have a role in real visuomotor control which fits well with other studies showing that tool-selective activation across both visual pathways when passively viewing (MacDonald & Culham, 2015) or manipulating real 3D tools (Brandi et al., 2014). Second, these findings imply that the roles of these visual tool-selective regions in relation to motor control may differ by region (e.g., tool-selective aIPS is relevant for grasping in general [for similar views see Tunik et al., 2005; Rice et al., 2006] but tool-selective pMTG is specifically relevant for the act of tool-use). Nevertheless, the representational content of a number of other visually tool-selective regions across the ventral and dorsal visual pathways remains to be tested using such procedures. Addressing this, the neuroimaging experiments in my thesis (Chapter 2 and 4) use a similar MVPA classification approach during real tool grasping with independently defined ROIs based on their selectivity to 2D pictures of tools.

1.4. Two-action systems model

In an important report, Rizzolatti & Matelli (2003) argued that the monkey dorsal visual stream can be divided into a further two streams: a medial dorso-dorsal stream and a lateral ventro-dorsal stream (for recent functional connectivity evidence see Borra & Luppino, 2016). Neuroimaging studies with humans have tended to confirm this view of separable dorsal networks, particularly when performing reaching and grasping actions (for reviews see Filimon, 2010; Turella & Lingnau, 2014; Gallivan & Culham, 2015). In fact, such a three-pathway division from early visual cortex resting state activity (i.e., via a dorsal, ventral and lateral pathway) is argued to capture the functional connectivity of the large Human Connectome Project dataset (Haak & Beckmann, 2018).

The *two-action systems model* proposed by Buxbaum and colleagues, describes how the ventro-dorsal stream plays a major role in tool-use (Buxbaum, 2001; Buxbaum & Kalenine, 2010; Watson & Buxbaum, 2015; Binkofski & Buxbaum, 2013; Buxbaum, 2017). In brief, Binkofski & Buxbaum (2013) argue that the left lateralised ventro-dorsal system (see green line Fig. 1.1.) is largely devoted to skilled, functional object-related actions (e.g., based on learnt properties of an object) while the bilateral dorso-dorsal system is proposed to be specialised for actions based on the structure of objects (e.g., based on size) that are currently visible (i.e., online visual properties). Tool-use, therefore, is predicted to be a result of the rich interactions (e.g., Buxbaum & Kalenine, 2010) between:

> ‘a left-lateralized ventro-dorsal system that subserves manipulation knowledge, from which information is translated into a specific motor plan, and a bilateral dorso-dorsal system specialized for sensory-motor mapping; for example, the translation of information from vision to motor execution (Frey, 2007).’ Buxbaum (2017, p.4).

Much like the DVST, some of the most compelling evidence in favour of this model can be drawn from neuropsychology. Patients with apraxia, a disorder of higher order motor control affecting skilled and learnt actions (see Rounis & Humphreys, 2015), tend to have suffered damage to left frontal and/or parietal lobe (though right brain damage cases exist; Donkervoort et al., 2000) and, broadly speaking, this leads to difficulties with tool using behaviours (e.g., Buxbaum, Shaprio & Coslett, 2014). Historically, apraxia patients have been classified into those suffering from ideational or ideomotor apraxia. Ideational apraxia refers to impairments of object or action knowledge where patients may misuse objects or present difficulty matching objects and actions (Leiguarda & Marsden, 2000; Petreska et al., 2007). Ideomotor apraxia typically refers to an inability where patients are typically unable to perform pantomimed actions such as a limb gesture (e.g., waving goodbye) or mimed tool-use (e.g., using a hammer without a hammer in the hand) as a result of a problem implementing conceptual knowledge into suitable motor acts (Wheaton & Hallet, 2007; Gross & Grossman, 2008). Nevertheless, definitions of these apraxia sub-classes are heavily debated, with patient behaviour rarely conforming to such distinctions (e.g., patients can exhibit impaired performance for both tool use and hand gesture tasks; Buxbaum, 2001; Buxbaum et al., 2007; also see Rounis & Humphreys, 2015).

For the purposes of making a distinction between the role of the ventro-dorsal and dorso-dorsal streams, the critical point is that both the behaviour and lesion sites associated with apraxia and optic ataxia can be viewed as dissociable (Binkofski & Buxbaum, 2013): apraxia deficits consist of both sensorimotor and cognitive components that support the ability to perform/understand object-related actions (Canzano, Scandola, Gobbetto, Moretto, D'Imperio & Moro, 2016) and are frequently associated with Inferior Parietal Lobule (IPL) and/or pMTG lesions (e.g., Varney & Damasio, 1987; Buxbaum, Kyle, Grossman & Coslett, 2007; Weiss, Rahbari, Hesse & Fink, 2008; Kalenine, Buxbaum & Coslett, 2010) whereas optic ataxia deficits are related to online motor control for reaching and grasping regardless of whether actions involve tools (e.g., Grea et al., 2002, Milner et al., 2001, Pisella et al., 2000; Tunik, Frey, & Grafton, 2005) and tend to follow damage of the superior parietal lobule (SPL) and/or the parieto-occipital sulcus (Karnath & Perenin, 2005, Perenin & Vighetto, 1988). This difference between optic ataxia and apraxia is in line with Gallivan et al.,'s (2013) findings described earlier where it was the left SMG and pMTG (i.e., parts of the ventro-dorsal stream), but not the aIPS (part of the dorsal stream), that specifically represented tool-based actions.

A fundamental assumption of the two-action pathway model is that the ventro-dorsal stream, including the left IPL (e.g., Buxbaum, 2001; Buxbaum, 2014; also see Osiurak & Badets, 2016; Osiurak et al., 2011) and posterior temporal lobe such as the pMTG (see Buxbaum, 2017), encodes stored parameters of internal representations about movements and body postures (e.g., Buxbaum, 2001; Buxbaum, 2014; also see Liepmann, 1920; Borghi, 2012; Borghi, Flumini, Natraj, & Wheaton, 2012; Caligiore, Borghi, Parisi, & Baldassarre, 2010; Thill et al., 2013). The information in these representations has been recently expressed in the form of *manipulation knowledge* which Buxbaum (2017, p.5) describes as 'shorthand for multisensory and motor memories learned when using objects and observing others using them'.

Many types of apraxic deficits can be explained as a result of breakdown in manipulation knowledge following IPL and/or pMTG lesions. This includes difficulties when matching pictures of hand postures to tools, relative to novel objects (Dawson, Buxbaum & Duff, 2010), an increased tendency to grasp tools in a way inappropriate for their use (Randerath, Li, Goldenberg, & Hermsdorfer, 2009) and impairments in the understanding or performance of skilled hand actions (e.g., Heilman, Gonzalez Rothi, Heilman & Valenstein, 1993; Halsband et al., 2001 Buxbaum & Saffran, 2002; Kalenine, Buxbaum & Coslett, 2010; Buxbaum, Shaprio & Coslett, 2014; for review see Vingerhoets, 2014).

The two-action pathway model shares important similarities with *schema* and *multiple routes to action* theories. First, a motor schema has been described as a predetermined set of sub-actions (e.g., for reaching, for grasping or for drinking; see Arbib, 1991) whose representations can be assembled together to create a higher order motor schema (e.g., to reach for, grasp and cut with a knife), which, if applied to apraxia, could explain the disorder as a breakdown in selecting and organising schemas into purposive action (see Jeannerod, 1997). Thus, both the two-action pathway and schema theory comparably appeal to the notion of stored internal representations to account for tool-using deficits. Second, Humphreys (2001) has argued for the existence of a semantic (i.e., indirect) and non-semantic (i.e., direct) route to action where the former route contains contextual and associative knowledge about tools while the latter route extracts a structural description of tools (e.g., their visual properties; Rumiati & Humphreys, 1998; Yoon, Heinke, & Humphreys, 2002; Yoon & Humphreys, 2005, 2007; also see Johnson & Grafton, 2003 for a similar view). The link here then is rather clear: both theories reference how action processing can occur in separable routes to action (e.g., the ventro-dorsal and dorso-dorsal stream).

However, the claim by the two-action systems model that the ventro-dorsal stream utilises *stored representations* about tool-related actions has been recently challenged by the *reasoning-based approach* (Osiurak & Badets, 2016; Osiurak et al., 2011; Reynaud et al., 2016) since it cannot account for some neuroimaging and neuropsychological evidence. For example, left hemisphere IPL-damaged apraxic patients show difficulty solving mechanical problems (e.g., selecting an appropriate object to use for retrieving a target out of a box; Goldenberg & Hagmann, 1998; Goldenberg & Spatt, 2009; also see Hodges, Spatt & Patterson, 1999) which cannot be attributed to a breakdown in utilising stored manipulation knowledge because the objects are novel (Osiurak & Badets, 2016). Likewise, if acquired knowledge was processed in the left IPL then activity may be stronger for actions involving familiar, relative to unfamiliar, tools, yet these areas (as well as almost all other areas) activate to a similar degree during tool pantomiming, regardless of familiarity (Vingerhoets, Vandekerckhove, Honore, Vandemaele, & Achten, 2011).

The key idea behind the *reasoning-based approach* is that tool-use is achieved via mechanical knowledge where online reasoning is carried out about the properties of a physical object (e.g., hardness, width) so that an appropriate tool can be selected and, thus, tool-use can be mentally simulated and performed (Osiurak & Badets, 2016). A major strength of this approach is that it accounts for the act of using novel objects as a tool (e.g., a stick to acquire an out of reach object), or even when using a tool for its unconventional purposes (e.g., a shoe for pounding a nail). From a neural perspective, Osiurak & Badets (2017) have parcellated the IPL and reinterpreted its roles: area PF of the SMG is important for technical reasoning (e.g., reasoning about tool object relationships) and a more anterior part of the SMG (aSMG) is responsible for integrating signals from PF with those of the dorso-dorsal stream which are relevant for motor control (i.e., processing hand and object relationships).

Considered together, both the two-action systems model and the reasoning-based approach agree that the ventro-dorsal stream is critical for tool-use (see

Osiurak, Rossetti & Badets, 2017), but this reasoning-based approach denies the existence of stored sensory-motor memories. Instead, the reasoning, based approach views tool-use as achieved largely through processes that are carried out *de novo* (Buxbaum, 2017). With relevance to this controversy, the experiments in my thesis provide one of the first tests (also see Gallivan et al., 2013) that ventro-dorsal stream regions have a role in real hand-tool interactions and if their activity is sensitive to learnt aspects of tool-use (i.e., grasping a tool in a way consistent with its learnt use or not).

Another feature of the two-action systems model worth highlighting is that manipulation knowledge is argued to participate in semantic memory-based representations (I consider semantic memory as ‘a large division of long-term memory containing knowledge about the world including facts, ideas, beliefs and concepts’ Martin, 2007, p.26) of tools themselves (Buxbaum, 2017). This has been argued due the fact that, as manipulation knowledge degrades, the ability to recognise a tool’s identity becomes slower (Lee, Mirman, & Buxbaum, 2014). This link between manipulation and semantic knowledge conforms with embodied or grounded cognition accounts (see Mahon, 2015), but, as I next review, findings are mixed as to whether *manipulation-based knowledge* of a tool (e.g., knowing an appropriate grasp) shares neural correlates with that of *function-based knowledge* (e.g., knowing the appropriate purpose).

1.4.1. Segregated processing of knowledge about tool manipulation & function?

Clinically, cases of apraxia indicate that the knowledge of a tool’s function is dissociable from knowledge about how to manipulate it (Buxbaum et al., 2000; Hartmann, Goldenberg, Daumuller & Joachim, 2005; Warrington & Taylor, 1978).

For example, apraxia patients have been described who can name, and identify from name, tools that they could neither use nor explain how to use (Ochipa, Rothi, & Heilman, 1989; also see Buxbaum, Veramontil, & Schwartz, 2000), whereas another patient F.B. has shown the opposite pattern of deficits where they can match objects by the way they are manipulated but is unable to match them by function or name (Sirigu, Duhamel, & Poncet, 1991). Semantic dementia patients are also a good example of this latter pattern where their Anterior Temporal Lobe (ATL) deterioration has been associated with retained abilities to use tools correctly (Snowden et al., 1996; Graham et al., 1997; Hodges et al., 1998, 1992; Buxbaum, Schwartz & Carew, 1997; Lauro-Grotto, Piccini & Shallice, 1997), despite their characteristic impairments when retrieving conceptual knowledge about objects (e.g., calling a banana an apple; Lambon-Ralph, Jefferies, Patterson & Rogers, 2017; Snowden et al., 2018).

Consistently, decision-making paradigms have shown that such forms of knowledge are dissociable at the behavioural level (e.g., recall the function of a tool or the way that a tool would be held; Garcea & Mahon, 2012). Further, neuroimaging has shown that function-related knowledge retrieval selectively activates the lateral anterior infero-temporal lobe (Canessa et al., 2008; Chen, Garcea, & Mahon, 2016; also see Peelen & Caramazza, 2012), fusiform gyrus (Valyear et al., 2006; Rice et al., 2007; Chen et al., 2017; also see Kleineberg, Dovern, Binder, Grefkes, Eickhoff, Fink & Weiss, 2018) and possibly the pMTG (see functional connectivity evidence in Bach, Peelen & Tipper, 2010). Likewise, stimulation of the left ATL and pMTG can selectively interfere with the recall of tool functions (Ishibashi et al., 2011; Ishibashi, Mima, Fukuyama, & Pobric, 2018; Andres et al., 2013) while that to the left SMG selectively interferes with recalling manipulation-based knowledge (Pelgrims, Olivier & Andres, 2011; Andres, Pelgrims, Olivier & Vannuscorps, 2017).

However, it is possible to refute the claim that the regions needed to retrieve both manipulation- and function-based knowledge are dissociable (see Vingerhoets, 2014 for a review). For example, Hodges, Spatt & Patterson (1999) and Hamanaka, Matsui, Yoshida et al., (1996) have each described two semantic dementia patients with losses of object-conceptual knowledge that are also associated with failures in using those objects (also see Hodges, Bozeat, Lambon Ralph, Patterson & Spatt, 2000). Similarly, a Voxel Lesion Symptom Mapping (VLSM) study with 38 chronic stroke patients showed that the deficits affecting their ability to either match common tools to recipient objects or to perform associated tool actions were both associated with fronto-parietal lesions (Goldenberg & Spatt, 2009), suggesting links between these two aspects of knowledge. Even some approaches to this question utilising neuroimaging have failed to find any neural region responding more during the retrieval of a tool's functional properties, rather than those related to their typical manipulation (e.g., Boronat et al., 2005; Kellenbach, Brett, & Patterson, 2003).

The complex picture being drawn so far is reflected in two sets of findings from a recent VLSM study of 136 left hemisphere stroke patients (Martin, Beume, Kummerer et al., 2016). Martin et al., (2016) had their patients perform tasks that neatly map on to the distinction between manipulation- and function-based tool knowledge, namely, that of tool use (e.g., hammer the nail) and tool selection (e.g., choosing the nail for the hammer), respectively. First, the left IPL was found to be associated with impairments on both tasks. Second, the left ATL and pMTG, amongst some other parts of frontal cortex, were more strongly associated with tool selection, than tool use, deficits. Thus, despite a notable divide in processing of tool function (e.g., selectively processed by ATL and pMTG) the IPL here was required for utilising both aspects of manipulation- and function-based knowledge.

This may help to explain why the IPL is important for both physical tool use (e.g., McDowell, Holmes, Sunderland & Schurmann, 2018) and processing more abstract knowledge needed to, for example, sort objects according to their use (Boronat et al., 2005; Canessa et al., 2008; Chen et al., 2015). Equally, this division of labour between the left IPL and pMTG is captured in another VSLM study showing that lesions to these regions are linked to spatial and semantic gesture recognition deficits (i.e., incorrectly matching *sawing* with a different manipulation of a saw versus a different tool), respectively (Kalenine, Buxbaum & Coslett, 2010).

A remaining issue, however, is why the left pMTG appears to play a role in action-related tasks with tools that do not require the declarative recall or selection of a tool based on its function (e.g., see results described earlier by Gallivan et al., 2013): contradicting the VLSM results just described, Gallivan et al.,'s (2013) results suggest that the pMTG and the IPL are both relevant for function- and manipulation-based knowledge. This highlights the difficulties in attempting to segregate the regions required for retrieving these two types of knowledge. Indeed, the exact role of the left pMTG continues to be debated, and perhaps unsurprisingly so, given that activation of the left MTG during tool recognition and the processing of tool attributes continues to be the most robust finding from the neuroimaging literature (for reviews see Binder et al., 2009; Martin, 2007) and that it has dense anatomical interconnections with parietal cortex (Bi et al., 2015; Ramayya, Glasser, & Rilling, 2010).

Currently, a leading view argues that the pMTG is a multimodal integration site (e.g., Hein & Knight, 2008; Willems, Ozyurek & Hagoort, 2009) that, in the case of tool-use, may play a primary role in representing knowledge about hand-tool relationships derived from experience in a visual (Watson & Buxbaum, 2015) or visuo-kinesthetic format (Buxbaum, 2017; Kalénine et al., 2010, Orban & Caruana, 2014; Watson, Cardillo, Ianni, & Chatterjee, 2013; but for additional evidence in the auditory domain also see Beauchamp, Argall, et al., 2004; Beauchamp, Lee et al., 2004). According to Buxbaum (2017) this information about what hand-tool actions look and feel like is an aspect of *manipulation knowledge* (see the quote provided in the previous section) which does not neatly align with either manipulation- or function-based knowledge. Overall then, whilst the case could be made that there are regions relevant for specifically processing function-, rather than manipulation-based knowledge (e.g., the ATL), parcellating areas of the ventro-dorsal stream according to this distinction may not be so simple. By matching the tool stimuli used in the first fMRI experiment of my thesis (see Chapter 2) to different primary functions (e.g., a knife and pizzacutter are used for cutting), it was possible to further examine which brain regions (e.g., parts of the ventro-dorsal stream) were sensitive to the different functions of tools.

1.5. Theory of Affordances

Coined by Gibson (1979), the term affordance was initially used to describe what the environment *affords* the individual (e.g., a hammer affords pounding or pavement affords walking across), with the core of his philosophy being that perception, by its nature, carries information about afforded actions. This ecological view is radically different from traditional views of perception that suggest it involves building an accurate representation of the external world and instead depicts a tight interrelation between perception and action (for contemporary ideas sharing this view see for example Creem-Regehr, 2005; Creem-Regehr & Kunz, 2010; Decety & Grezes, 1999; Loomis, Da Silva, Fujita & Fukusima, 1992).

For Gibson (1979) affordances do not simply reflect objective or subjective object properties (e.g., the hammer's head is made from metal or is heavy, respectively). Rather, affordances are better viewed as relations between the features of a situation and the abilities of an individual (Chemero, 2001; 2003; 2009) such that, for example, a hammer affords pounding for an adult with the motor capacity to lift the object, but not a baby who lacks the required strength. Building on this idea, the concept of affordances has been widely expanded over the past 40 years (for reviews see Borghi & Riggio, 2015; Oisurak, Rosetti & Badets, 2017), particularly since Tucker & Ellis's (1998) influential evidence of an *affordance effect* from a Stimulus Response Compatibility (SRC) paradigm.

Typically, an SRC paradigm involves testing whether behavioural responses are faster if the spatial position of a stimulus is compatible, relative to incompatible, with the required response (e.g., a left sided target is compatible with a left, but not right, sided button-press; Proctor & Vu, 2006). Tucker & Ellis (1998) had participants judge via left or right handed button presses whether pictures of familiar graspable objects with handles (e.g., a frying pan) were inverted. Reaction times (RTs) were faster when the object's handle was oriented towards the hand used to respond, even though the handle orientation was irrelevant to inversion judgements. In line with affordance theory, this evidence is commonly interpreted to show that the motor programs afforded by an object (e.g., grasping the handle) are integral to its representation; a point that is supported by numerous other reports (e.g., Costantini, Ambrosini, Scorolli & Borghi, 2011; Yang & Beilock, 2011; Costantini, Ambrosini et al., 2010; Ferri et al., 2011; Wamain et al., 2016; Godard, Wamain &

Kalenine, 2019), most notably in experiments involving more naturalistic responses such as squeezing (Tucker & Ellis, 2001) or reaching-to-grasp (Bub, Masson & Kumar, 2018).

Based on this, it is often described how merely perceiving an object leads to the automatic planning, or evocation, of the movements afforded by that object (e.g., Tipper, Paul & Hayes, 2006; Ferri, Riggion, Gallese & Costantini, 2011; Bub, Masson & Kumar, 2018). Rather convincingly, seminal electrophysiological evidence in the monkey brain has also shown that, even if a monkey does not move, grasp-related neurons respond to the visual presentation of objects according to their importance for action (Rizzollatti, Camarda, Fogassi, Gentilucci, Luppino & Matelli, 1988; also see Cisek & Kalaska, 2010). In fact, the already described tool-specific fMRI activation in the human dorsal visual stream during tool picture viewing paradigms (see section 1.3.1.) is often interpreted in the same way (e.g., Chao & Martin, 2000) with recent evidence even showing that these effects can occur without perceptual awareness of even having seen a tool (Tettamanti, Conca, Falini & Perani, 2017). This evidence is supplemented by other *affordance effects* where viewing objects can increase measures of motor excitability, perhaps suggesting a plan to move (Buccino, Sato, Cattaneo, Roda & Riggio, 2009; Makris, Hadar & Yarrow, 2011; Franca, Turella, Canto, Brunelli et al., 2012; cf. Fadiga, Fogassi, Pavesi & Rizzolatti, 1995). Altogether then, it is apparent that object vision can evoke motor affordances, even in the absence of an intention to act.

This said, the automaticity of affordance effects is not a generalisable principle and is instead sensitive to context and intentions of the actor (e.g., Buxbaum & Kalénine, 2010; Osiurak et al., 2010; 2011; Valyear et al., 2011).

For example, automatic affordance effects in behaviour have been shown to occur only if task demands are relatively undemanding (e.g., if a pantomime does not involve forward planning; Randerath, Martin & Frey, 2013) and can be enhanced based on past behaviour (e.g., if tool-use was performed earlier; Jax & Buxbaum, 2010).

Nevertheless, the conditions under which object perception can trigger affordances are relatively underspecified. Macdonald & Culham (2015) recently failed to find any significant fMRI activation during a passive viewing task when the hand and the handle of a real 3D tool were of matching orientations. This effect is rather surprising given that these objects afforded genuine action, unlike images of tools that have been predominantly studied in the past (see Snow et al., 2011). To further investigate the neural basis of object affordances, the experiments in my thesis involve graspable 3D that authentically afford action.

1.5.1. Tools and functional affordances

Motor affordances can be evoked that relate to the learnt function of a tool (e.g., Kalenine, Wamain, Decroix & Coello, 2016; Mizelle, Kelly & Wheaton, 2013; Hartson, 2003; Stoytchev, 2005; Awaad, Kraetzschmar & Hertzberg, 2015; Young, 2006; Masson, Bub & Breuer, 2011; Mon-Williams & Bingham, 2011; Pellicano, Iani, Borghi, Rubichi & Nicoletti, 2010; Valyear et al., 2013). For example, when Tucker & Ellis (1998) found that compatible handle positions evoked actions, this could be attributable to the fact that we have learnt to grasp the handle of such objects (e.g., a knife) because it is how they would be held for subsequent use (e.g., cutting). A *functional affordance* is the term that some authors have adopted to capture this notion (e.g., Mon-Williams & Bingham, 2011; Pellicano, Iani, Borghi, Rubichi & Nicoletti, 2010; Young, 2006).

As a brief note, functional affordances are treated separately here to the notion of stable affordances. Both types of affordance are based on previous experience, but stable affordances do not necessarily rely on learnt knowledge about an object's function and instead reflect any learnt properties of an object (e.g., shape or size), as is indicated in the following example: 'we know a marble is graspable with a precision grip' (Sakreida, Effnert, Thill, Mereike et al., 2016, p.90).

To appreciate this concept, first consider that *functional affordances* are evocable much like pure physical/structural affordances are (Symes, Ellis & Tucker, 2007), where this latter type of affordance is simply based on the structure of an object (e.g., a cylinder oriented toward the hand can still facilitate RTs in an SRC paradigm based on the fact that it affords grasping; Symes, Tucker & Ellis, 2006; see Chapter 3 for further discussion). For example, Bub, Masson & Creek (2008) demonstrate that hand kinematics (e.g., RTs) are facilitated regardless of whether an action is performed that is consistent with the functional (e.g., a whole hand grasp for pliers) or structural affordance (e.g., a whole hand grasp for a spray bottle) of a pictured tool. Similarly, Jax & Rosenbaum (2010) found that RTs are slower when responding to objects with a mismatched structural and functional affordance that could perhaps indicate a time-consuming inhibition process for the irrelevantly evoked action (also see Kalenine, Wamain, Decroix & Coello, 2016; cf. Bub, Masson & van Mook, 2018). Together, these studies demonstrate that affordances are not simply dictated based on an object's structure but can be based on the learnt knowledge about how to manipulate that object (i.e., as is critical for tools).

To provide an additional example from neuropsychology, Riddoch, Humphreys & Price (1989) have also presented a patient with cortico-basal degeneration who showed over-utilisation deficits (i.e., a strong tendency to automatically perform grasp actions toward objects even when not explicitly intended) and asked her to grasp a cup using the hand that was on the matching side of the table (i.e., left versus right). In line with affordance theory, her actions were cued by the orientation of the cup's handle in relation to the patient's preferred hand. Crucially, however, the frequency of this grasp action decreased when the cup was inverted, even though the physical positioning of the handle was identical as to when it was upright. Therefore, again, it was not simply the structure of the object that led to overutilization of the affordance, but it was presence of a functional affordance that altered the patient's propensity for action.

Perhaps the most compelling evidence of the existence of functional affordances comes from one of the rare fMRI experiments where participants interacted with real 3D tools. Specifically, Valyear, Gallivan, McLean & Culham (2012) found that select parieto-frontal regions, including the left aIPS, precentral gyrus and right SPL displayed suppressed activity when demonstrating the well learned action of a tool after having passively viewing that tool in the same trial. Crucially, this neural adaptation was absent if the task instead required the tool to be viewed, but this time, then used for demonstrating a control movement that was newly learned and cued by colour (e.g., trace a circle with a red tool-handle). Therefore, it appears that simply viewing a tool can evoke the well learnt action it is associated with, though it is worth noting that such a conclusion lies on the assumption that suppression truly reflects planning (also see *Theory of affordances:* section 5.3.3.).

Returning to the frameworks described in earlier sections, functional affordances are proposed to be processed by the ventral (e.g., Oisurak, Rosetti & Badets, 2017; Young, 2006) and/or ventro-dorsal streams (e.g., Buxbaum &

Kalenine, 2010; Buxbaum, 2017) whereas structural affordances would are expected to be processed by the dorsal/dorso-dorsal stream (e.g., Osiurak, Rosetti & Badets, 2017; Buxbaum, 2017). Rather interestingly, the most recent form of the two-action systems model (i.e., the two action-systems *plus* model), Buxbaum (2017) argues that the left SMG may act as a buffer that prepares multiple afforded actions. These actions are apparently able to be based on either structural affordances processed by the dorso-dorsal stream or functional affordances processed by the ventro-dorsal stream (e.g., the pMTG or possibly IPL; Buxbaum, 2017). The action that is ultimately performed is expected to be based on contextual information (e.g., such as the actor's intention; also see Cisek & Kalaska, 2010) processed by the Inferior Frontal Gyrus (IFG) (see Garcea, Stoll & Buxbaum, 2019 for recent VLSM evidence in favour of this view; also described in Chapter 2 discussion). In this way, the two-action-systems model now clearly provides a division of labour between the posterior temporal cortex and the IPL (see *Segregated processing of knowledge about tool manipulation & function?:* section 1.4.1.).

To further explore the notion of functional affordances, the experiments in my thesis had participants grasp tools in a way that was consistent with the functional affordance of that tool (i.e., by the handle). Though, crucially, they never actually performed their associated *use-based* actions - in this way, results might be linked to automatic triggering of affordances because there is no intention to carry out such actions.

1.6. A tool processing network

Neuroimaging studies investigating the brain regions linked to processing tools has become an incredibly popular area of study. This type of stimulus is suited to overcome the common criticism that the DVST offers little account of how visual information from the ventral and dorsal visual pathways become integrated (e.g., Schenk & McIntosh, 2010; but see Milner 2017 and Cloutman, 2013). Likewise, these special objects are critical for testing hypotheses drawn by the ventro-dorsal stream models that describe how learned knowledge is integrated with online visual information, regardless of whether these models focus on gesturing (e.g., Buxbaum, 2001) or problem-solving (Osiurak et al., 2013). In fact, these stimuli have been popular throughout cognitive neuroscience since they are able to help understand category selectivity (e.g., do related categories overlap; Bracci et al., 2012; Peelen & Downing, 2019), affordances (see *Tools and functional affordances*: section 1.5.1.), neural connectivity (e.g., Bi, Han, Zhong, Ma, Gong et al., 2015) and neurocognitive development (e.g., Dekker, Mareschal, Sereno & Johnson, 2011; Kersey, Clark, Lussier, Mahon & Cantlon, 2015).

Meta-analyses now highlight a robust network of brain regions, often with a strong degree of left lateralisation, that activate when viewing, hearing, imagining, naming, pantomiming and, in some rare studies, acting with tools (for reviews see Lewis, 2006; Martin, 2007; 2016). Following the nomenclature of others (e.g., Garcea & Mahon, 2014), I refer to this collection of regions as the *tool processing network* (see Fig. 1.2A. for an example of these areas).

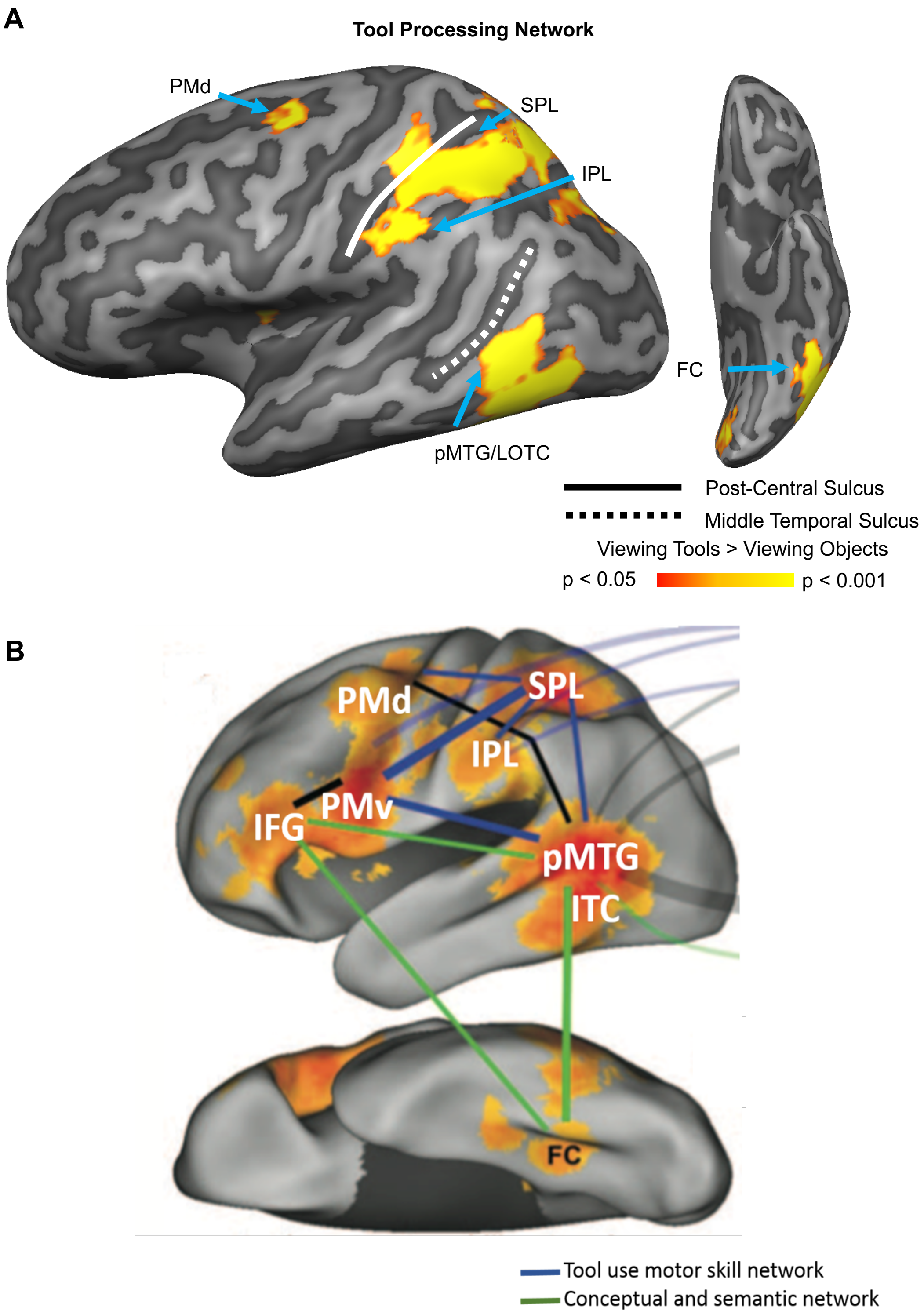

Fig. 1.2. (A) The tool processing network. Left hemisphere activation generated from contrasting viewing 2D tools and viewing 2D objects (i.e., chairs) based on data from 31 participants who completed a Bodies, Objects, Tools and Hands fMRI functional localiser across Chapters 2 and 4 (see *fMRI visual localiser paradigm:* section 2.2.4. and section 4.2.4.). (B) The tool use motor skill network (blue lines)

and conceptual and semantic tool networks (green lines) are displayed on the left hemisphere as proposed by Lewis (2006). Acronyms: ITC, Inferotemporal Cortex; FC, Fusiform Cortex; Inferior Frontal Gyrus, IFG. Figure 1.2B. is adapted and reprinted from Lewis (2006).

In a highly cited meta-analysis, Lewis (2006) examined the results of 31 tool-related neuroimaging studies that clearly shows this tool processing network and drew a distinction between a conceptual versus manipulation tool use network based on the number of paradigms showing activation overlap for a given type of task (see Fig. 1.2B.). The conceptual network was derived from findings that similar regions were found to be activated regardless of the sensory modality that tools were presented in. For instance, simply reading words depicting tools, relative to animals or other object categories (Mummery et al., 1998; Chao et al., 1999; Moore & Price, 1999; Perani, et al., 1999; Grossman et al., 2002; Phillips et al., 2002) can activate the posterior temporal and fusiform cortex (for review see Binder, Desai, Graves & Conant, 2009). Likewise, studies investigating hearing tools (e.g., Bunzeck, Wuestenberg, Lutz, Heinze & Jancke, 2005; Lewis et al., 2005) also shows a strong tool-selective left lateralisation of activity throughout parieto-premotor and posterior temporal cortex. As for the tool use motor skill network, this was based on neuroimaging experiments where participants either pantomimed the use a tool without the object in hand (e.g., Inoue et al., 2001) or imagined performing these actions (e.g., Grafton, Arbib, Fadiga & Rizzolatti, 1996; Fridman, Immisch, Hanakawa, Bohlhalter, Waldvogel, Kansaku, Wheaton, Wu & Hallet, 2006; Wadsworth & Kana, 2011).

Importantly, the tool-use motor skill network described by Lewis (2006) is based only on a single study investigating tool-use where participants manipulated chopsticks (Inoue et al., 2001). These pantomiming or imagination based studies are beneficial from a practical perspective (presenting tools in the confined space of an MRI scanner is technically challenging and increases the risk of motion artefacts driven by performing real actions), but, as highlighted by Lewis (2006), processing related to these behaviours may or may not reflect levels of abstraction needed during actual tool use. This point is emphasised by evidence that apraxia patients' symptoms can become less severe if allowed to manipulate a real tool, as opposed to pantomime their use (Buxbaum et al., 2000; Clark et al., 1994; Goldenberg & Hagmann, 1998; Goldenberg et al., 2004; Hermsdörfer et al., 2006; Laimgruber et al., 2005; Liepmann, 1908; Wada et al., 1999; Rapcsak et al., 1995; DeRenzi & Lucchelli, 1988).

The lack of real tool-use tasks during neuroimaging remains to be a major weakness in the field, possibly contributing to inconclusive findings in more recent meta-analyses. To demonstrate this point, consider a recent Activation Likelihood Estimate (ALE) analysis (Ishibashi, Pobric, Saito & Lambon Ralph, 2016) which investigated the neural clusters relevant to the retrieval of identity- (i.e., recognising or naming tasks) versus action-related properties of tools (i.e., planning, imagining and executing tool-use behaviour). These authors found a significant likelihood of activation for action processing within the left PMd and SPL, yet, the same areas were not found to be tool-selective when Valyear et al., (2017) collated clusters of activation from studies involving real grasping relative to tool-related actions (e.g., pantomiming, real manipulation) in another meta-analysis. I suspect difficulties in understanding which brain regions are critical for the retrieval of action-related knowledge needed for real tool-use will continue until further studies overcome difficulties of measuring real actions during neuroimaging. Thus, another aim of my thesis was to assess which of the regions in the tool processing network carry information relevant to performing tool-related actions.

1.6.1. Imagining or pantomiming tool-use as a proxy for real action

Remarkably, imagining to perform an action is known to share neural correlates with action observation and even motor production (e.g., Grezes & Decety, 2001; Case, Pineda & Ramachandran, 2015). Accordingly, motor imagery provides a way to explore tool-using behaviours during neuroimaging without increasing the risk of motion-artefacts that may be caused by moving the upper-limb or hand when performing real actions (see Culham et al., 2003) and would thus confound results (e.g., Friston, Williams, Howard, Frackowiak & Turner, 1996).

These imagination-based paradigms have revealed findings highly consistent with principles described earlier, indicating their usefulness in understanding the neural correlates of real tool-use. For example, left lateralisation is a key feature of multiple neuroscientific models that focus on tool-use (e.g., Binkofski & Buxbaum, 2013; Lewis, 2006) and imagining to use a tool correspondingly leads to activation within the IPL, SPL, IFG, MTG and FC that is strongly lateralised to the left hemisphere (e.g., Moll et al., 2000; Gerardin, Sirigu, Lehericy, Poline, Gaymartd, Marsault, Agid & Bihan, 2000; Creem-Regehr & Lee, 2005; Imazu, Sugio, Tanaka & Inui, 2007; Wadsworth & Kana, 2011). Likewise, Tomasino, Weiss & Fink (2012) have found that simply imagining tool-use can lead to increased functional connectivity between the left IPL and another brain area that represents the body (i.e., the extrastriate body area; Downing, Jiang, Shuman & Kanwisher, 2001; Urgesi, Candidi, Ionta & Aglioti, 2007; Downing & Peelen, 2016) - this reflects popular claims that tool-use involves the incorporation of these objects into a representation of the body (Iriki, Tanaka & Iwamura, 1996; Arbib, Bonaiuto, Jacobs

& Frey, 2009; Cardinali, Jacobs, Brozzoli et al., 2012; Farne, Serino & ladavas, 2007; Jacobs, Bussel, Combeaud & Roby-Brami, 2009; Maravita & Irki, 2004).

Another fMRI experiment utilising motor imagery also holds useful insights regarding claims made by the two-action systems model. Specifically, Vingerhoets, Acke, Vandemaele & Achten (2009) had participants imagine performing tool-related actions that were relevant to its *use* (i.e., grasp to use or grasp and use) as well as other intransitive actions (i.e., grasp to move or pointing to an object) and contrasted these with other objects that decreased in familiarity (i.e., unfamiliar tools well as for neutral shapes). The findings here showed that imagining actions based on tool-use increased activity within the left IPS, while those with more familiar tools activated the IPL in both hemispheres (though more strongly on the left). Thus, use-relevant actions appeared to be linked to the dorso-dorsal stream while tool familiarity was linked to activity within the ventro-dorsal stream, demonstrating that (1) there may be rich interactivity between the streams for tool-use (Kalenine & Buxbaum, 2010) and (2) that the dorso-dorsal stream may have access to stored knowledge (for a consistent link between the IPS and tool-related knowledge also see Valyear et al., 2007).

There are, however, well recognised drawbacks of using motor imagery as a proxy for real actions. Compliance to task demands cannot be directly assessed in imagination-based paradigms (though see Decety, Jeannerod & Prablanc, 1989) and the neural correlates of motor imagery and overt action do not perfectly overlap (Hetu, Gregoire, Saimpont, Coll, Eugene, Michon & Jackson, 2015). It could be argued the that neural differences between these two task types is mainly linked to differences in visual/sensorimotor feedback such that increased activation should only occur within primary sensory and motor areas (Gerardin et al., 2000; Hanakawa et al., 2003; Lotze et al., 1999). However, recent TMS evidence highlights that even the left IPL is critical for motor imagery (Kraeutner, Serafi, Lee & Boe, 2019) and, upon direct comparison, Imazu et al., (2007) show that actual chopstick use, relative to imagined chopstick use, can differentially activate this area. Accordingly, generalising findings from imagination-based tasks to real action behaviours should be carried out cautiously, particularly given that they can rarely be compared with real tool-use because only few neuroimaging studies have measured such behaviour.

A similar number of important findings can be drawn for tool-pantomiming studies, which involve participants pantomiming the action of a tool without it in their hand. For instance, these tasks commonly implicate the left parietal and/or frontal cortex, often independent of the hand used (Moll, Oliverira-Souza, Passman, Cunha, Souza-Lima & Andreiuolo, 2000; Choi, Na, Kang, Lee, Lee & Na, 2001; Oghami, Matsuo, Uchida & Nakai, 2004; Johnson-Frey, Newman-Norlund & Grafton, 2005; Bohlhalter et al., 2009; Kroliczak & Frey, 2009; Vingerhoets, Acke, Alderweireldt, Nys, Vandemaele & Achten, 2012). This effect being hand-independent rules out the important possibility that left lateralisation for tool-use merely reflects the tendency for action-related neuroimaging experiments to involve participants performing right-handed actions and that there is a contralesional mapping between the acting side of the body and sensorimotor cortex (e.g., Rice, Tunik, Cross & Grafton, 2007).

Similarly, a few of these pantomiming studies have indicated that many of the brain regions required to execute a tool-related pantomime are similarly active when simply planning these actions (i.e., after being instructed which pantomime to later perform; Johnson-Frey, Newman-Norlund & Grafton, 2005; Fridman et al., 2006). This approach not only mitigates the risk of motion-artefacts confounding results during tool pantomiming (i.e., there is no overt movement during planning) but also clearly informs the study of motor planning, a popular topic which motor control theories frequently identify as being distinct from motor execution (e.g., Wolpert, 1997; see Chapter 4 for further discussion).

However, atleast two points indicate that caution should still be taken before generalising actions related to tool pantomiming to that of real tool-use. First, the neural correlates of real tool-use are likely to dissociate from those for pantomimed tool-use given that such deficits dissociate in apraxia (De Renzi et al., 1982, Goldenberg, 2013, Hermsdörfer et al., 2012, Jarry et al., 2013, Randerath et al., 2011). Second, upon a direct contrast of tool pantomime and tool demonstration (i.e., pantomiming action with the tool in hand), Lausberg, Kazzer, Heekeren & Wartenburger (2015) have found that, independent of the hand used, pantomiming specifically activates the left middle and superior temporal gyri (Lausberg, Kazzer, Heekeren & Wartenburger, 2015) a region presumed to be critical for planning tool-pantomimes (Johnson-Frey et al., 2005).

In fact, Randerath, Goldenberg, Spijkers, Li & Hermsdorfer (2011) have described a number of differences between the act of pantomiming and actually using tools that may, in turn, lead to distinct activations for tool pantomiming. These include the fact that tool pantomiming involves more degrees of freedom (i.e., visual/proprioceptive cues about the tool are absent) and places a larger demand on working memory (i.e., representations of the tool and recipient object need to be maintained). Likewise, others view pantomiming in general as a highly communicative behaviour (Goldenberg 20013; Goldenberg et al. 2003) which could explain its tendency to recruit left lateralised networks (Frost, Binder, Springer, Hammeke, Bellgowan, Rao & Cox, 1999).

Of course, one could argue that these pantomiming actions are a suitable measure of regions required for processing stored long-term knowledge about tools because they contrast tool-pantomimes with other types of intransitive pantomimes (e.g., communicatory gestures). However, as I highlighted when describing findings from imagination tool-based studies, validation of this claim requires additional studies of real tool-related actions to be carried out to assess whether they do in fact show converging findings. Altogether, it is not yet clear if imagination- or pantomime-based tasks are optimal to investigate which brain regions are relevant for real tool-use because such behaviour is rarely studied. Accordingly, a real grasping paradigm was utilised for the experiments in my thesis.

1.7. Current Projects

The principal aim of my thesis was to investigate which brain regions carry learnt information about tools during a real grasping paradigm (Project 1 [Chapter 2] and Project 3 [Chapter 4]) and to explore if this is manifested in the kinematics of these actions (Project 2 [Chapter 3]). I reasoned that this was an important area of study because (1) knowledge about tools (e.g., their typical manipulations and functions) is key to human tool-use and (2) only very rarely has neuroimaging been performed when the hand is used to interact with a tool. To this end, I carried out two fMRI experiments as well as a motion-tracking investigation, all involving variations of the same 3D tool grasping paradigm.

This paradigm involved participants grasping tools in ways that were considered to be typical (i.e., by the tool's handle) or atypical (i.e., by the tool's head) for its subsequent use. A few neuroimaging experiments have employed observational tasks of a similar nature (e.g., Johnson-Frey et al., 2003; Mizelle & Wheaton, 2010), perhaps most comparably, in a movie viewing task where participants watched movies of these actions (Valyear & Culham, 2010). But, to my knowledge, this is the first time this task has been adapted for real grasping. As in Valyear & Culham (2010), a brain region sensitive to these conditions was taken to reflect a sensitivity to the learnt aspects of tool-use.

Careful consideration was given to the design of this paradigm in order to provide insights into a number of points raised during this introduction. First and foremost, a real grasping paradigm was chosen since the vast majority of tool-related experiments involving passively viewing tools or utilise pantomime or imagination-based tasks that might not truly reflect the neural processing required for real human tool-use (see *Seeing 2D tools to using 3D tools:* section 1.3.1. and *Imagining or pantomiming tool-use as a proxy for real action:* section 1.6.1.). Therefore, these experiments offer a rather unique test of the claims that tool-use is supported by the ventral visual (see *Dual visual stream theory:* section 1.3.). and ventro-dorsal pathways (see *Two-action systems model:* section 1.4.). Second, non-tool stimuli matched for important properties such as grasp kinematics and elongation were also used as (1) a control for the tool grasping conditions and (2) to investigate which brain regions were sensitive to object category (see in particular *Seeing 2D tools to using 3D tools:* section 1.3.1.). Third, by including different tool exemplars, manipulation- and function-based knowledge of tools could be experimentally teased apart (see *Segregated processing of knowledge about tool manipulation & function:* section 1.4.1.). Fourth, since we focused on grasping, rather than real tool-use actions, results may bare relation to the concept of affordances (see *Theory of affordances:* sections 1.5. and *Tools and functional affordances:* section 1.5.1.) because tool-related differences would not be attributable to an explicit intention to use these objects (note that by measuring grasping instead of tool-use, the conditions could also be more easily equated for kinematic complexity). Finally, by using a localiser ROI MVPA approach (described below) it was possible to assess whether parts of the tool-processing network usually identified during picture viewing paradigms are also sensitive to the performance of real tool-related actions (see *Seeing 2D tools to using 3D tools:* section 1.3.1. and *A tool processing network:* section 1.6.).

Project 1 (Chapter 2) used a powerful fMRI block design that was well suited to avoid motion artefacts to investigate which regions were sensitive to the learnt aspects of tool use. This was achieved using state-of-the-art MVPA classification techniques: first, in a ROI approach involving category selective areas (e.g., tool-selective areas) based on each participant's activity from an independent fMRI visual localiser (Bracci et al. 2012) and, second, in a searchlight approach that was performed throughout the entire brain. I hypothesised that much of the tool processing network (see Fig. 1.2.) would carry information regarding tool knowledge. In particular the hypothesis was made that key regions of the ventral (e.g., LOTC, pFs) and ventro-dorsal (e.g., SMG, pMTG) pathways would be sensitive to the way that the tools were grasped (e.g., typically or atypically).

Project 2 (Chapter 3) was a behavioural follow-up experiment in which participants repeated the just described investigation in a motion-tracking lab. Primarily, this experiment was designed to validate the paradigm by assessing for hallmark behavioural grasping characteristics (e.g., whether grip size scaled with object size) despite the unconventional nature of the block-design task (i.e., laying supine and making repetitive actions within a block). Second, this experiment also served to characterise the kinematics associated with the reaching (e.g., reaction time) and grasping (e.g., maximum grip aperture) portions of the movements, allowing the novel tests of two questions. First, I hypothesised that there would be differences between hand kinematics between grasping objects of a different category (i.e., the tools and non-tools) due to related evidence from motion-capture when grasping tools in order to use, relative to move, them. Second, I hypothesised that that typicality of a tool action may influence RT due to related evidence from other behavioural experiments modifying similar properties.

Project 3 (Chapter 4), involved a slow-event fMRI design that could disentangle whether the same representations described in Project 1 (Chapter 2) were decodable during motor planning, that is, before the hand moved. In this case, participants were instructed how to act but withheld this action during a delay period. The same MVPA procedures were used as in Project 1 (Chapter 2) and involved decoding during phases where participants simply viewed a tool (i.e., a preview phase), instructed how to grasp (i.e., a plan phase) and actually performed this movement (i.e., a grasp phase). Predictions were made based on the results of Project 1 and it was considered that PMv may play an important role here due to its hypothesised role in motor planning. During the preview phase, it was also predicted that ventral and, possibly, ventro-dorsal stream regions would code information about tool identity (e.g., is a knife being viewed or a pizzacutter) and object category (e.g., is a tool being viewed or a non-tool) because viewing 3D tools might be largely similar to results reported when participants have viewed 2D tools.

Chapter 2

Hand-selective areas in the dorsal and ventral visual streams represent how to grasp real 3D tools for use

2.1. Introduction

Humans' extraordinary ability to develop and use tools has co-occurred with neural evolution (e.g., Stout & Chaminade, 2012; Orban & Caruana, 2014). Comparative fMRI across humans and rhesus monkeys indicates that activation within an anterior part of the left Supramarginal Gyrus (SMG) is uniquely found when humans observe tool-use, even if the animals had previously been trained to use the tools (Peeters, Rizzolatti & Orban, 2013; Peeters, Simone, Nelissen, Fabbri-Destro, Vanduffel, Rizzolatti & Orban, 2009). Nevertheless, as will be made clear here, there is remarkably little neuroimaging evidence demonstrating which human brain regions support the ability to skilfully manipulate real tools with the hand (e.g., rather than the ability to perceive tools presented on a screen).

When we pick up tools, there is a propensity to grasp them by the handle. This behaviour persists even when the handle is oriented away from the hand and is found to cease only if performing a concurrent and taxing task involving semantic memory (Creem & Proffit, 2001). The influential Dual Visual Stream Theory (DVST; Milner & Goodale, 1995; 2006) considers these *use-appropriate* actions as a special form of visuomotor behaviour because they do not rely solely on processing within the dorsal visual stream, a pathway hypothesised to transform visual information about an object's structural properties (e.g., width, orientation) into real-world metrical coordinates for visually guided motor control (e.g., grasping). Instead, these actions are thought to additionally rely on processing from the ventral visual stream, another pathway which is differently hypothesised to process visual information for the purpose of object recognition. These perceptual mechanisms in the ventral stream would be critical for identifying a tool (e.g., Goodale & Milner, 2010) and to be involved in the selection of the appropriate hand posture for using it (Milner & Goodale, 2006; Goodale, 2014).

The behaviour of visual form agnosia patient D.F., a case study whose brain damage has been traditionally linked to the bilateral ventral (e.g., Lateral Occipital Temporal Cortex; LOTC) but not dorsal (e.g., Intraparietal Sulcus; IPS), visual stream (James, Culham, Humphrey, Milner & Goodale, 2003), clearly implicates this ventral pathway in the act of tool-use. When visually presented with a series of tools, patient D.F. does not necessarily grasp these objects by their handles, despite the fact that her actions are well-formed (e.g., her grip size is well scaled to object size) and that she has no impairment in retrieving learnt knowledge about these objects (e.g., following tactile exploration D.F. can pantomime the use of the tool; Carey, Harvey & Milner, 1996). Having a stable grasp on any portion of a tool (e.g., by the head of a tool) is suitable for purposes such as moving them from one location to another, but it is choosing to grasp the handle that reflects the successful transformation of stored knowledge about a tool into motor programs for prehension (Johnson-Frey, 2007). Accordingly, the retrieval of learnt information about object-associated actions is contingent on accessing the identity of the object and this is likely to be subserved by the ventral visual pathway (also see Almeida, Fintzi & Mahon, 2013).

Building on this, the two-action systems model (e.g., Binkofski Buxbaum, 2013; Buxbaum, 2017) theorises that tool-use is supported by a left lateralised ventro-dorsal stream that courses through the left posterior temporal cortex (e.g., Middle Temporal Gyrus [MTG]) / Inferior Parietal Lobule (IPL) to left frontal areas including the Ventral Premotor Cortex (PMv) and Inferior Frontal Gyrus (IFG; see

Rizzolatti & Matelli, 2003 and Fig. 1.1. in Chapter 1). More specifically, the ventro-dorsal pathway is predicted to be devoted to skilled actions that depend on previously learned information about familiar objects such as their identity, function and the way that it would be typically be manipulated (e.g., grasping a tool for its use; Buxbaum, 2001, Fridman et al., 2006, Glover, 2004; Buxbaum & Kalénine, 2010; Johnson-Frey, 2004, Pisella et al., 2006, Randerath et al., 2010, Vingerhoets et al., 2009). This pathway is contrasted with the bilateral dorso-dorsal stream that, instead, runs through the Superior Parietal Lobule (SPL), IPS and dorsal premotor cortex (PMd; Rizzolatti & Matelli, 2003) and is supposedly for processing information based on currently available visual and proprioceptive information (e.g., grasping a tool based on its structure; Binkofski & Buxbaum, 2013).

Behaviour from patients with apraxia clearly illustrate claims made about the ventro-dorsal stream by the two-action systems model (e.g., Watson & Buxbaum, 2015). These patients tend to be impaired during tasks that involve retrieving stored knowledge about an object, such as when having to pantomime the use of a tool (Buxbaum, Sirigu, Schwartz & Klatzky, 2003; Sirigu et al., 1995; Poizner, Mack, Verfaellie, Rothi & Heilman, 1990) and when having to interact with a real tool (e.g., Hermsdorger, Li, Randerath, Roby-Brami & Goldenberg, 2013; Sperber, Christensen, Llg, Giese & Karnath, 2018), which can even be detected when simply grasping the handle of a tool in order to demonstrate its use (Randerath, Li, Goldenberg, & Hermsdorfer, 2009; also see Goldenberg & Hagmann, 1998). Crucially, these apraxic deficits are often apparent despite no impairments when performing or recognising hand actions based on the structure of an unfamiliar object (e.g., when matching hand postures to a novel object; Sirigu et al., 1995; Buxbaum, Sirigu, Schwartz & Klatzky, 2003) and tend to follow lesions to the ventro-dorsal stream such as the left IPL (e.g., Buxbaum, Kyle, Grossman & Coslett, 2007; Haaland, Harrington, & Knight, 2000; Heilman, Rothi & Valenstein, 1982; Randerath, Goldenberg, Spijkers, Li, & Hermsdörfer, 2010), or, less commonly, the left premotor areas and middle/inferior frontal gyri (e.g., Goldenberg, 2009),

Theoretically, the ventro-dorsal stream is proposed to support tool-use through its access to manipulation knowledge which is predicted to be in the form of stored multisensory and motor memories that are learnt from using objects (Buxbaum, 2017). Specifically, it is predicted that the posterior temporal cortex (e.g., the posterior MTG [pMTG]) encodes information about the learnt relationship between the hand and tool (e.g., visually and kinaesthetic representations of the hand and the tool's handle), while the SMG prepares candidate movements (e.g., grasping by the handle or grasping by the head) and the IFG uses contextual information to select which of those movements should ultimately be executed (e.g., confirming if the goal is to use the tool; also see Cisek, 2007; Cisek & Kalaska, 2010). This process is expected to be supplemented by processing within the dorso-dorsal visual stream that translates learned representations of a tool-related movement into an action suited for the current situation (e.g., based on real-time sensory input about the exact tool exemplar).

Ideally, these hypotheses from the DVST and two-action systems model would be heavily tested with neuroimaging techniques (e.g., fMRI, PET) by examining the brain's responses when humans interact with real 3D tools. However, obvious technical constraints make this approach challenging, particularly in the case of fMRI (e.g., limitations of space, required use of non-ferrous equipment). This said, a few studies do involve participants using a single tool throughout the scanning session (e.g., a pair of chopsticks or tongs; Tsuda, Aoki, Oku, Kimura, Hatazawa & Kinoshita, 2009; Imazu, Sugio, Tanaka & Inui, 2007; Ogawa, Schormann, Zilles & Fukuda, 2001; Yoo, Sohn & Jeong, 2013; Gallivan et al., 2013) and, most notably, two studies (i.e., Valyear, Gallivan, McLean & Culham, 2012; Brandi Wohlschlager, Sorg & Hermsdorfer, 2014; also see Stark & Zohary, 2008) have utilised specialist equipment (see Culham et al., 2003) to facilitate paradigms where participants manipulate a series of real tools during fMRI (see Valyear et al., 2017 for a review).

Those two fMRI experiments that overcome the difficulty of presenting a series of 3D tools during scanning have revealed that actions linked to tool-use (e.g., a spatula for flipping), rather than tool-related actions that do not rely on stored knowledge (e.g., moving a tool or performing an arbitrarily cued action), is linked to processing throughout parieto-frontal (Valyear, et al., 2012; Brandi, et al., 2014) and, to some extent, occipito-temporal (Brandi et al., 2014) cortex. In the first study, Valyear et al., (2012) found a series of regions including the bilateral SMG, left anterior IPS (aIPS) and right SPL that were more active, or exhibited neural adaptation (see Chapter 1 for further description of this study) for performing well learnt actions. In the second study, Brandi et al., (2014) presented participants with an impressive number of tool and manipulable bar shaped non-tool objects in order to contrast neural activity when these stimuli were used or simply moved. Most relevant here, it was revealed that performing the functional use of a tool (e.g., cutting string with scissors), relative to either the use of a non-tool (e.g., fitting a bar into an inset) or moving a tool (e.g., lifting scissors), preferentially activated the left Middle Occipital Gyrus, as well as areas within the ventro-dorsal stream (i.e., MTG, SMG and PMv).

From a critical perspective, however, performing learnt actions in these studies did not implicate canonically described ventral visual stream regions such as the LOTC (i.e., area LO and the posterior Fusiform Gyrus [FG]; Grill-Spector & Malach, 2004). In fact, close inspection of results obtained from Brandi et al., (2014) reveals that the left LOTC co-activated with critical substrates of the dorso-dorsal stream (e.g., bilateral SPL and left PMd) when an object was used, regardless of whether it was tool or a non-tool. This fits rather poorly with the DVST claim that the ventral visual pathway is specifically involved in tool-use.

All of this said, over two decades of neuroimaging evidence clearly pinpoints a tool-processing network that activates when imagining or perceiving stimuli depicting tools regardless of whether they are presented in the form of pictures, words, movies or sounds (for reviews Ishibashi, Pobric, Saito & Lambon Ralph, 2016; Chouinard & Goodale, 2010; Lewis, 2006). The tool processing network is largely left lateralised and encompasses occipito-temporal and parieto-frontal areas most of which were already described earlier in relation to the DVST and two-action systems model (see Fig. 1.2. in Chapter 1). Neuroimaging studies using these non-action tasks continue to demonstrate that many parts of the tool-processing network are sensitive to the functions (e.g., Mahon, Milleville, Negri, Rumiati, Caramazza & Martin, 2007; Canessa, Borgo, Cappa, Perani, Falini, Buccino & Shallice, 2008; Peelen & Caramazza, 2012; Leshinskaya & Caramazza, 2015; Tonin, 2018) and identities of tools (e.g., Mahon & Caramazza, 2010). Recently, Chen et al., (2017) even showed that viewing tools, relative to similarly elongated non-tool objects, increases fMRI functional connectivity between core nodes within the ventral (i.e., left Fusiform Gyrus; FG) and ventro-dorsal stream (i.e., left MTG) to another node in the dorsal stream (i.e., the anterior IPS; aIPS), as may be expected by the DVST and two-action systems model.

How relevant this tool-processing network is to real tool-use remains an open question, however. Images of tools are a popular choice of stimuli, yet there is growing evidence that real 3D objects are represented differently than a 2D picture of that same object within the ventral and dorsal visual streams (Snow, Pettypiece, McAdam, McLean, Stroman, Goodale & Culham, 2011; Freud, Macdonald, Chen, Quinlan, Goodale & Culham, 2018). This is perhaps unsurprising given that real objects offer richer cues about depth as well as a genuine possibility for action, as demonstrated by the fact that performing a grasp towards a flat picture follows a fundamental psychophysical principle (i.e., Weber's law) but real object grasping does not (Holmes & Heath, 2013).

One particularly interesting avenue worth exploring is whether overlapping portions of the left LOTC and IPS that are selective to pictures of tools or hands (i.e., LOTC-Tool, LOTC-Hand, IPS-Tool and IPS-Hand; Op de Beeck, Brants, Baeck & Wagemans, 2010; Bracci, Ietswaart, Peelen & Cavina-Pratesi, 2010; Bracci, Cavina-Pratesi, Ietwaart, Caramazza & Peelen, 2012; Bracci & Peelen, 2010; Striem-Amit, Vannuscorps & Caramazza, 2017; Perini, Caramazza & Peelen, 2014) play a role in real tool interactions. A number of picture viewing studies suggest that these areas, particularly in the LOTC, carry information about action-related properties of hand movements (e.g., Bracci, Cavina-Pratesi, Connolly & Ietswaart, 2016; Peelen, Bracci, Lu, He, Caramazza & Bi, 2013), such as the type of grasp (e.g., precision versus power grasp; Bracci, Caramazza & Peelen, 2018) or action that is associated with a tool (e.g., squeezing versus rotating; Perini, Caramazza & Peelen, 2014).

Driven by the fact that the sensitivity of an fMRI analysis can be optimised by using multivariate techniques (Haxby, Gobbini, Furey, Ishai, Schouten & Pietrini, 2001; Kamitani & Tong, 2005; Kriegeskorte & Bandettini, 2007), it has become increasingly popular to use Multi-Voxel Pattern Analysis (MVPA) to understand where representations about real actions are stored (for reviews see Gallivan & Culham, 2015; Hutchinson & Gallivan, 2018). One technique, known as MVPA classification, involves passing voxel activity patterns from a region into a machine learning algorithm to test if different types of experimental condition can be *decoded* (Haxby, Gobbini, Furey, Ishai, Schouten & Pietrini, 2001).

This MVPA classification approach has revealed that patterns of activity throughout the primary motor cortex as well as the dorso-dorsal stream, such as the premotor cortex, SPL, and IPS can be used to discriminate between movements involving different reach directions (e.g., left versus right; Fabbri, Stubbs, Cusak & Culham, 2016; Gallivan, McLean, Smith & Culham, 2011; Gallivan, McLean, Flanagan & Culham, 2013), degree of grip precision (touch versus grasp; Gallivan, McLean, Valyear, Pettypiece & Culham, 2011; Fabbri, Stubbs, Cusak & Culham, 2016; Ariani, Wurm & Lingnau 2015; Ariani, Oosterhof & Lingnau, 2018), hand rotation (e.g., Shay, Chen, Garcea & Mahon, 2019) or even individual finger movements (Diedrichsen, Wiestler & Krakauer, 2013).

Recently, a few studies have shown that decoding is possible for various abstract aspects of a tool-related pantomime that cannot simply be attributed to specific movement kinematics. For example, the left FG has been shown to carry representations about the function associated with a tool (i.e., open versus cut) whereas regions including the pMTG, premotor cortex and IPL represent their related action types (i.e., rotate versus squeeze; Chen, Garcea & Mahon, 2016; Chen, Garcea, Jacobs & Mahon, 2017). Likewise, the aIPS has been shown to code the identity of a tool (Ogawa & Imai, 2016) while many regions including the ventral part of the LOTC, IPS, premotor cortex, MTG and SMG code functional tool grasping (Buchwald, Przybylski & Kroliczak, 2018). However, how well these results reflect those that would be obtained from real tool interactions is unclear, particularly given that pantomiming places additional demands on the ventral visual stream (e.g., Westwood & Goodale, 2003; Tonin, 2018).

The primary goal of the current experiment was to examine which brain regions contain activity patterns that are sensitive to grasping a tool in a way that is consistent with its learnt use. A few picture/movie viewing fMRI experiments have used stimuli depicting hands grasping a tool in conditions that can be considered as either typical (i.e., by the tool’s handle) or atypical (i.e., by the tool’s head) in relation to the object’s ordinary use (e.g., Johnson-Frey, Maloof, Newman-Norlund, Farrer, Inati & Grafton, 2003; Valyear & Culham, 2010; Mizelle & Wheaton, 2010a; Mizelle & Wheaton, 2010b; also see Hoeren, Kaller, Glauche, Vry et al., 2013 and Roberts & Humphreys, 2010). Consistent with visual form agnosia patient D.F.’s failure to grasp tools in a way consistent with their learnt use (Carey, Harvey & Milner, 1996), most of these studies report that activity in the ventral visual (and ventro-dorsal) stream is sensitive to the typicality of viewed grasp (e.g., Valyear & Culham, 2010; Mizelle & Wheaton, 2010a). For example, Valyear & Culham (2010) have demonstrated that ventral stream regions including the bilateral pMTG and LOTC were more greatly active when participants viewed movies of typical, than atypical, tool grasping. Likewise, Mizelle Kelly & Wheaton (2013) similarly reported large clusters of activity throughout bilateral occipitotemporal and parietofrontal cortex were influenced by the appropriateness of how a tool was held (e.g., a hammer held by its handle so that its head is over a nail versus a hammer held by its head so the hand is over a nail). The nature of this task, then, appears suitable for identifying the regions sensitive to the learnt aspects of tool-use.

Here, we measured brain activity with fMRI while participants reached-to-grasp 3D-printed tool (i.e., kitchen utensils) and bar shaped non-tool (i.e., bar-shaped) objects matched for their degree of elongation, required grip size and reach distance (Fig. 2.1A). A ROI and searchlight MVPA classification strategy was employed to assess which brain regions exhibited activity patterns that could be used to decode the *typicality* of tool grasping - this entailed decoding between tool grasps that were considered to be *typical* (i.e., by the tool's handle) versus *atypical* (i.e., by the tool' head) for subsequent use. As a control, we also assessed whether decoding was possible for the *grasp direction* of non-tool grasping - this entailed decoding between non-tool grasps that were located on their *right* versus *left* sides (i.e., the sides of the non-tools that corresponded to the typical and atypical grasping of tools, respectively). We reasoned that a region containing representations that are tuned to the learnt aspects of tool-use would display decoding accuracies for typicality that were significantly higher than (1) chance and (2) the decoding accuracy obtained from the same ROI when discriminating between grasp direction.

For the ROI MVPA, an independent fMRI visual localiser to define left-hemisphere tool-processing network ROIs (LOTC-Tool, IPS-Tool, pMTG, PMv, PMd, aSMG, posterior Fusiform sulcus [pFs]) per subject. Additionally, the localiser allowed us to define other left hemisphere category selective portions of the IPS and LOTC that were selective to pictures of hands (LOTC-Hand, IPS-Hand), bodies (LOTC-Body) and objects (LOTC-Object) as well as control ROI in the left Early Visual Cortex (EVC). The searchlight MVPA approach was used to test if this information could be decoded from activity patterns from any other brain region across either hemisphere.

Based on the DVST (Milner & Goodale, 1995; 2006), we predicted that ventral visual stream regions would specifically represent typicality (e.g., the LOTC and pFs), particularly in parts of the LOTC selective to pictures of tools and hands because they are known to process information about object-directed actions (e.g., Perini, et al., 2014; Striem-Amit, Vannuscorps & Caramazza, 2017). The same pattern of results was anticipated to occur in the ventro-dorsal stream ROIs, including the pMTG, aSMG and PMv, because of their access to manipulation knowledge as predicted by the two-action pathways model.

As a secondary goal, stimuli were designed to enable us to examine which brain regions coded additional features relevant to tool-directed actions including *object category* (i.e., grasping *tools* versus *non-tools*) as well as *tool function* (i.e., grasping tools strongly associated with *cutting* versus *scooping*) and *tool identity* (i.e., grasping a *knife* versus *spoon* versus *pizzacutter*). In particular, it was predicted that ventral stream regions (i.e., LOTC and FG) would code information about object category and tool identity given their role in object identification (Milner & Goodale, 1995; 2006) and ventro-dorsal stream regions (i.e., pMTG, aSMG, PMv) would code information about tool function due to their roles in retrieving learnt object-related knowledge (e.g., Buxbaum, Veramontil & Schwartz, 2000; Boronat, Buxbaum, Coslett, Tang, Saffran, Kimberg & Detre, 2005).

2.2. Method

2.2.1. Participants

A total of twenty right-handed (Edinburgh Handedness Questionnaire; Oldfield, 1971) healthy volunteers were recruited from the University of East

Anglia’s (UEA’s) paid participant panel. One participant was excluded due to excessive head motion during scan sessions (see *Data preprocessing:* section 2.2.7.) leaving a total sample of nineteen participants (10 males, 18-34 years of age; mean age [standard deviation] = 23.4 [4.2]). Fifteen of the participants were naïve to the purpose of the study and the remaining five were authors. All had normal or corrected-to-normal vision, no history of motor, psychiatric or neurological disorders and gave informed consent in accordance with the ethical committee at the UEA. Financial compensation was provided for all volunteers.

2.2.2. Stimuli & apparatus

Two different categories of stimuli were presented during the experiment: tools and non-tools (Fig. 2.1A). The tool set comprised three commonly used kitchen utensils (i.e., a knife, pizza-cutter and spoon). The non-tool set included three bar shaped objects (also see Brandi et al., 2014) that were each paired to a single tool by matching their degree of elongation and maximum width. To closely match the required kinematics (i.e., reach distances and required grip aperture) needed to grasp the tools typically/atypically with that of grasping the paired non-tools on either side, two black squares (0.6cm x 0.6cm) were located on the left and right sides of each stimulus indicating where the object should be precision grasped widthways (i.e., finger on top and thumb on bottom). These black markers were positioned at the widest part of the functional-end of the tools and then, equidistantly from the middle, on their handles (identical positions were transposed on to the non-tools). Note that the knife tool and non-tool pair were controlled most effectively where the required grip size was identical throughout all conditions.

The tools had identical handles (maximum dimensions for length x width x depth: 11.6cm x 1.9cm x 1.1cm) attached to different functional-ends (pizza-cutter:

10.1cm x 7.5cm x 0.2cm, spoon: 10.1cm x 4.1cm x 0.7cm & knife: 10.1cm x 1.9cm x 0.2cm). The non-tool objects were built from two cylindrical shapes. These were an identical length to the paired tools' handle or functional-end. To minimise the resemblance of the non-tools to a tool (e.g., a spatula), the maximum width and depth of *both* cylinders were matched to the paired tools' functional-end (i.e., the non-tool cylinders matching the length of the handles for the spoon and pizza-cutter were thus wider than the handles of the paired tools). Both cylinders were connected using a third cylindrical shape with the same size dimensions as the paired tools' neck (e.g., the non-functional part such as the non-serrated part of the knife blade). In foil trials, a fourth whisk tool (10.1cm x 5.6cm x 5.6cm) and the pizzacutter non-tool (i.e., the non-tool with a width most similar to the whisk's functional end) were presented but excluded from further analysis to keep the number of experimental trials per exemplar equal. All objects were digitally designed (Autodesk Inc., San Rafael, CA, USA) and 3D-printed (Objet30 Desktop) in VeroGray material (Stratasys) material.

Two back-to-back pedestals rested on a custom-built turntable (e.g., Gallivan, Cavina-Pratesi & Culham, 2009) that sat above the subjects' pelvis when lying supine in the scanner (Fig. 2.1B). Stimuli were secured to a backboard so that they could be inserted on to the sloped platform (~10-15° away from the horizontal) at a distance comfortably within reach (the mean distance between the resting hand and centre of an object was 43cm [SD = 4cm]). To achieve direct vision of stimuli without the use of mirrors, the head coil was tilted and foam cushions (NoMoCo Pillow, La Jolla, CA, USA) were used to support the head (head tilt = ~30°). The likelihood of motion artefacts related to performing reach-to-grasp actions was reduced by restraining the upper-right arm and providing support with additional cushions so that movements were performed by flexion around the elbow only.

During the experiment, objects were only visible when illuminated by white Light Emitting Diodes (LEDs) attached to a flexible plastic stalk (LOC-LINE; Lockwood Products, Inc., Lake Oswego, OR, USA) positioned above the participant's left shoulder. Earphones (Sensimetrics MRI-Compatible Insert Earphones Model S14, USA) were worn for receiving verbal instructions and a centrally aligned red fixation LED was located above objects (subtending a mean visual angle of ~20° [SD = 0.7°] from the centre of stimuli). Movements of the right eye and arm were recorded using two infrared cameras (MRC Systems GmbH, Germany). A custom designed script written in Matlab (The MathWorks, USA R2010a), using the Psychophysics Toolbox extensions (Brainard, 1997) controlled all equipment.

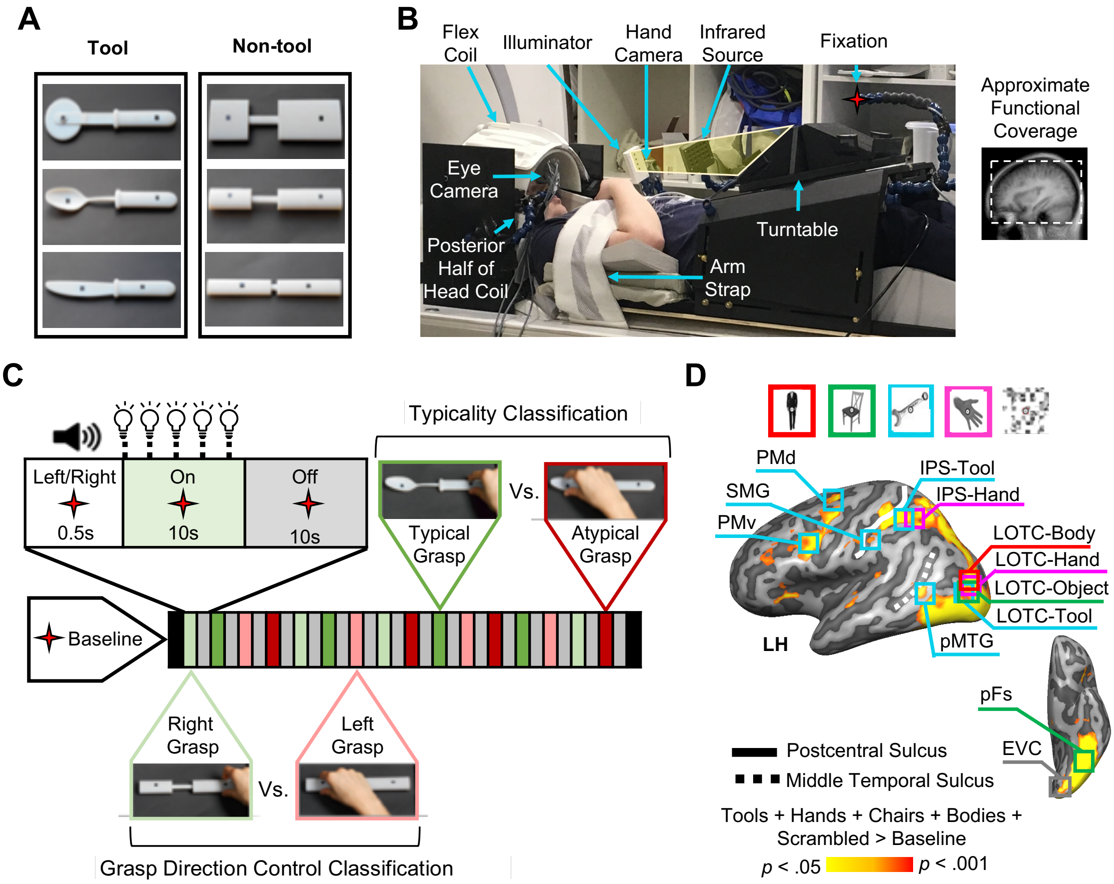

Figure 2.1. Methods and materials. (A) 3D-printed tool and non-tool stimuli. (B) Turntable apparatus used to present graspable objects shown from the side (the experiment is completed in the dark, thus lighting here is for illustration only). The upper limb and hand are shown at the starting location. The red star represents the fixation LED and the delineated yellow zone represents the workspace that was illuminated by white LEDs. Cameras recording eye and hand movements in the dark were supported by an infrared source. Approximate functional coverage is presented (right) and was achieved by suspending a flex coil over the head. (C) Timing of the fMRI block design. A schematic of a single ON-OFF block period is highlighted (top left) that always consisted of an auditory instruction period (white block, where participants heard the word ‘left’ or ‘right’), an ON block where the object is illuminated and subsequently grasped five times (green block, where grasping is performed once every two seconds on the side of the object previously instructed) and followed by an OFF block where the workspace remained dark (grey block, where participants continue maintaining fixation). For analysis, a classifier received input from the rightward and leftward grasping blocks for both the tool and non-tools objects independently. For the tools blocks these right and left grasps corresponded to grasping the tool in ways that were typical (i.e., by the handle) and atypical (i.e., by the functional-end) for use, respectively (also see Fig. 2.3). (D) Representative locations of functionally defined perceptual ROIs are depicted by colour coded cubes based on the type of contrast used from a Bodies, Objects, Hands and Tools (BOTH) localiser per participant (see Section 2.2.8. for more information). Group activation during the BOTH visual localiser is displayed for [all conditions > (baseline*5)] and projected onto a left hemisphere cortical surface reconstruction of a reference brain (COLIN27 Talairach) available from the neuroElf package (http://neuroelf.net).

2.2.3. fMRI grasping paradigm

In an fMRI block design 10s ON/OFF blocks were used because they have been shown to optimally detect BOLD signal changes without significant motion artifacts (Birn, Cox & Bandettini, 2004; Fig. 2.1C). In an ON block, the object was briefly illuminated (0.25s) five times with two second intervals. Every illumination of the object acted as a cue for participants to perform a precision grasp (i.e., using index finger and thumb to grasp the top and bottom of the object, respectively) using their right hand at a natural pace in open-loop conditions (e.g., Monaco, Sedda, Cavina-Pratesi & Culham, 2015). Between illumination periods, the hand returned to the starting location (i.e., closed and resting on the middle of the chest; see Fig. 2.1B). The workspace remained dark in the OFF blocks that followed each ON block. This flashing presentation cycle within the ON blocks has been shown to maximise the signal-to-noise ratio in previous perceptual decoding experiments (Kay, Naselaris, Prenger & Gallant, 2008; also see Smith & Muckli, 2010). Participants were asked to maintain fixation throughout each run and all 3D objects appeared in their lower peripheral visual field (Rossit et al. 2011).

Importantly, before each ON block began, a verbal ‘Left’ or ‘Right’ auditory cues (0.5s) informed the participant which side of the object was to be grasped. Crucially, the tools’ handles (and the side of the non-tools matching the length of these handles) were always oriented to the right so that right- and left-ward grasping for the tool conditions were could be labelled as typical and atypical, respectively. Participants were never instructed to use the objects and all stimuli were described as objects rather than tools to volunteers.

Each functional run included 16 ON blocks. For the 12 experimental ON blocks, three repetitions were completed per condition (i.e., tool typical, tool atypical, non-tool right and non-tool left). Specifically, every exemplar was presented twice per run, once for a left and once for a right grasp. The remaining foil ON blocks involved grasping the tool and non-tool by each side but were excluded from analysis. On average participants completed six runs (minimum five, maximum seven), equalling 18 reps per the primary conditions (i.e., tool typical, tool atypical, non-tool right and non-tool left). Block orders were pseudorandomised so that conditions were never repeated (two-back) and preceded an equal amount of times by other conditions. Including the start and end baseline fixation periods (14s), each functional scan lasted 356s (5:56 minutes), making the length of a single session ~1 hour 45 minutes. Prior to the fMRI experiment, participants were familiarised with the setup and practiced grasping each side of every exemplar in a separate lab session (30 minutes) outside of the scanner.

2.2.4. fMRI visual localiser paradigm

Following the real action experiment, all participants returned for a separate session where we used a Bodies, Objects, Hands and Tools (BOTH) fMRI visual localiser (Bracci, Ietswaart, Peelen & Cavina-Pratesi, 2010; Bracci, Cavina-Pratesi, Ietswaart, Caramazza & Peelen 2011; Bracci, Cavina-Pratesi, Connolly & Iettswaart, 2016). This enabled ROIs to be defined based on independent functional data in regions commonly reported to activate when participants view 2D pictures of tools (Fig. 2.1D.). In separate blocks (14s) 14 different images (0.5 seconds) were presented and interleaved by blank white screens (0.5 seconds) for a given stimulus category (Fig. 2.2.). Every fifth block contained fixation-only scrambled image epochs and the order of the four experimental conditions were randomised between these baseline periods.

To match, as much as possible, characteristics within the tool (i.e., identity & orientation), body (i.e., gender, body position & amount of skin shown), hand (i.e., position & orientation) and chair (i.e., materials, type & style) categories, two sets of 24 individual 2D grayscale images depicting an isolated stimuli against a white background (400 x 400 pixels) were selected from previous stimuli sets (Bracci, et al., 2010; Bracci, Cavina-Pratesi, Ietswaart, Caramazza & Peelen 2011; Bracci, Cavina-Pratesi, Connolly & Iettswaart, 2016). Image sets were presented in alternated runs that were counterbalanced across the sample and had a central black and white bullseye fixation overlaid throughout the experiment. Stimuli were rear-projected (SilentVision SV-6011 LCD, Avotech Inc., Stuart, FL, USA) on to a screen and were viewed through a head-coil mounted mirror while participants laid supine in the scanner. A one-back detection task was performed with responses collected via button press (FORP, Current Design, Inc., USA). Individual orders of stimulus exemplars were randomised, and a single run included 24 category blocks (6 reps per condition) with blank fixation baseline periods (14s) at the beginning and the end of the experiment. Each localiser scan lasted 448 seconds (7:28 minutes) and, on average, participants completed 4 runs (minimum 3, maximum 4). The entire localiser session lasted ~50 minutes after including the time taken for an anatomical scan plus setting up (~10 minutes each).

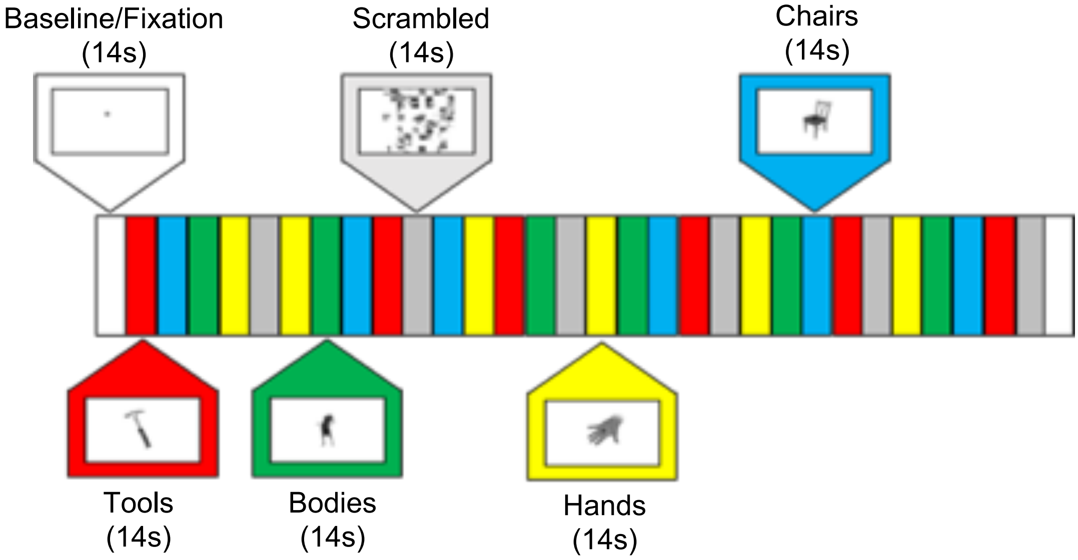

Figure 2.2. Experimental timing of the Bodies, Objects, Hands and Tools (BOTH) perceptual localiser fMRI block design with example stimulus images. Adapted from Bracci, Ietswaart, Peelen & Cavina-Pratesi (2010), Bracci, Cavina-Pratesi, Ietswaart, Caramazza & Peelen (2011) and Bracci, Cavina-Pratesi, Connolly & Ietswaart (2016).

2.2.5. Data acquisition

The BOLD fMRI measurements were acquired using a 3T wide bore GE-750 MR scanner. To achieve a good signal to noise ratio during the grasping paradigm, whilst enabling direct vision of the workspace without the use of mirrors, the head rested in a tilted posterior half of a 21-channel receive-only coil and a 16-channel receive-only flex coil was suspended over the anterior-superior part of the skull. A full 21-channel head coil was used for the BOTH localiser paradigm.

Functional MRI volumes were acquired using T2*-weighted single-shot gradient Echo-Planer Imaging (EPI) sequences during both the grasping experiment and the BOTH visual localiser (Time to Repetition [TR] = 2000ms; Voxel Resolution [VR] = 3.3 x 3.3 x 3.3mm; Time to Echo [TE] = 30ms; Flip Angle [FA] = 78°; Field of View [FOV] = 211x 211mm; Matrix Size [MS] = 64 x 64). Each volume comprised 35 contiguous (no gap) oblique slices acquired through axial orientation, providing near whole-brain coverage. A T1-weighted anatomical image was acquired at the start of each paradigm using BRAVO sequences (TR = 2000ms; TE = 30ms; FOV = 230mm x 230mm x 230mm; FA = 9°; MS = 256 x 256; Voxel size = 0.9 x 0.9 x 0.9mm) with 196 slices providing near whole-brain coverage. The MR imaging for the real action paradigm and 18 of the localiser paradigms was performed at the Norfolk & Norwich University Hospital (Norwich, UK). Datasets for the two remaining localiser sessions were retrieved from Rossit, Tonin & Smith (2018) where a Siemens whole-body 3T MAGNETON Prisma fit scanner with a 64-channel head coil and integrated parallel imaging techniques was used at the Scannexus imaging centre (Maastricht, Netherlands). In these cases the same number of slices were acquired for the functional T2*-weighted images (TR = 2000 ms; TE = 30 ms, FA = 77°; FOV = 216 mm; matrix size = 72 x 72), whilst the T1-weighted anatomical image had 192 slices (TR = 2250 ms; TE = 2.21ms; FA = 9°; FOV = 256 mm; matrix size = 256 x 256).

2.2.6. Data preprocessing

To ensure that participants performed the real action paradigm correctly and that they maintained eye fixation, the recorded videos of the right eye (available of 8 participants due to technical issues) and workspace (available for 14 participants due to technical issues) were screened. Two runs (of two separate participants) from the entire experiment were excluded from further analysis. In one of these blocks the participant failed to follow the grasping task instructions correctly (i.e., performing alternated left and right grasps) and for the remaining block another participant did not maintain fixation (i.e., saccaded downward to object). In the remaining runs that were analysed, participants made performance errors in <1% of experimental trials. The types of errors included not reaching after every illumination (3 trials, 2 participants), reaching in the wrong direction (1 trial, 1 participant) and downward eye saccades (5 trials, 3 participants). A one-way Repeated Measures (RM) ANOVA with 12 levels (i.e., the six exemplars across both left versus right grasping conditions) showed that these percentage of errors were equally distributed amongst trial types regardless of whether the percentage of hand and eye errors were analysed after being combined or treated separately (all *p*'s > 0.28).

Preprocessing of the raw functional datasets and the subsequent ROI definitions were carried out using BrainVoyager QX [version 2.8.2] (Brain Innovation, Maastricht, The Netherlands). BrainVoyager's 3D motion correction (sinc interpolation) aligned each functional volume within a participant to the functional volume acquired closest in time to the anatomical scan (e.g., Fabbri, Stubbs, Cusack & Culham, 2016; Rossit, McAdam, Mclean, Goodale & Culham, 2013). One subject was excluded from further analysis because of excessive head movements (i.e., x, y & z translation and rotation spikes exceeded 1mm and 1° rotation, respectively) as revealed by screening the time-course movies and motion plots created with the motion-correction algorithms for each run. Slice scan time correction (ascending and interleaved) and high-pass temporal filtering (2 cycles/run) was also performed. Functional data were superimposed on to the anatomical brain images acquired during the localiser paradigm that were previously aligned to the plane of the anterior-posterior commissure and transformed into standard stereotaxic space (Talairach & Tournoux, 1988). No additional spatial smoothing was applied.

To identify ROIs from the BOTH localiser datasets per participant we used independent fixed-effects General Linear Model (GLM) analyses. The predictors for each image condition (i.e., Bodies, Objects, Tools, Hands and Scrambled) were created from boxcar functions that were then convolved with a two gamma Boynton (Boynton, Engel, Glover & Heeger, 1996) hemodynamic response function (HRF). A boxcar HRF was aligned to the onset of the stimulus block with the same duration as block length. The baseline epochs were excluded from the model, and therefore, all regression coefficients (betas) were defined relative to this baseline activity.

2.2.7. ROI definitions

Twelve ROIs (see Fig. 2.1D and Table 1) that could be functionally defined from the BOTH localiser activity were selected based on their well-documented roles in processing information related to tools (see Lewis, 2006 and Valyear, Fitzpatrick & McManus, 2017 for reviews), body parts (Bracci, Iettswaart, Peelen & Cavina-Pratesi, 2010; Bracci, Cavina-Pratesi, Ietswaart, Caramazza & Peelen, 2011; Bracci, Cavina-Pratesi, Connolly & Iettswaart, 2016) and/or objects (see Grill-Spector & Weiner, 2014 for a review). These included multiple ROIs in the LOTC (i.e., LOTC-Hand, LOTC-Body, LOTC-Tool & LOTC-Object) and IPS (i.e., IPS-Hand & IPS-Tool) that were defined based on their selectivity to different categories of stimuli, as well as the pMTG, posterior Fusiform sulcus (pFs), SMG, PMd, PMv and, as a control, the Early Visual Cortex (EVC). All of these areas were identified in the left hemisphere because of evidence the strong left lateralisation for tool processing (Lewis, 2006).

ROIs were defined by drawing a cube (15 voxels^3) around the peak of activity from previously reported volumetric contrasts set at a threshold of $t = 3$ which equated to $p < 0.005$ (Gallivan, McLean, Valyear, & Culham, 2013). If no activity was identified a more liberal threshold was applied ($t = 2.581$, $p < .01$) (Bracci, Cavina-Pratesi, Connolly & Ietswaart, 2016) and in cases where no activity was observed these ROIs were omitted for that participant (see Table 1 for mean

Talairach coordinates and frequencies of ROI per subject). The location of 22% ROIs were verified by a senior author (S.R.) with respect to the following anatomical guidelines:

- *Lateral Occipitotemporal Cortex-Object selective* (LOTC-Object) - [Chairs > Scrambled] (Hutchinson, Culham, Everling, Flanagan & Gallivan, 2014; Bracci & Op de Beeck, 2016) - defined by selecting the peak of activation near the Lateral Occipital Sulcus (LOS) (Malach, Reppas, Benson, Kwong, Jiang, Kennedy, Ledden, Brady, Rosen & Tootell, 1995; Grill-Spector, Kourtzi & Kanwisher, 2001; Grill-Spector, Kushnir, Edelman, Avidan, Itzchak & Malach, 1999; Bracci & Op de Beeck, 2016).
- *Lateral Occipitotemporal Cortex-Body selective* (LOTC-Body) - [Bodies > Chairs] (Bracci & Op de Beeck, 2016) - defined by selecting the peak of activation near the LOS and inferior to the left Extrastriate Body Area (EBA; Valyear & Culham, 2010) which was identified by the contrast [(Bodies + Hands > Chairs)] (adapted from Bracci, Ietswaart, Peelen & Cavina-Pratesi (2010) [(Whole Bodies + Body Parts) > (Hands + Chairs)]). EBA was not included in the analysis.
- *Lateral Occipitotemporal Cortex-Hand selective* (LOTC-Hand) - [(Hands > Chairs) AND (Hands > Bodies)] (Bracci & de Beeck, 2016) - defined by selecting the peak of activation near the LOS. These were often anterior to LOTC-Body (Bracci & Op de Beeck, 2016; Bracci, Ietswaart, Peelen & Cavina-Pratesi, 2010).
- *Lateral Occipitotemporal Cortex-Tool selective* (LOTC-Tool) - [Tools > Chairs] (Bracci, Cavina-Pratesi, Ietswaart, Caramazza & Peelen, 2012; Hutchinson, Culham, Everling, Flanagan & Gallivan, 2014) - defined by selecting the peak of activation near the LOS. These often closely overlapped LOTC-Hand (Bracci, Cavina-Pratesi, Ietswaart, Caramazza & Peelen, 2012).

- *Posterior Middle Temporal Gyrus* (pMTG) - [Tools > Chairs] (Hutchinson, Culham, Everling, Flanagan & Gallivan, 2014; Valyear & Culham, 2010) - defined by selecting the peak of activation on the pMTG, more lateral, ventral and anterior to EBA (Hutchison et al., 2014). We selected the peak anterior to the Anterior Occipital Sulcus (AOS), as the MTG is in the temporal lobe and the AOS separates the temporal from the occipital (Damasio, 1995).
- *Posterior Fusiform Sulcus* (pFs) - [Chairs > Scrambled] (Hutchinson, Culham, Everling, Flanagan & Gallivan, 2014) - defined by selecting the peak of activation in the posterior aspect of the fusiform gyrus, extending into the occipitotemporal sulcus (Hutchinson, Culham, Everling, Flanagan & Gallivan, 2014).
- *Intraparietal Sulcus-Hand selective* (IPS-Hand) - [Hands > Chairs] (Bracci, Cavina-Pratesi, Connolly & Ietswaart, 2016; Bracci & Op de Beeck, 2016) - defined by selecting the peak of activation on the IPS (Bracci & Op de Beeck, 2016).
- *Intraparietal Sulcus-Tool selective* (IPS-Tool) - [Tools > Scrambled] (Bracci, Cavina-Pratesi, Connolly & Ietswaart, 2016; Bracci et al., 2016) - defined by selecting the peak of activation on the IPS (Bracci & Op de Beeck, 2016).
- *Supramarginal Gyrus* (SMG) - [Tools > Scrambled] (Creem-Regehr, Dilda, Vicchrilli, Federer & Lee, 2007) - defined by selecting the peak of activation located most anterior along the SMG (Peeters, Rizzolatti & Orban, 2013), lateral to the anterior segment of the IPS (Gallivan, Chapman, McLean, Flanagan & Culham, 2013), posterior to the Precentral Suclus (PreCS) and superior to the lateral sulcus (Ariani, Wurm & Lingnau, 2015).
- *Dorsal Premotor Cortex* (PMd) - [Tools > Scrambled] - defined by selecting the peak of activation at the junction of the PreCS and the superior frontal sulcus

(Gallivan, Chapman, McLean, Flanagan & Culham, 2013; Ariani, Wurm & Lingnau, 2015).

- *Ventral Premotor Cortex* (PMv) - [Tools > Scrambled] (Creem-Regehr, Dilda, Vicchrilli, Federer & Lee, 2007) - defined by selecting the voxels inferior and posterior to the junction between the inferior frontal sulcus and the PreCS (Gallivan, Chapman, McLean, Flanagan & Culham, 2013).
- *Early Visual Cortex* (EVC) - [All Conditions > Baseline] (Bracci & Op de Beeck 2016) - defined by selecting the voxels in the occipital cortex near the calcarine sulcus (Singhal, Monaco, Kaufman, & Culham, 2013).

Table 2.1. Mean sizes and Talairach coordinates of ROIs from the BOTH visual localiser. Acronyms: SD = Standard Deviation.

ROI	Number of subjects	Mean voxel size (SEM)	Mean peak coordinates (SD)		
			X	Y	Z
EVC	19	114 (35)	-14 (6)	-89 (4)	-9 (9)
LOTC-Object	19	148 (34)	-42(4)	-77 (4)	-7 (4)
LOTC-Body	18	55 (30)	-45 (3)	-76 (5)	2 (6)
LOTC-Hand	17	81 (44)	-47 (4)	-71 (4)	-1 (5)
LOTC-Tool	17	77 (45)	-47 (5)	-71 (5)	-2 (6)
pMTG	17	96 (48)	-45 (4)	-57 (3)	3 (4)
pFs	19	105 (41)	-40 (4)	-54 (4)	-14 (4)
SMG	17	69 (43)	-53 (6)	-28 (4)	27 (6)
IPS-Hand	19	110 (57)	-38 (4)	-46 (7)	42 (3)
IPS-Tool	19	81 (55)	-37 (5)	-41 (7)	42 (5)
PMv	14	61 (19)	-45 (7)	-1 (6)	31 (5)
PMd	14	47 (43)	-29 (5)	-13 (4)	51 (4)

2.2.8. ROI MVPA

Pattern classification was performed with a combination of in-house scripts (Smith & Goodale, 2015) using Matlab with the Neuroelf toolbox [version 0.9c; http://neuroelf.net/] and a linear Support Vector Machine (SVM) classifier (libSVM 2.12 toolbox; https://csie.ntu.edu.tw/~cjlin/libsvm/). The SVM was trained to learn the mapping between multivariate observations of voxel activity within an ROI for the particular types of grasping blocks that had been performed (e.g., typical and atypical grasping blocks). Accuracy was then assessed by testing the classifier's ability to discriminate between these types of blocks on reserved data that was not included in the training. This was achieved using a "leave-one-run-out" N-fold cross-validation approach. As in previous studies (e.g., Smith & Goodale, 2015; Gallivan, Johnsrude, & Flanagan, 2016), we performed this N-1 cross validation procedure until all runs were tested and then averaged across N-iterations in order to produce a representative decoding accuracy measure for each participant, ROI and pairwise/multiclass classification (Duda, Hart & Stork, 2001). The input to the pattern classifier were individual voxel beta values for each ROI. The time course of each ROI's voxel per run was extracted and each block was modelled by a separate predictor variable that resulted from a convolving a standard double gamma HRF model with the block duration (Smith & Muckli, 2010; Vetter et al., 2014). Note that the activity of each ROI was normalised (separately for training and test data) within a range of -1 to +1 before input the SVM (Smith & Muckli, 2010) and the linear SVM algorithm was implemented using the default parameters provided in the LibSVM toolbox (C = 1).

2.2.9. Classification procedure

A combination of pairwise and multiclass discriminations were used for MVPA. To satisfy the primary goal of this study (i.e., to identify brain regions that contained learnt representations about how to grasp a tool in a way consistent with its learnt use) we were interested in the decoding accuracy for each ROI when classifying blocks of tool grasping movements that were considered to be typical versus atypical (i.e., the classification of typicality). As a control, we also assessed decoding accuracy for these ROIs when classifying blocks of similar non-tool grasping movements that were directed to the right versus left side of the non-tool control object (i.e., the control classification of grasp direction).

This control classification of grasp direction with the non-tools allowed us to ensure that successful decoding of typicality when grasping the tools was not simply explainable by the direction of grasp because typical grasping always consisted of rightward grasping and atypical grasping always consisted of leftward grasping. We reasoned that decoding accuracy would be stronger for typicality, than grasp direction, in regions that were sensitive to learnt information about tool-related actions. To this end, we first tested if decoding accuracy was significantly higher than chance (i.e., 50%) with one-samples t-tests when classifying typicality and grasp direction separately. Second, we tested if decoding accuracy was significantly higher for the classification of typicality, than grasp direction, using pairwise t-tests (see Fig. 2.3). These second pairwise comparisons were only used to compare accuracies from ROIs that displayed evidence of being sensitive to functional tool grasping; that is, where decoding accuracy was significantly above chance for the typicality, but not grasp direction.

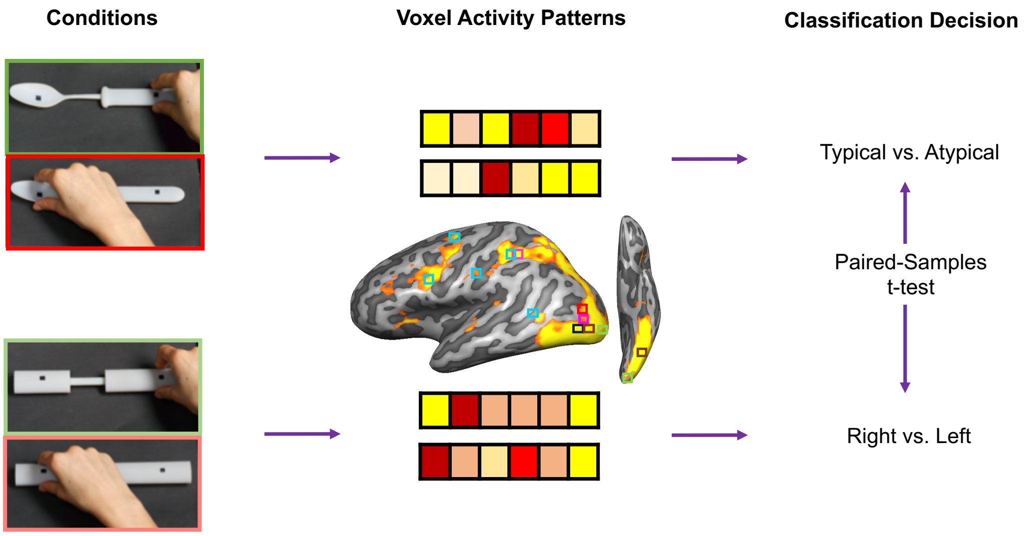

Figure 2.3. Example of MVPA classification for primary analysis. A classifier was trained to learn the mapping between the two types of grasping blocks for the tools and non-tools independently (left top and bottom). This was carried out per ROI by inputting the voxel activity patterns for these conditions (middle). A classification decision was then made for new data that had been reserved from training for the purpose of testing the accuracy of the classifier (right). The classifier discriminated between trials labelled to be *typical* versus *atypical* for the tool conditions (right top) and those labelled *right* versus *left* for non-tool conditions (left bottom). The cross-validated decoding accuracy was compared to that expected by chance (50%) using one-samples t-tests. If activity patterns in a ROI could be used to decode typicality (i.e., from the tool conditions) but not grasp direction (i.e., from the non-tool conditions) paired samples t-tests were then used to test if decoding accuracy for grasping was significantly higher than grasp direction. This pattern of results would be taken as evidence that an ROI carried learnt representations about how to grasp a tool in a way consistent with its learnt use.

As another control, we also tested the extent to which the patterns of activity in these ROIs were sensitive to object size regardless of object category (see Fig.

2.4.). This was important because the tool blocks (i.e., typical and atypical grasping) sometimes included trial pairs that differed in object size (i.e., smaller grasping versus larger head for the spoon and pizza-cutter tools). As this did not occur within the non-tool blocks (i.e., both sides were the same width), tool-specific decoding for the spoon and pizzacutter objects could be attributed to having differential demands on size perception and/or scaling grip aperture. Secondary aims of the study were to assess which brain regions coded other information about object category, tool function and tool identity (see Fig. 2.4.), all of which have been reported to be coded in when viewing or pantomiming 2D presented tools.

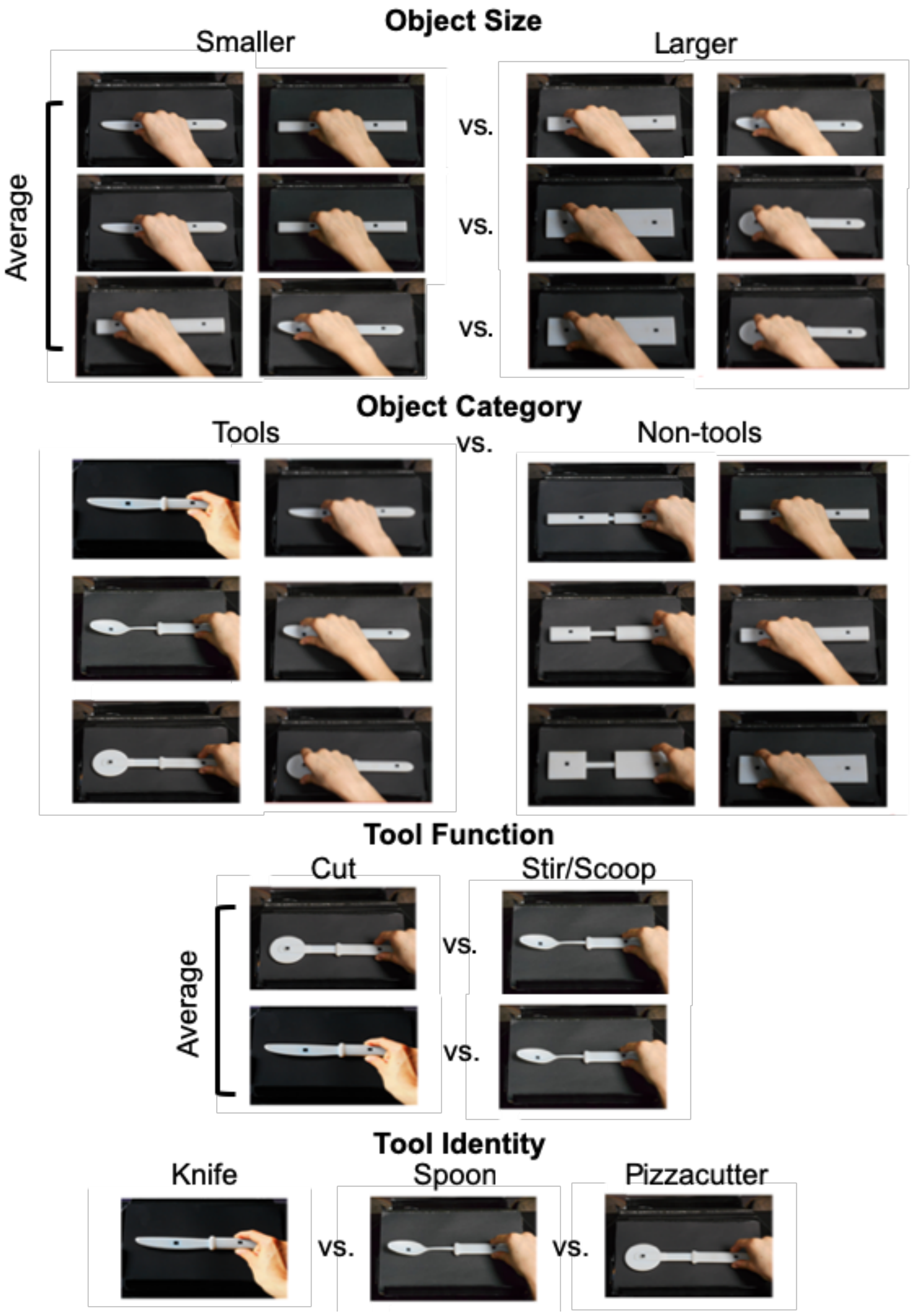

Fig. 2.4. Classification labels for control and secondary analyses. Object size (Top). This classification was a control analysis that was possible because the heads of the knife, spoon and pizzacutter tools (and their paired non-tools) had small, medium and large widths when considered relative to one another. Thus, a classifier was used to test if discrimination was possible between object of a *larger* versus *smaller* size. This was achieved by averaging the decoding results from three separate pairwise classifications of object size that pitted one set of exemplars versus one of the other

two sets (the 3 rows of stimuli are separated to show the individual pairwise classifications between the objects that were the size of the small knife versus medium spoon, small knife versus large pizza-cutter and medium spoon versus large pizza-cutter). Object category (Upper middle). This classification was performed using a pairwise discriminations of *tools* versus *non-tool*s. Tool function (Lower middle). This classification was performed using two pairwise discrimination of the tools that were strongly associated with *cutting* versus *scooping* and averaging the decoding accuracies (as for object size, the rows of stimuli show the individual pairwise comparisons between the knife versus spoon and pizzacutter versus spoon). Tool identity (Bottom). This classification was performed using a single multiclass discrimination of the different tool exemplars (*knife* versus *spoon* versus *pizza-cutter*). For all analyses reach direction(s) were controlled. Object size involved left grasping blocks only (i.e., conditions where the tools and their paired non-tools had identical widths). Object category involved both right and left grasping blocks (i.e., to maximise power). Tool function and identity involved right grasping blocks only (i.e., handles of the tools were identical).

All statistical tests were one-tailed because (1) decoding was not expected to occur below chance when using one-samples t-tests (Walther, Caddigan, Fei-Fei & Beck, 2009; Walther, Chai, Caddigan, Beck & Fei-Fei, 2011; Chen, Namburi, Elliott, Heinzle, Soon, Chee & Haynes, 2011; Smith & Goodale, 2015) and (2) we predicted that paired-samples t-tests for the functional tool grasping analysis would show significantly higher decoding accuracy for typicality than grasp direction. To control for the problem of multiple comparisons, a False Discovery Rate (FDR) correction of $q \leq 0.05$ was applied to all t-tests performed for each ROI per classification.

2.2.10. Searchlight MVPA

In addition to the ROI analysis above, we repeated these classification procedures with a whole-brain searchlight (Kriegeskorte, Goebel & Bandettini, 2006; Walther, Caddigan, Fei-Fei & Beck, 2009; Pereira & Botvinick, 2011). The SearchMight toolbox (Pereira & Botvinick, 2011) implemented in Matlab was used to shift a cube (5 x 5 x 5 voxel length, equal to 125 voxels) throughout the whole-brain volume and perform the same decoding analyses as described in the ROI MVPA (see Section 2.2.9) independently at each different centre voxel position (Smith & Goodale, 2015). These analyses were performed independently for each participant, using a common group mask and the accuracy values for each voxel were converted to unsmoothed statistical maps. The common group mask was defined by voxels with a mean BOLD signal > 100 for every participant's fMRI runs to ensure that all voxels included in searchlight MVPA contained suitable activation values.

To assess where in the brain coded information about typicality, we used a paired samples t-test approach. The non-tool accuracy maps were subtracted from the tool accuracy map per subject. A group tool > non-tool difference map was then produced based on the mean, where statistical significance was assessed by testing whether decoding accuracies were higher than zero at each voxel. Group accuracy maps resulting from the remaining classifications (i.e., object size, object category, tool function and tool identity) were tested against the value expected by chance for that classification (i.e., 50% or 33%). BrainVoyager's cluster-level statistical threshold estimator (Goebel et al., 2006; Forman et al., 1995) was used for cluster correction (voxelwise thresholds were set to $p = 0.01$ and then the cluster-wise thresholds were set to $p < .05$ using a Monte Carlo simulation of 1000 iterations; for similar approaches see Morrison, Tipper, Fenton-Adams & Bach, 2013; Monaco, Sedda, Cavina-Pratesi & Culham, 2015) and results are projected on to an averaged anatomical scan generated from the 19 subjects.

2.3. Results

2.3.1. Typicality versus grasp direction decoding

Decoding accuracies for the typicality classification (i.e., based on tool grasping) was found to be significantly above chance when based on activity patterns in the LOTC-Hand (56%, $t(16) = 2.73$, $p = 0.007$, $d = 0.66$ [chance: 50%]) and IPS-Hand ROIs (57%, $t(18) = 2.72$, $p = 0.007$, $d = 0.62$). The activity patterns in these ROIs could not, however, be used to decode the control grasp direction classification (i.e., based on non-tool grasping) significantly higher than chance (both p's > 0.22), ruling out the possibility that these regions were merely encoding different grasp directions. In fact, classification accuracy was significantly higher for typicality, than grasp direction, in these LOTC-Hand ($t(16) = 2.11$, $p = 0.026$, $d = 0.51$) and IPS-Hand ROIs ($t(18) = 3.26$, $p = 0.002$, $d = 0.75$; Fig 2.5A.). No other ROIs showed a similar pattern of results, including parts of the LOTC and IPS that were sensitive to other stimulus categories (i.e., tools, bodies, hands or objects). Instead, significant above-chance decoding was observed in LOTC-Body and pFs for the classification of both tool typicality (59%, $t(17) = 4.75$, $p < 0.001$, $d =1.12$ and 58%, $t(18)$ 2.57, $p = 0.01$, $d = 0.59$, respectively) and grasp direction (56%, $t(17) = 2.46$, $p = 0.012$, $d = 0.58$ [chance = 50%] and 57%, $t(18) = 2.59$, $p = 0.009$, $d = 0.59$, respectively). The PMd ROI displayed significant decoding of reach direction for non-tool grasping only (59%, $t(13) = 4.11$, $p = 0.001$, $d = 1.1$). All remaining one-samples t-tests were not significant.

As in the ROI analysis, the decoding accuracies obtained from the searchlight for typicality when grasping the tools were compared with that for grasp direction when grasping the non-tools (see the typicality difference map in Fig. 2.5B.). Significantly higher decoding accuracy for typicality than grasp direction was observed in a large cluster (see Table 2.2. for cluster sizes) comprising an anterior portion of the left Superior and Middle Temporal Gyri (STG; MTG) that extended into the Parahippocampal Gyrus (PHG). Other clusters meeting these criteria were found in the right hemisphere within the Fusiform Gyrus (FG), anterior Superior Parieto-Occipital Cortex (aSPOC) and posterior Superior Temporal Sulcus (pSTS). Additionally, to explore whether searchlight results corroborated results from the ROI analysis, we also examined the uncorrected map at a more liberal threshold ($p < 0.05$) and observed higher tool decoding accuracy within the IPS that overlapped the IPS-Hand ROIs (Fig. 2.5C.). The difference map revealed no evidence of significantly higher decoding accuracy in the opposite direction, that is, where grasp direction decoding was significantly higher than typicality decoding.

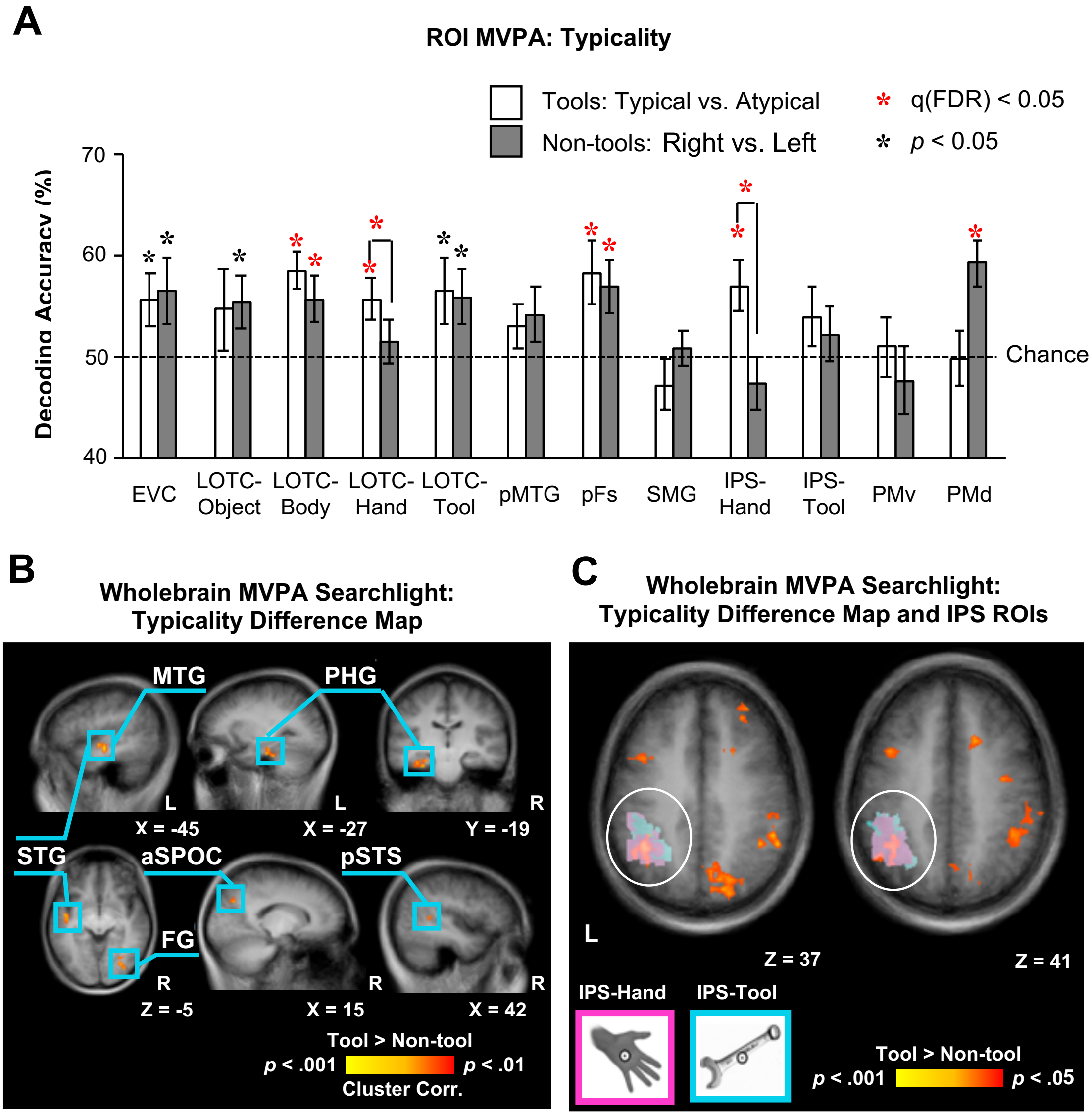

Figure 2.5. (A) Left hemisphere ROI MVPA results for the classifications of typicality (i.e., when grasping tools) and, as a control, grasp direction (i.e., when grasping non-tools). Decoding accuracies obtained using activity patterns from the LOTC-Hand and IPS-Hand ROIs were significantly higher than (1) chance and (2) that for grasp direction. (B) Typicality difference map derived from a searchlight analysis. Tool and non-tool decoding accuracies were acquired per voxel independently and then the values from the tool map were subtracted from the non-tool map for each participant. The resulting maps were finally tested against zero to reveal where decoding accuracies were significantly higher for tools than non-tools.

(C) Individual IPS-Hand and IPS-Tool ROIs for each subject are overlaid on the typicality difference map set at a lower threshold that is not cluster corrected. Visually, the cluster clearly overlaps with the IPS-Hand ROIs. Errors bars represent SEM.

2.3.2. Object size decoding

Decoding accuracies for the classification of object size did not significantly differ from chance for any of the visual localiser ROIs (all p's < 0.18; Fig. 2.6A.). Reflecting the ROI analysis, the searchlight also did not show evidence that the areas around the IPS-Hand or LOTC-Hand could discriminate size significantly above chance (Fig. 2.6B.). Instead, significant size decoding was observed in a posterior part of the right IPS (pIPS), left Pre-Supplementary Motor Area (Pre-SMA), posterior Middle Temporal Gyrus (pMTG), Insula (INS), Retrosplenial Cortex (RSC) and bilateral cerebellum around layers I-IV in the left and layer VI in the right hemispheres. A superior portion of the left LOTC was also found to discriminate object size significantly above chance, and this overlapped with a probalistic map of the LOTC-Body ROIs, but not that of LOTC-Hand (Fig. 2.6C.; probalistic maps were generated using the volume-of-Interest based function in BrainVoyager QX).

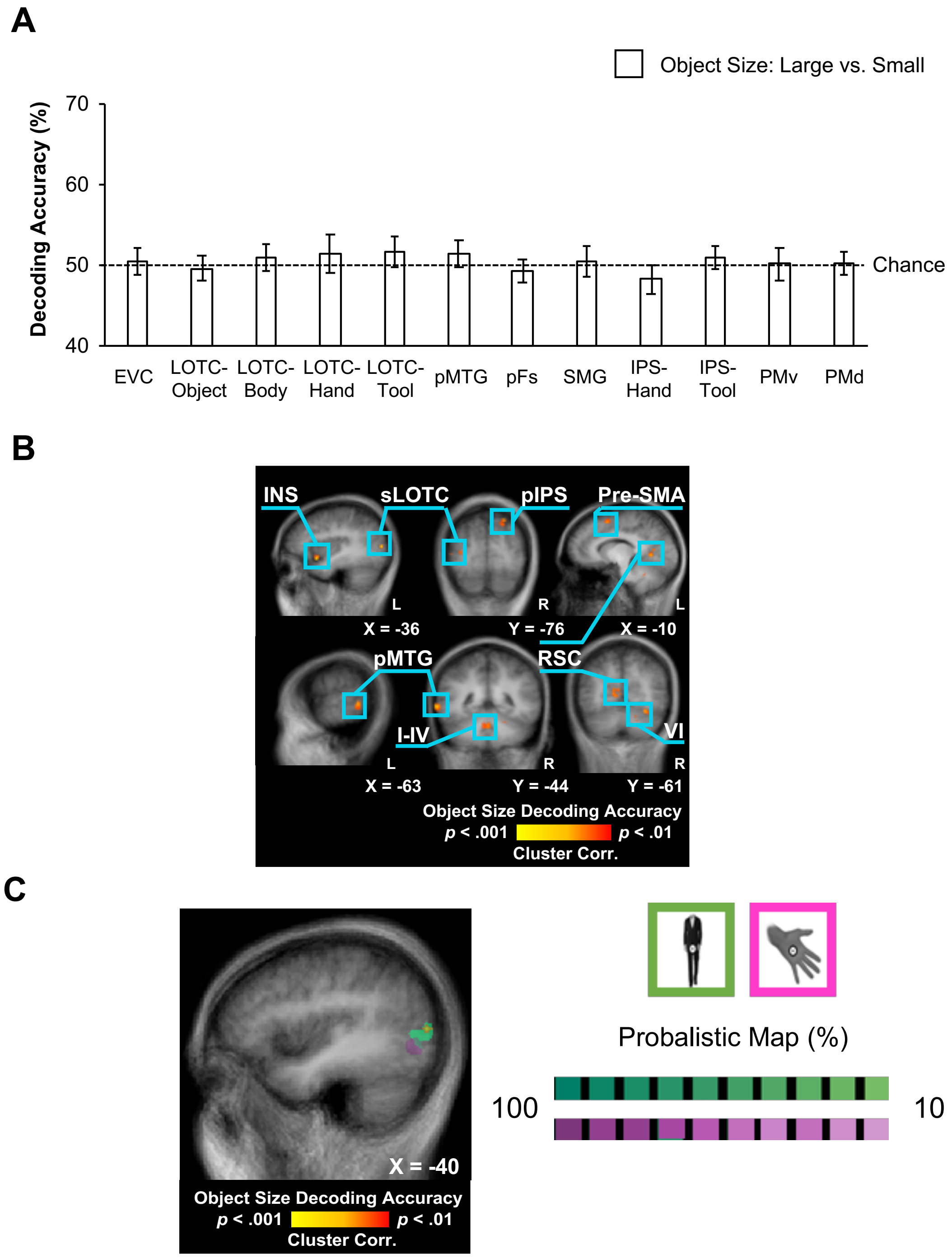

Figure 2.6. (A) Left hemisphere ROI MVPA results for the classification of object size. No perceptual ROIs decoded object size significantly higher than chance. (B) Searchlight results for the classification of object size. (C) Probalistic maps of LOTC-Body and LOTC-Hand ROIs are overlaid on the superior LOTC cluster that

was found by the searchlight to decode object size significantly above chance. Error bars represent SEM.

2.3.3. Object category decoding

Decoding accuracy for the classification of object category was found to be above chance for the LOTC-Object ROI, though this did not survive FDR correction for multiple comparisons (53%, $t(18) = 2.86$, $p = 0.005$, $d = 0.66$ [chance = 50%]; see Fig. 2.7.). No significant clusters by the searchlight for decoding object category.

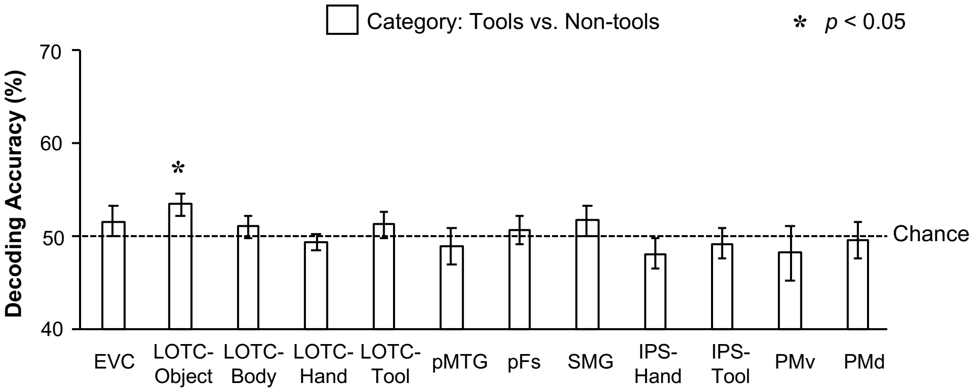

Fig. 2.7. Left hemisphere ROI MVPA results for the classification of object category. Error bars represent SEM.

2.3.4. Tool function decoding

Decoding accuracy for the classification of tool function was found to be above chance for the SMG ROI, though this did not survive FDR correction for multiple comparisons (56%, $t(16) = 2.2$, $p = 0.022$, $d = 0.53$ [chance = 50%]; see Fig. 2.8A.). The searchlight identified significant clusters for decoding tool function within the left secondary somatosensory cortex (S2) and posterior SPOC (pSPOC), plus the right Inferior Frontal Gyrus (IFG) and MTG (Fig. 2.8B.).

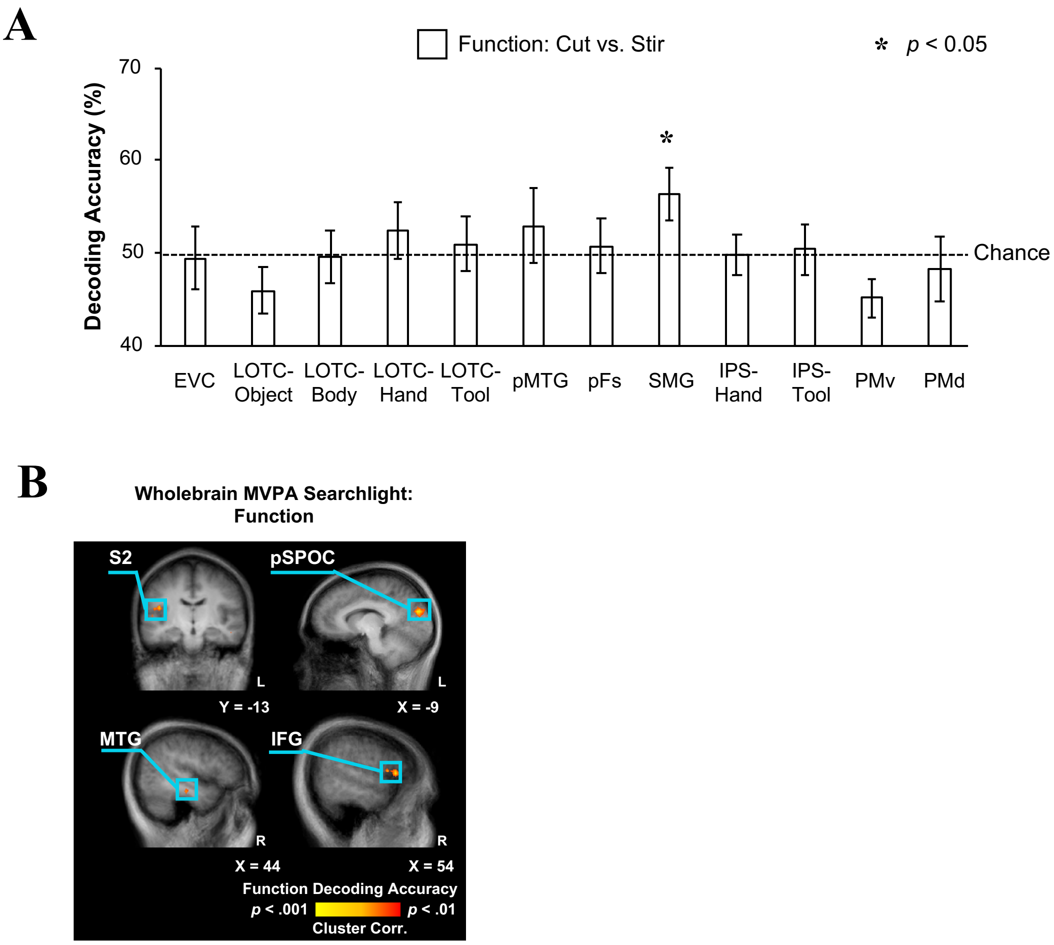

Fig. 2.8. (A) Left hemisphere ROI MVPA results for the classification of tool function. (B) Searchlight results for the classification of tool function. Error bars represent SEM.

2.3.5. Tool identity decoding

As was the case for the decoding of tool function, decoding accuracy was above chance for the classification of tool identity for the SMG ROI, though this again did not survive FDR correction (41%, $t(16) = 2.28$, $p = 0.018$, $d = 0.55$ [chance = 33%]; see Fig. 2.9A.). The searchlight revealed a cluster in the left pre-SMA that decoded tool identity significantly above chance (see Fig. 2.9B.).

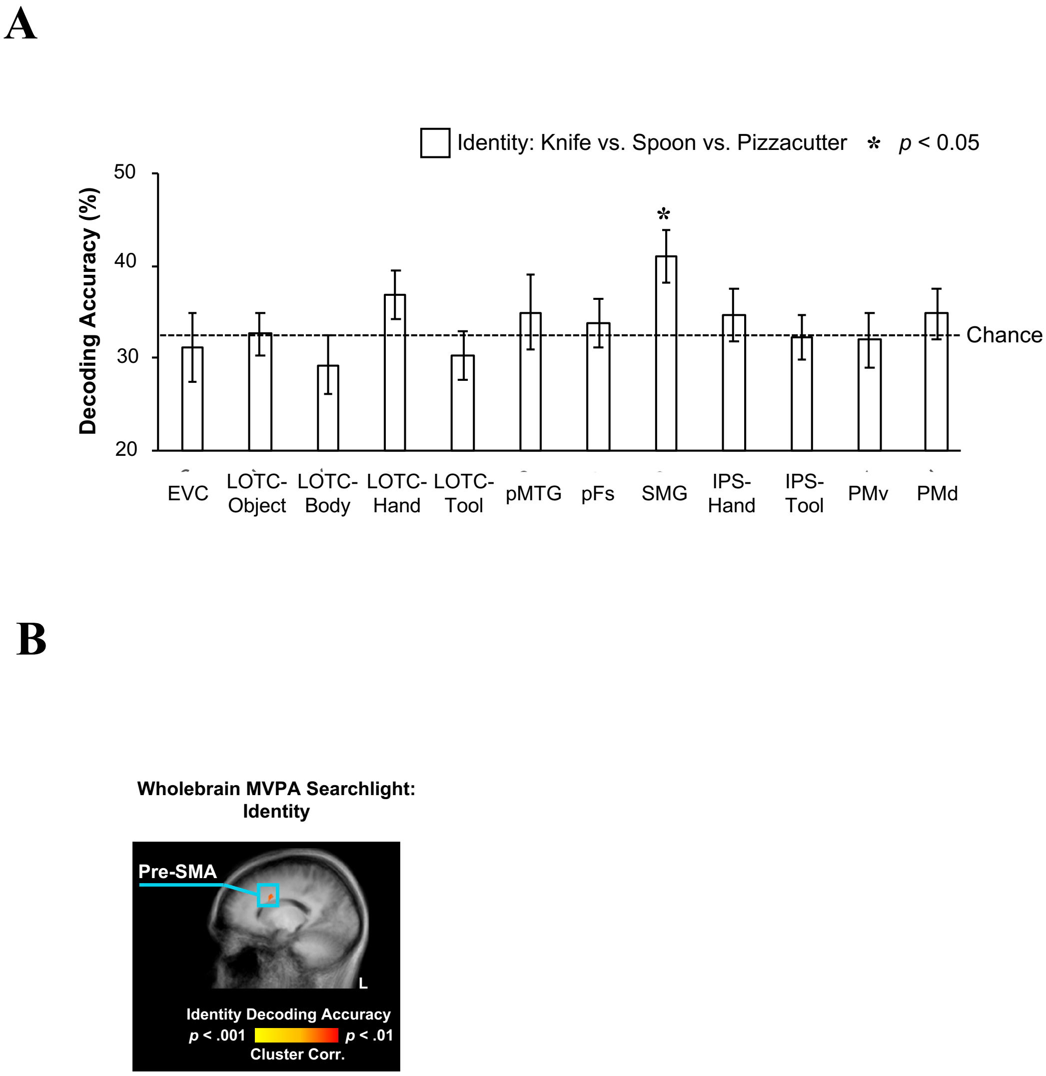

Fig. 2.9. (A) Left hemisphere ROI MVPA results for the classification of tool identity. (B) Searchlight results for the classification of tool identity. Error bars represent SEM.

Table 2.2. Searchlight cluster sizes, peak coordinates (Talairach) & statistical values.

Region of activation	Cluster voxel size	Peak coordinates			*t*	*p*
		X	Y	Z		
Typicality Difference Map						
Typicality > Grasp direction						
L-MTG	1674	-39	-16	-11	5.6	< 0.001
L-STG		-45	-7	-5	5	< 0.001
L-PHG		-27	-19	-23	4.8	< 0.001
R-FG	1410	30	-73	-5	4.8	< 0.001
R-aSPOC	278	15	-67	31	4.64	< 0.001
R-pSTS	242	36	-43	7	4.7	< 0.001
Size						
L-INS	228	-36	14	-12	5.18	< 0.001
L-MOG	281	-36	-79	7	6.56	< 0.001
L-MTG	447	-63	-43	-2	4.8	< 0.001
L-RSC	548	-9	-58	1	5.29	< 0.001
L-SMA	282	-9	8	52	4.58	< 0.001
R-aSPOC	194	21	-76	47	4.42	< 0.001
L-I-IV	1294	-3	-46	-29	4.66	< 0.001
R-VI	568	27	-61	-20	4.9	< 0.001
Function						
L-S2	254	-42	-13	16	4.52	< 0.001
L-SPOC	887	-9	-82	22	5	< 0.001
R-IFG	408	54	20	7	4.88	< 0.001
R-MTG	213	44	-19	-14	4.05	< 0.001

Tool Identity						
Pre-SMA	201	-9	8	22	4.54	< 0.001

2.4. Discussion

During a real 3D tool grasping paradigm, fMRI MVPA was used to examine which brain regions contain representations about the learnt aspects of tool-use. After controlling for very similar actions with a series of non-tools, regions selective for viewing pictures of hands in the dorsal and ventral visual streams (IPS-Hand and LOTC-Hand) were found to be sensitive to whether a tool is grasped in a way that is typical for use (i.e., when grasping the tool's handle) or not (i.e., when grasping the tool's head). These representations, as well as others regarding the identity, function or category of an object, were also decodable from grasp-related activity within parieto-frontal and temporo-occipital cortex across hemispheres, including a large portion of left anterior temporal cortex (i.e., MTG, PHG & STG). Together, these findings imply that these regions have a role in humans' highly evolved ability to interact with tools.

2.4.1. Hand-selective cortex and learnt actions

The human brain contains multiple areas that respond preferentially to the sight of a pictured hand in both the sensorimotor and visual systems (e.g., Perini, Caramazza & Peelen, 2014; Bracci, Cavina-Pratesi, Ietswaart, Caramazza & Peelen, 2012; Bracci & Op de Beeck, 2016). These regions are proposed to be relevant for object-directed action (e.g., Bracci, Cavina-Pratesi, Connolly & Ietswaart, 2016; Striem-Amit, Vannuscorps & Caramazza, 2017; Bracci, Caramazza & Peelen, 2018) such as for storing the hand movements or hand postures associated with specific tools (Peelen, Bracci, Lu & He, Caramazza & Bi, 2013). Our results clearly fit with this view, showing that hand-selective cortex is sensitive to whether a hand movement matches the way in which a tool is typically grasped for use.

This interpretation relies on the assumption that representations within these hand-selective areas can be shaped through learning (i.e., the link between tool-use and hand movements are learnt through experience; Sirigu et al., 1995; Buxbaum, Sirigu, Schwartz & Klatzky, 2003). A number of cases now argue that prior knowledge can indeed alter representations within occipito-temporal cortex (Gallivan & Culham, 2015; Lingnau & Downing, 2015), particularly for body-selective regions (Downing & Peelen, 2016). Likewise, compelling fMRI evidence from one-handed participants (e.g., amputees) indicates that responses within such LOTC and IPS areas could be experience-dependent because their responses are related to the amount they use a prosthetic limb, with this degree of experience even modulating LOTC-Hand’s connectivity with primary somatomotor cortices (van den Heiligenberg, Macdonald, Duff, Henderson, Johansen-berg, Culham & Makin, 2015; van den Heiligenberg, Orlov, Macdonald, Duff, Slater, Beckmann, Johansen-Berg, Culham & Makin, 2018). Thus, good evidence supports this interpretation, though further study is needed to identify how learning affects processing within these regions (e.g., what experience is necessary to distinguish between functional and non-functional grasping; e.g., Dempsey-Jones, Wesselink, Friedman & Makin, 2019) and is well suited by tool-training interventions (e.g., Weisberg, Van Turrenout & Martin, 2006; Kiefer, Sim, Liebich, Hauk & Tanaka, 2007; Bellebaum, Tettamanti, Marchetta et al., 2013) that have, so far, been used only during perceptual experiments (see *Future directions:* section 5.6.).

Of particular interest, typicality decoding was successful using activity patterns from hand-selective, but not overlapping parts of tool-selective cortex. Not only do these LOTC-/IPS-Hand and LOTC-/IPS-Tool ROIs share a number of voxels anatomically, picture viewing experiments have shown that these overlapping areas exhibit similar responses (e.g., Bracci, Cavina-Pratesi, Ietswaart, Caramazza & Peelen, 2012; Bracci & Peelen, 2013; Bracci, Cavina-Pratesi, Connolly & Ietswaart, 2016). The results here, then, uniquely suggest that these tool- and hand-selective sites may reflect distinct neural populations (for consideration of this point see Bracci, Cavina-Pratesi, Ietswaart, Caramazza & Peelen, 2012; Striem-Amit, Vannuscorps & Caramazza, 2017), a claim that could be investigated using high-resolution fMRI (e.g., Grill-Spector, Sayres & Ress, 2006; Schwarzlose, Baker & Kanwisher, 2005; McGugin, Gatenby, Gore & Gauthier, 2012).

Perhaps, we found that typicality was specifically decodable from hand-selective regions because, in this experiment, we examined hand, rather than tool, movements. Indeed, Gallivan et al., (2013) have differently found that a tool-selective area around the pMTG (even described as LOTC-Tool by Gallivan, 2014), carries information about whether a pair of tongs is used to perform grasping versus reaching. This suggests a potential difference between these tool- and hand-selective areas, but it is worth highlighting that reaching and grasping are not necessarily equated for kinematic complexity (e.g., grasping may take longer or demand more exact positioning of the tool) making such a conclusion from the Gallivan et al. (2013) study tentative. Continuing to carefully design control tool-related actions (e.g., Valyear et al., 2012; Brandi et al., 2014) will be important and might benefit from, for example, highlighting contact points as was the case for our reach-to-grasp movements.

An unlikely explanation, however, of the specific decoding of typicality for hand-, but not tool-selective regions, is that they are caused by differences in the number of voxels between these ROIs (i.e., hand-selective regions were larger than tool-selective regions; see Etzel, Zacks & Braver, 2013). In LOTC the mean voxel sizes of these ROIs were almost identical (i.e., LOTC-Hand mean size was 4 voxels larger than LOTC-Tool). Similarly, the IPS ROI that did differ to a greater extent (i.e., IPS-Hand mean size was 29 voxels larger than IPS-Tool) were replicated by a searchlight (i.e., the typicality cluster showed substantial overlap with IPS-Hand, not IPS-Tool) that used identically sized cubic inputs. In fact, the only result I suspect may be influenced by average voxel size is the decoding of object category in left LOTC-Object; of the neighbouring LOTC ROIs this was clearly the largest and was the only one to show any evidence of decoding object category (i.e., tool versus non-tool), suggesting a possible link between voxel size and decoding accuracy (see Eger, Ashburner, Haynes, Dolan & Rees, 2008; Walther, Caddigan, Fei-Fei & Beck, 2009; Axelrod, Bar, Rees & Yovel, 2014; Said, Moore, Engell, Todorov & Haxby, 2010). Therefore, I interpret this data to suggest that hand-selective cortex carries information that could serve tool-use and, accordingly, indicates that these regions in the LOTC and IPS (and possibly those described by others within the left ventral temporal cortex, bilateral pSTS, inferior precentral gyrus and IFG; see Grosbras, Beaton & Eickhoff, 2012; Bracci, Cavina-Pratesi, Connolly & Ietswaart, 2016), deserve particular attention by future investigations of tool-related processing.

2.4.2. Visual streams & a semantic hub in learnt actions

As in closely-related perceptual (e.g., Valyear & Culham, 2010; Mizelle et al., 2014; also see uncorrected results from Yoon, Humphreys, Kumar & Rotshtein, 2012) and pantomiming experiments (e.g., Przybylski & Króliczak, 2017; Buchwald, Przybylski & Króliczak, 2018) a sensitivity to the typicality of a tool grasping movement was observed in the ventral visual stream (i.e., left LOTC-Hand and right

FG). This is consistent with the DVST's claim that, even though visuomotor control is processed by the dorsal visual stream, the ventral visual stream is needed for actions involving tools because such movements rely on information that has been previously learnt (e.g., how they should be grasped; Milner & Goodale, 1995; 2006; also see Carey, Harvey & Milner, 1996). In fact, many contemporary arguments have consistently made the claim that the ventral visual stream plays a role in the storage and integration of knowledge about learned hand-tool interactions (e.g., Johnson-Frey, 2004; Culham & Valyear, 2006; Johnson-Frey, 2007; Mahon, Milleville, Negri, Rumiati, Caramazza & Martin, 2007; Watson & Chatterjee, 2011; van Elk, van Schie & Bekkering, 2014; Orban & Caruana, 2014).

Only recently, however, has there been direct evidence that these ventral stream regions contain neural representations relevant to object-directed actions (for reviews see Lingnau & Downing, 2015; Gallivan & Culham, 2015). These representations have ranged from those linked to basic kinematic components of a movement (e.g., reach direction; Gallivan, Chapman, McLean, Flanagan & Culham, 2013; Gallivan, McLean, Valyear & Culham, 2013; Gallivan, Johnsrude & Flanagan, 2016) to those that are abstract and independent of such kinematics (e.g., lifting versus punching/lifting heavy versus light objects; Ooserhof, Wiggett, Diedrichsen, Tipper & Downing, 2010; Gallivan, Cant, Goodale & Flanagan, 2014; Ariani, Oosterhof & Lingnau, 2018; also see Wurm & Lingnau, 2015 and Wurm, Ariani, Greenlee & Lingnau, 2016 for similar evidence when viewing object-directed actions). Our findings add to both growing bodies of evidence: the ventral stream contains abstract representations, in the form of typicality and object-category decoding (see *Hand-selective cortex and learnt actions:* section 2.4.1.), as well as representations that simply reflect kinematic properties including those of grasp direction and/or object size (e.g., within the left LOTC-Body and pFs ROIs; see Fig. 2.5A. and searchlight results in the LOTC in Fig. 2.6C.).

As for the dorsal visual stream, the findings here are not entirely consistent with original claims of the DVST (nor the two-action systems model; Buxbaum, 2017), because areas of the dorso-dorsal stream coded typicality (i.e., left IPS-Hand and right pSPOC; see Fig. 2.5.) and tool function (i.e., left aSPOC; see Fig. 2.8B.). These regions were not identified in important control classifications of grasp direction (i.e., grasping the right versus left sides of non-tools) or object size (i.e., grasping smaller versus larger objects) implying that these results are not attributable to basic kinematic differences (e.g., smaller versus larger grip size). Importantly, the control classifications appear to be a valid approach to identify such kinematic confounds because they revealed findings matching previous MVPA real action experiments regarding other parts of the dorso-dorsal stream including the decoding of grasp direction in the left PMd (see Fig. 2.5A. and the left PMd/Frontal Eye Field ROI in Gallivan, McLean, Smith & Culham, 2011) and object size in the right pIPS (see Fig. 2.6B. and the left pIPS ROI in Gallivan, McLean, Valyear, Pettypiece & Culham, 2011). In fact, results from the control searchlight classification of object size (Fig. 2.6B.) clearly implicated other areas known to be responsible for motor control including the left pre-SMA and bilateral cerebellar areas (e.g., Nowak, Topka, Timmann, Boecker & Hermsdorfer, 2007; Glover, Wall & Smith, 2012; King, Hernandez-Castillo, Poldrack, Ivry & Diedrichsen, 2019; for review see Hardwick, Caspers, Eickhoff & Swinnen, 2018) advocating this techniques capability of detecting representations about less abstract properties.

Like the results here, a number of related studies have found that parts of the IPS are sensitive to the learnt aspects of tool-use (e.g., Chen, Garcea & Mahon, 2016; Chen, Garcea, Jacobs & Mahon, 2017). Most comparably to the experiment here, this has been demonstrated when participants view typical and atypical grasping (Valyear & Culham, 2010) as well as when pretending to grasp a pictured tool by its handle (Przybylski & Króliczak, 2017; Buchwald et al., 2018). Accordingly, an interesting inference is that perhaps distinct parts of the dorso-dorsal stream do have access to stored knowledge (cf. Milner & Goodale, 2006; Buxbaum, 2001). A similar conclusion could be drawn from results reported by Valyear, Cavina-Pratesi, Stiglick & Culham (2007) where they found that a portion of the aIPS which is selectively activated when naming tools (relative to other graspable non-tools) was distinctly posterior from another region of the aIPS that was active when these participants grasped novel objects.

More unique, however, are the pattern of decoding results in SPOC. Detailed experimentation of reaching and grasping behaviour has most commonly linked SPOC activity, often bilaterally (see Monaco, Cavina-Pratesi, Sedda, Fattori, Galletti & Culham, 2011) to the processing of hand kinematics (e.g., wrist orientation or reach distance; Karnath & Perenin, 2005; Monaco, Cavina-Pratesi, Sedda, Fattori, Galletti & Culham, 2011; Cavina-Pratesi, Monaco, Fattori, Galletti, McAdam, Quinlan, Goodale & Culham, 2010; Gallivan, Cavina-Pratesi & Culham, 2009). Nevertheless, I believe these findings are unlikely to be attributable to subtle differences in hand kinematics, especially in the case of the left pSPOC because this region decoded tool function which involved grasping the identical handles of stimuli that simply had different heads attached. A nearby precuneus area has been similarly implicated in the processing of conceptual knowledge before (Fairhall & Caramazza, 2013) and SPOC even preferentially responds to the areas where actions are most typically performed (i.e., the lower, relative to upper, visual field; Rossit, McAdam, McLean, Goodale & Culham, 2013), suggesting, perhaps, that this region's activity is sensitive to past experience (also see Scholz, Klein, Behrens & Johansen-Berg, 2009 for experience-dependent structural changes around the nearby Posterior Occipital Sulcus bilaterally).

Rather surprisingly, the left pMTG, a canonical part of the ventro-dorsal stream that is presumed to process manipulation knowledge (Buxbaum, 2017) was not found to decode typicality, tool function or tool identity. Activation in this area is argued to be the most robust finding in tool-related literature (e.g., Chao, Haxby & Martin, 1999; Beauchamp, Lee, Haxby & Martin, 2003; Lewis, 2006; Martin, 2016) but, taking a critical stance, null results from select studies have previously questioned whether function- and action-related information is represented here (Chen, Garcea & Mahon, 2016 and Chen, Garcea, Jacobs & Mahon, 2018) or if this area is even tool-selective at all (e.g., Kellenbach, Brett & Patterson, 2003; Downing, Chan, Peelen, Dodds & Kanwisher, 2006).

An important puzzle here is why Valyear & Culham (2010) found typical grasping selectivity in the left pMTG (in addition to LOTC) during their picture viewing paradigm, whereas we did not when participants actually performed these actions (also see Mizelle et al., 2014). I suspect this is related to the observational nature of Valyear & Culham's (2010) task because action observation, relative to imitation, has been shown to specifically activate the left pMTG (Caspers, Zilles, Laird & Eickhoff, 2010). In fact, action observation, relative to simply grasping a cued side of an object, is likely to be more semantically taxing (e.g., attributing intentions to an actor; Catmur, 2015) and an increase in such demands has been shown to shift tool-related activity anteriorly (e.g., from LOTC toward the MTG; Bracci & Peelen, 2013; Simmons & Martin, 2012; Simmons, Reddish, Bellgowan &

Martin, 2010). This presents a potential division between the roles of the left LOTC (i.e., LOTC-Hand) and pMTG, however these regions have rarely been explicitly distinguished between (e.g., Lingnau & Downing, 2015). The use of specific labels within the LOTC (see Weiner & Grill-Spector, 2012) will deepen our understanding of tool-related neural activity (Gallivan, 2014; Chen, Garcea, Jacobs & Mahon, 2017; Perini et al., 2014; Bracci & Peelen, 2013) and could facilitate comparisons with lesion methodologies that tend to implicate large portions of the left posterior temporal cortex in action production and/or recognition deficits (e.g., Campanella et al., 2010; Kalenine et al., 2010; Tranel et al., 2003; Tarhan, Watson & Buxbaum, 2015).

Other ventro-dorsal stream areas (i.e., left SMG and PMv) also displayed no evidence that they could be used to decode typicality. Again, this is inconsistent with previous research involving real actions (e.g., Oosterhof, Tipper & Downing, 2012) showing, for example, that the left IPL represents various action-related properties during tool pantomiming (e.g., Chen et al., 2015; Chen et al., 2017) as well as TMS evidence that it is causally linked to tool grasping (McDowell, Holmes, Sunderland & Schurmann, 2018). Nevertheless, notice that many of these studies have not included important non-tool control actions (as was the case here) impeding the conclusion that these areas have a role in the performance of tool-specific actions, rather than actions, per se (in fact see Reader, Royce, Marsh, Chivers & Holmes, 2018 for evidence that TMS of SMG disrupts actions regardless of whether they are well learnt or not). Likewise, even stimulation evidence is difficult to link to this exact region because effects may be outside of the SMG (though see Andres, Pelgrims, Olivier & Vannuscorps, 2017).

An important difference between this study and the highly related tool-use paradigms described earlier which did implicate ventro-dorsal stream regions in learnt tool-use (Brandi, Wohlschlager, Sort & Hermsdorfer, 2014; Valyear, Gallivan, McLean & Culham, 2012; Gallivan et al., 2013), is that those paradigms contrasted rather kinematically distinctive real hand-tool actions (e.g., reaching versus grasping, using versus lifting). In line with lesion evidence showing that tool-use, but not functional tool grasping, deficits are clustered around the SMG (Randerath, Goldenberg, Spijkers, Li & Hermsdorfer, 2010), perhaps such regions are involved only during more demanding tool-use acts.

This said, the pattern of results we found for decoding tool function and tool identity in the left SMG and, sometimes, the right IFG did closely resemble recent results showing these that these regions are part of a pathway mediating action competition that arises between- (i.e., a difficulty inhibiting the action associated with a distractor tool), but not within-tools (i.e., a difficulty inhibiting the conflicting actions associated with a single tool; Garcea et al., 2019; also see Buxbaum, 2017). Here these regions consistently showed evidence for decoding the functions and identities between-tools (e.g., coding what is a knife as opposed to a spoon or pizzacutter), rather than within-tool differences (e.g., grasping a knife by its handle versus blade). Of note, the SMG decoding evidence of this was rather weak and might imply that a larger number of tool exemplars will be useful in clarifying this point.

The remaining regions that did represent typicality included those known to be highly relevant to semantic processing (see Binder et al., 2009), that is, those within the anterior portions of the left temporal lobe (e.g., Mummery et al., 2000) as well as the right pSTS (see Hocking & Price, 2009; Hasan, Valdes-Sosa, Gross &

Belin, 2016; Mion, Patterson, Acosta-Cabronero, Pengas et al., 2010) and FG (e.g., Baker et al., 2001). In fact, involvement of the anterior-ventral and/or posterior-superior temporal cortex has been detected during innovative tool-related tasks (e.g., tool-manufacturing, reasoning where a tool is typically found; Stout, Toth, Schick, Stout & Hutchins, 2000; Putt, Wijeakumar, Franciscus & Spencer, 2017; Vingerhoets, 2008; Peelen & Caramazza, 2012). Likewise the right pSTS is argued to be integral for understanding the meaning of hand actions (e.g., Puce, Allison, Bentin, Gore & McCarthy, 1998; Pelphrey, Morris & McCarthy, 2004; Pelphrey, Morris, Michelich, Allison & McCarthy, 2005) and has even been shown to grow in the macaque after learning to use a tool (Quallo, Price, Ueno, et al., 2009), denoting their relevance to tool grasping.

The hub-and-spoke theory for semantic representation (e.g., Lambon Ralph, Jefferies, Patterson & Rogers, 2017) offers a viable account of the widespread coding of typicality reported here that, importantly, does not preclude related embodied cognition views (e.g., Damasio & Damasio, 1994; Barsalou, 1999; Pulvermuller, 2005, Martin, 2007). Based on data spanning TMS, fMRI and semantic dementia cases (e.g., Hodges et al., 1995, Binney, Embleton, Jefferies, Parker & Lambon Ralph, 2010), the bilateral Anterior Temporal Lobe (ATL) is predicted to constitute a semantic *hub* that mediates cross-modal semantic processing through its connections to *spokes* in the sensory and motor cortices (Lambon Ralph et al., 2017). Under this framework, it could be speculated that it is through bidirectional connections with the left ATL (see Chen, Lambon Ralph & Rogers, 2017) that other brain regions (e.g., left hand-selective cortex, right FG) come to represent typicality. From here, aspects of the results here raise intriguing questions about this model such as the role of lateralisation (e.g., were ATL representations only identified in the left hemisphere here due to the lateralisation of tool-processing? For a similar left ATL lateralisation in language processing see Visser & Lambon Ralph, 2011), interhemispheric connections (e.g., can information transfer between left ATL and right FG/pSTS? For evidence in favour of this possibility see Ramayya et al., 2009; Anzellotti et al., 2016) and ATL sub-regions (e.g., does the large cluster encompassing anterior STG, MTG and PHG reflect the multimodal nature of tool-use?; For related discussions see Visser & Lambon Ralph, 2011; Visser, Jefferies, Embleton & Lambon Ralph, 2012; Jackson, Hoffman, Pobric & Lambon Ralph, 2015; Martin, Simmons, Beauchamp & Gotts, 2014).

2.4.3. Limitations

I have focused my interpretation of successful decoding between the grasping of typical and atypical grasping as a reflection of the learnt aspects of tool-use (i.e., handle grasping is considered to be typical for use because we have learnt the association between this action and the function of that object) but there are alternative views. First, it could be argued that typicality decoding is caused by differences in somatosensory stimulation associated with grasping the tools' handles versus heads (e.g., differences in smoothness), but an explanation based wholly on somatosensation cannot explain these results since a ROI in left somatosensory cortex did not show the same pattern of results as the left hand-selective cortex ROIs (i.e., decoding was possible for typicality as well as grasp direction based on non-tool grasping; see Appendix A). Second, perhaps these results were driven by differences in attention (e.g., attention is drawn towards the head of the tool; Skiba & Snow, 2016; Xiong, Proctor & Zelaznik, 2019). Great care was taken to control many properties between the respective portions of the handles and heads of the tools and non-tools (e.g., maximum width, reach distance, required grip aperture), though, as is often the case, further studies with additional control stimuli would be useful in ruling out this possibility (e.g., using scrambled non-tools; see Macdonald & Culham, 2015). Finally, the decoding of typicality could be linked to familiarity (e.g., maybe we grasp tools by their handles more often than the head). As discussed further in Chapter 5, I consider familiarity and typicality to be closely related (e.g., as familiarity with an object increases there may be a better understanding of its typically associated action), though I appreciate that tool-training paradigms would be particularly suitable for further elucidating this point.

In order to optimise this project's experimental power (see Methods), participants performed highly unnatural consecutive grasping actions five times within a block. Whether this unusual behaviour affected movement kinematics is unknown and is a particularly interesting point given our unexpected findings that hand-, but not tool-selective, cortex decoded typicality (e.g., are representations in hand-selective cortex related to hand kinematics?). Accordingly, the next chapter (Chapter 3) presents a follow-up behavioural motion-capture experiment that closely examines hand kinematics during the same paradigm. Likewise, the final experimental chapter (Chapter 4) used adapted this paradigm for use with a slow event-related fMRI approach (with a more natural single grasping action) to investigate whether decoding of typicality decoding was also possible during motor planning, that is, before the hand even moved.

2.4.4. Conclusion

Simply grasping a tool by its handle, even when the intention to use it is absent, appears sufficient to evoke representations about learnt tool-use. Regions spread across both hemispheres were found to carry such information, perhaps most notably within hand-, but not overlapping tool-, selective cortex. A huge amount of neuroimaging research has focused on examining neural responses associated with perceiving or thinking about tools. The results here give the impression that directing further attention to areas specialised for hand-related processing may yield valuable insights into the neural bases of human tool-use. After all, for the vast majority of us, our hands are fundamental to the skilled use of these objects.

Chapter 3

Hand kinematics during tool grasping: A motion-capture investigation

3.1. Introduction

Tools are central to our world with humans being able to handle them with remarkable dexterity. Our understanding of how this behaviour unfolds at the kinematic level is hugely unexplored, even when simply reaching toward and grasping these objects. This is despite there being more extensive study of reach-to-grasp kinematics in general (for review see Castiello & Dadda, 2019) as well as a detailed understanding of how tools influence behaviour when measured in other ways (e.g., eye-tracking, button-presses). Addressing this, a behavioural follow-up experiment to the previous fMRI study (Project 1, Chapter 2) is presented in this chapter, where hand kinematics during the same tool and non-tool grasping paradigm were measured with motion-capture.

When the hand approaches an object, the point where grip size (i.e., the distance between the thumb and index finger) is at its largest has been described as a clearly identifiable landmark since early film and motion analysis (e.g., Jeannerod, 1984; Wing, Turton & Fraser, 1986; Gentilucci et al., 1991). This measure, often referred to as Peak Grip Aperture (PGA), has been reliably shown to covary with object size (Marteniuk et al., 1990; Gentilucci et al., 1991; Castiello et al., 1992; Castiello, Bennet & Stelmach, 1993), with the relationship between MGA and object size being commonly used to quantify a degree of *grip scaling* (e.g., Jackson & Shaw, 2000; Jackson, Newport & Shaw, 2002; Vishton, Rea, Cutting & Nunez, 1999; Sedda, Monaco, Bottini & Goodale, 2011).

Inspecting such measures continues to be invaluable for refining influential theories related to motor control (e.g., Smeets & Brenner 1999; 2018), including that of the Dual Visual Stream Theory (DVST) that specifically offers an explanation of the processes underlying tool-use behaviour (e.g., Milner & Goodale, 1995; 2006). Likewise, hand kinematic analyses also offer key insights about the aetiology (e.g., Perenin & Vighetto, 1998; Pisella, Rossetti & Rode, 2017) and rehabilitation (e.g., Levin, 2016; Kapur, Jensen, Buxbaum, Jax & Kuchenbecker, 2010; Buxbaum & Randerath, 2018) of clinical disorders (e.g., visual neglect; optic ataxia, visual form agnosia), including apraxia, a disorder specifically linked to tool misuse (e.g., Hermsdorfer, Randerath, Goldenberg & Johannsen, 2012; Sperber et al., 2018). Considering the epistemological criticism that neural measures alone cannot derive the processes underlying a given behaviour (Krakauer, Ghazanfar, Gomez, Malcolm, Maclver & Poeppel, 2017; also see Gramann, Ferris, Gwin & Makeig, 2014), kinematic investigations of tool grasping are needed to understand the mechanisms that support tool-use.

Unlike fMRI investigations where participants must lay supine, grasping kinematic measures are nearly always taken when participants sit upright at a table (e.g., Holt, Lefevre, Flatters et al., 2013; Paulun, Gegenfurtner, Goodale & Fleming, 2014), as would be the case for much everyday behaviour (e.g., when grasping the computer mouse at a desk). Moreover, most grasping studies focus on single reach-to-grasp actions (e.g., Lukos, Ansuini & Santello, 2008; though see Castiello, 1997; Quinlan & Culham, 2015), whereas the particular fMRI block-design utilised in Project 1 entailed an unnatural repetitive grasping action (i.e., grasp an object five times within a trial). These points raise the question as to whether the actions performed during the fMRI study would share the same characteristics as those normally studied in laboratory-based grasping experiments, particularly since other types of *awkward* grasps have been shown to influence hand kinematics (e.g., when using the ring finger and thumb or the non-dominant hand; Gonzalez, Ganel, Whitwell, Morrissey & Goodale, 2008; Franz, Hesse & Kollath, 2009; Janczyk, Franz & Kunde, 2010; Tang, Whitwell & Goodale, 2014; Eloka, Feuerhake, Janczyk & Franz, 2015).

A primary aim of the experiment here, therefore, was to clarify whether participants were likely to have been scaling their grip according to object size during the fMRI grasping paradigm presented in Project 1. To this end, a separate behavioural motion-capture experiment was carried out using a highly similar design and setup (see Methods and Fig. 2.1B). Supplementary kinematic measures have been recorded for other fMRI grasping paradigms (e.g., Begliomini, Caria, Grodd & Castiello, 2007; Bernier & Grafton, 2010; Rossit, McAdam, McLean, Goodale, Culham, 2013), but only rarely are the constraints (e.g., laying supine) matched between neuroimaging and behavioural assessment (Grol, Majdandzic, Stephan, Verhagen, Dijkerman et al., 2007; Cavina-Pratesi, Monaco, Fattori, Galletti et al., 2010; Monaco, Cavina-Pratesi, Sedda, Fattori, Galletti & Culham, 2011).

By using the same tool and non-tool stimuli (see Methods and Fig. 2.1A), this grasping experiment is unique from most related studies that instead examine actions involving unfamiliar geometric shapes that have no obvious use (e.g., Efron blocks; Efron, 1969). Even the rarer experiments that investigate the grasping of other everyday objects often use stimuli such as cups, fruits or balls (e.g., Castiello, 1996; Riddoch, Edwards, Humphreys, West & Heafield, 1998; Gentilucci, 2003; Parma, Ghirardello, Tiriindelli & Castiello, 2011; Sartori, Ciani, Bulgheroni & Castiello, 2013; Glover, Rosenbaum, Graham & Dixon, 2004) that closely resemble classes of objects (e.g., vegetables or sports equipment) which, when passively viewed during neuroimaging, do not activate the brain in the same way as viewing a picture of a tool does (e.g., Kraut, Moo, Segal & Hart Jr, 2002; Valyear, Cavina-Pratesi, Stiglick & Culham, 2007; Bracci & Op de Beeck, 2016; cf. Downing, Chan, Peelen, Dodds & Kanwisher, 2005).

This said, important studies have already investigated tool-related actions at the kinematic level, often focusing on how behaviour is altered by the movement intended to be performed with the tool. For example, Jax & Buxbaum (2010) have shown that the reaction time (RT) is generally slower if grasping a tool when the intention is to demonstrate its use, relative to simply moving the tool to another location. Sensitive motion-capture technology has been used to replicate this RT effect and has additionally revealed that grasping a tool for using, rather than moving, is linked to a prolonged movement times (MT) and enlarged PGA in both young (Valyear, Chapman, Gallivan, Mark & Culham, 2011; Cicerale, Ambron, Lingnau & Rumiati, 2014) and elderly adults (Cicerale, Ambron, Lingnau & Rumiati, 2014).

Identification of unique hand kinematics when using, rather than moving, a tool fits well with the view that there are distinct neural mechanisms required for using a tool for its well-learnt purpose (e.g., Milner & Goodale, 1995; 2006; Buxbaum, 2017). In fact, a number of accounts on this topic clearly contrast this knowledge-based action with others, such as when distinguishing between prehension (versus utilisation) (Johnson-Frey, 2003), acting-with (versus acting-on) an object (Johnson-Frey & Grafton, 2003) or acting consistently with object properties that are functional (versus structural/volumetric) (Bub, Masson & Cree, 2008). Common to all of these views is that such actions rely on access to stored knowledge about how to manipulate the tool. Nonetheless, two important details should be considered before presuming that different hand kinematics when using, versus moving, a tool are specifically based on retrieving stored tool-action associations.

First, tool-use may rely on more extensive planning than tool-moving (Valyear, Chapman, Gallivan, Mark & Culham, 2011), a point easily drawn if considering the amount of concrete steps between the former (e.g., grasp the knife, demonstrate a slicing action and place it down) and latter task (e.g., grasp the knife and place it down). In fact, the findings that RTs are actually faster for using a tool if this action is instead compared to passing the tool to another person (Oisurak, Roche, Ramone & Chainay, 2013) suggests that the degree of movement extent is an important consideration because, in this case, the amount of steps are more closely matched (i.e., grasp the knife, rotate the knife, pass the knife), with RT being thought to correspond to motor planning (e.g., Delmas, Casamento-Moran, Park, Yacoubi & Christou, 2018).

Second, accuracy demands are poorly specified in these tool-use tasks (i.e., demonstrating its use in mid-air without a real object to contact), particularly since the tool-move conditions have a real marked goal (e.g., lay it on a foam pad; Cicerale, et al., 2014). Not only are kinematic variables related to both grasping (e.g., grip scaling) and reaching (e.g., peak velocity, MT) influenced by whether an action is real or pantomimed (e.g., Goodale, Jakobson & Keillor, 1994), the realness of a tool-related action has also been shown to influence kinematics (Lulic, Maciukiewicz, Gonzalez, Roy & Dickerson, 2018), even when specifically comparing the demonstration versus actual contextual use of a tool (Hermsdorfer, Randerath, Goldenberg & Johannsen, 2012).

Worth highlighting, the highly relevant motion-capture studies (i.e., Valyear, Chapman, Gallivan, Mark & Culham, 2011; Cicerale, Ambron, Lingnau & Rumiati, 2014) carefully restricted their kinematic analyses to the point where the hand first contacted the object, thus, minimising the influences of these two methodological considerations (i.e., differences in movement extent or accuracy demands are constant when initially grasping the tool). However, it is clear that upcoming movements in an action sequence can influence the way that the object is initially grasped (e.g., when grasping to throw versus to place; Rosenbaum, Vaughan, Barnes, & Jorgensen, 1992; Cohen and Rosenbaum 2004; Marteniuk et al., 1987; Ansuini et al., 2006; Ansuini, Giosa, Turella, Altoe & Castiello, 2008; Schuboe, Maldonado, Stork & Beetz, 2008; Johnson-Frey, McCarty & Keen, 2004; Gentilucci, Negrotti & Gangitano, 1997; Rosenbaum, Chapman, Weigelt, Weiss & van der Wel, 2012; Rosenbaum & Feghhi, 2019). Thus, additional investigations with different tool grasping tasks where movement extent and accuracy demands are more similar would be useful to further clarify whether tool-related movements do rely on access to learnt knowledge.

Accordingly, another aim of this experiment was to test whether there were distinct kinematics between tool and non-tool grasping because tool, but not non-tool, actions are linked to stored knowledge (e.g., Milner & Goodale, 1995; 2006; Buxbaum, 2017; Osiurak et al., 2014; Johnson-Frey, 2003; Johnson-Frey & Grafton, 2003; Bub, Masson & Cree, 2008) yet movement extent and accuracy demands are tightly matched if simply grasping these objects. Indeed, there is already kinematic evidence indicating that tool grasping which takes into consideration the object’s functional properties (i.e., for demonstrating its use) is slower with a wider PGA than if grasping the same tool when only needed to consider its structural properties (i.e., for moving it elsewhere; Valyear, Chapman, Gallivan, Mark & Culham, 2011; Cicerale, Ambron, Lingnau & Rumiati, 2014; also see Jax & Buxbaum, 2010). A key hypothesis, then, was that tool, relative to non-tool grasping would share the same characteristics (i.e., slower with a wider PGA).

Importantly, these findings were predicted even for the simple act of grasping (i.e., rather than using a tool) because even passively viewing a tool (e.g., as a prime) can influence subsequent grasping behaviour (e.g., Bub, Masson & Cree, 2008; Valyear et al., 2011). In fact, many other behavioural studies, besides those involving grasping, examining tool-related processing have found that the presentation of tool can, atleast under certain conditions (see Tipper et al., 2006; Pellicano et al., 2010; Costantini, Ambrosini, Scorolli & Borghi, 2010; Costantini, Committeri & Sinigaglia, 2011; Ambrosini, Scorolli, Borghi & Costantini, 2012; also see Valyear et al., 2011 for an example of how strategy affects tool priming during grasping), automatically evoke motor preparation (for reviews see Thill, Caligiore, Borghi, Ziemke & Baldassarre, 2013; van Elk et al., 2014; Borghi & Riggio, 2015; Osiurak, Rossetti & Badets, 2017).

Rather interestingly, a selection of these other behavioural studies involving button-press judgements have consistently shown that RTs are faster if pictures or videos of tools depict their typical manipulation (for review see Humphreys, Kumar, Yoon, Wulff, Roberts & Riddoch, 2013). For example, action decision RTs (e.g., when naming a tool or its action) are faster if watching an axe be swung or even simply gripped in such a way, relative to if they consistent with an atypical action such as wiping (Yoon & Humphreys, 2005; Kumar, Yoon & Humphreys, 2012; Yoon, Humphreys, Kumar & Rotshtein, 2012). Likewise, faster action decision RTs also occur if pictured tools appear in locations such that its handle is congruently positioned with the responding hand (Yoon & Humphreys, 2007; Yoon, Humphreys & Riddoch, 2010). In fact, Valyear et al.,'s (2011) video viewing experiment of which the grasping paradigm in Chapter 2 was adapted from, similarly found a faster voice onset when naming tools being grasped in a way that was typical (e.g., by the handle), relative to atypical (e.g., by the head) or not being grasped at all.

Whether the typicality of an action also affects 3D tool grasping is, to my knowledge, yet to be explored. Unlike 2D pictures, 3D objects have features (e.g., shape, depth) that are directly extractable by the visual system and offer the possibility of a genuine action (Snow, Pettypiece, McAdam, McLean, Stroman, Goodale & Culham, 2011). Reasonably then, the final aim of this experiment was to investigate whether motor planning may indeed be faster for actions involving the handle of a tool, relative to its head (see below for a specific prediction).

Here, motion-capture was used to record kinematics of the right hand when participants performed tool and non-tool grasping in conditions highly similar to the previous fMRI project (see Chapter 2, Project 1). First and foremost, this behavioural follow-up experiment was designed to assess whether participants were likely to have been scaling their grip during the previous fMRI project despite the fact that these actions were performed under unconventional conditions (i.e., while laying supine and when grasping five times in within a trial). This was tested by examining whether PGA significantly changed as a function of the three object sizes (i.e., small, medium and large). A second aim of this experiment was to examine whether there were differences between *tool* and *non-tool* grasping, that is, a difference between grasps based on *object category*. Specifically, I predicted that tool, relative to non-tool, grasping would be significantly different for the *reach* (e.g., RT, MT) and *grasp* (e.g., PGA, grip scaling) portions of the movement, since previous evidence

(Jax & Buxbaum, 2010; Valyear, Chapman, Gallivan, Mark & Culham, 2011; Cicerale, Ambron, Lingnau & Rumiati, 2014) shows that tool grasps are slower and with a wider PGA if the action is based on their functional (i.e., when using the tool), relative to structural, properties (i.e., when moving the tool). The final aim was to examine whether responses were significantly faster for *typical* (i.e., grasp by the tool's handle), relative to *atypical,* tool grasps (i.e., grasp by the tool's head). Based on evidence that RTs are faster when 2D depictions of tools match the way that tools are typically manipulated (e.g., Yoon & Humphreys, 2005; Yoon & Humphreys, 2007), I predicted that RTs may also be modulated by the *typicality* of tool grasping. This could have been in the form of an additional interaction between *object category* and *typicality* for the analysis of RT where measures would be faster for non-tool, relative to atypical tool grasping, but not relative to typical tool grasping.

3.2. Method

3.2.1. Participants

Twenty-two right-handed (Edinburgh Handedness Questionnaire; Oldfield, 1971) healthy volunteers completed this experiment (6 males, 19-29 years of age, Mean Age = 22.3, SD = 2.4). Ten of these participants had completed the previous fMRI experiment, while the rest were naïve to study's purpose. All had normal or corrected-to-normal vision, no history of motor, psychiatric or neurological disorders and gave informed consent in accordance with the ethical committee at the University of East Anglia. In return for participation, volunteers were compensated £12.

3.2.2. Stimuli & apparatus

Stimuli were the same 3D-printed tools (i.e., knife, spoon and pizzacutter) and non-tools (i.e., cylinders with widths the same size as the heads of the knife, spoon or pizzacutter) described in the fMRI experiment (Project 1, Chapter 2; Fig. 2.1A; see *Stimuli & Apparatus*: section 2.2.2.). Participants laid supine in the turntable apparatus described previously (Fig. 2.1B) which was set-up in the Vision & Action laboratory at the UEA (Fig. 3.1.). The relative distances between the participants and the fixation or stimuli were based on the average measurements taken from the fMRI experiment such that stimuli were again directly reachable (the resting hand and object centre for every participant was at a distance of 43cm) and that the centrally aligned red fixation LED was located above the objects (subtending a mean visual angle of ~20° from the centre of stimuli). A head tilt comparable to the fMRI experiment (i.e., ~20°) was achieved in this experiment by using two pillows. Only several minor differences existed between the apparatus used for fMRI and the behavioural follow-up experiment. First, no arm-strap nor eye monitoring cameras were used here; though participants did complete the same pre-experiment training period as for in Project 1 and received verbal reminders between experimental blocks to maintain fixation and to minimise upper arm movements. Second, noise-cancelling headphones (Bose Corporation, USA) were worn to ensure that the sound of stimulus placement did not provide cues about an upcoming trial.

A Qualisys Oqus (AB, Gothenberg, Sweden) sampling at 179 Hz measured the position of small passive markers affixed to the participants' right wrist and the nails of the right index finger and thumb (Fig. 3.1.). A custom script written in Matlab (The MathWorks, USA R2010a), supported by the Psychophysics Toolbox (Brainard, 1997), received a trigger from the workstation at the beginning of each run to control the electronic equipment (i.e., fixation, object illuminator, audio and the motion-capture system).

3.2.3. Procedure

The procedure here was largely the same as for the previous fMRI experiment (see *Procedure*: section 2.2.3.). In brief, the experiment was completed in darkness, where participants rested their hands on their chest. First, an audio cue was heard (i.e., Left or Right) and the stimulus was then illuminated (500ms later) cueing the reach-to-grasp action which was to be directed to the side of the stimulus that was auditorily instructed. Crucially, the tools' handles (and the side of the non-tools matching the length of these handles) were always oriented to the right so that right- and left-ward grasping for the tool conditions were labelled as typical and atypical tool grasping, respectively. As before, stimuli were illuminated five times (i.e., open loop conditions with illumination lasting 250ms each) in a given trial with an interval of two seconds - the marker positions were recorded for these five grasping repetitions within a trial using a continuous 10 second recording.

Grasping was performed using a precision grip where the objects were grasped from across their width (hereon referred to as size) from the top to bottom with the index finger and thumb, respectively (Fig. 3.1.). Actions were instructed to be performed at a natural pace and the objects were never instructed to be used. The elements critical for modelling the haemodynamic response during fMRI were not carried out in this behavioural experiment: we removed the baseline periods at the beginning/end of each experimental block and periods of darkness (i.e., fMRI off-blocks) were not interspersed between trials.

The same pseudorandomised trial orders were used as in Project 1 with 16 trials per block. For the 12 experimental trials the three repetitions were completed per condition (i.e., tool typical, tool atypical, non-tool right and non-tool left) with each exemplar (e.g., knife tool/non-tool, spoon tool/non-tool and pizzacutter tool/non-tool) being grasped by their right and left sides once. The foil tool and non-tool were grasped by each side in the remaining four trials and were excluded from analysis. On average participants completed seven runs (minimum six, maximum seven) and this totalled on average 84 experimental trials and 21 repetitions per condition for each participant. The entire experiment lasted approximately one hour and the extra run that was collected in comparison to the fMRI experiment ensured that sufficient repetitions remained after accounting for excluded trials that would arise from the occlusion of markers (see *Data preprocessing:* section 3.2.4).

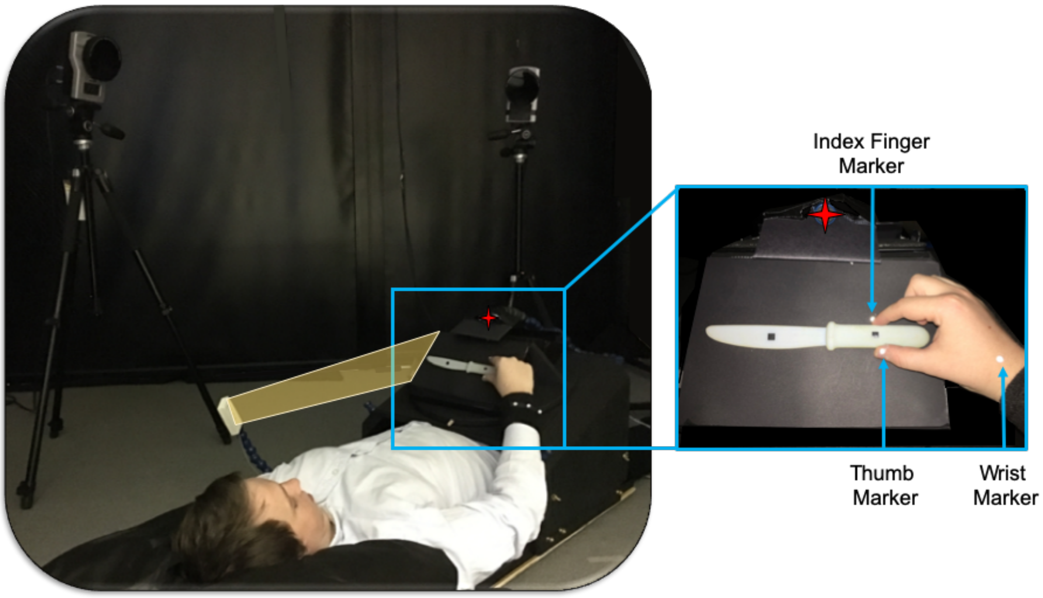

Fig. 3.1. Apparatus for motion tracking experiment. (*Left*) The 3D graspable objects were presented using the same turntable equipment as described in the fMRI experiment. The setup is presented here from behind and is surrounded by motion tracking cameras (four additional cameras are ceiling-mounted, out of camera shot). The red star represents the fixation LED and the delineated yellow zone represents the illuminated workspace emitted by white LEDs. (*Right*) Marker positions are labelled on the index finger, thumb and wrist. The hand is shown at its final contact points for an example of a typical tool grasp. Note that the experiment is completed in the dark, thus lighting here is for illustration only.

3.2.4. Data preprocessing

Kinematic data were obtained by localising the x, y and z positions of the markers attached to the index finger, thumb and wrist of the participants' right hand (see Fig. 3.1. for positions). Analyses were conducted off-line using a customised software written in Matlab. These 3D positions for each marker were filtered using a low-pass Butterworth filter (10 Hz-cut-off, 2nd order) (Krigolson & Heath, 2004; Binsted, Brownell, Vorontsova, Heath & Saucier, 2007; Davarpanah & Heath, 2016). The wrist marker position was then used to determine the onset and offset of the movement toward objects using a velocity threshold of 50mm/s (e.g., Cohen et al., 2009).

Like a similar study that measured reaches with an outward (i.e., reach toward object) and inward (i.e., return hand to home position) reaching component (Quinlan & Culham, 2015), the local minimum of the velocity trace was used as the offset of the outward reach (i.e., the floor velocity value) if this value did not fall between the 50mm/s criteria. This end velocity criteria had to be manipulated on <1% of trials. A one-way Repeated Measures ANOVA (RM ANOVA) with all 12 individual grasping conditions per exemplar as factors (i.e., knife tool typical, knife tool atypical, spoon tool typical, spoon tool atypical, pizzacutter tool typical, pizzacutter tool atypical, knife non-tool typical, knife non-tool atypical, spoon non-tool typical, spoon non-tool atypical, pizzacutter non-tool typical and pizzacutter non-tool atypical) and the frequency of trials where this value had to be manipulated as a dependent variable, indicated that there was no significant differences between the conditions in which this end velocity criteria had to be manipulated ($F(11) = 1.4$, $p = 0.16$, $\eta p^2 = 0.06$).

Table 3.1. Kinematic dependent variables. Acronyms: ms = milliseconds, mm/s = millimetres per second; - = Same as above.

Dependent Measures	Name	Unit	Marker(s)	Description
		Reach Kinematics		
Reaction Time	RT	ms	Wrist	Time interval between illumination cue and the onset of the movement.
Movement Time	MT	ms	Wrist	Time interval between movement onset to movement offset.
Time to Peak Velocity	tPV	ms	Wrist	Time interval between movement onset and PV.
Peak Velocity	PV	mm/s		Peak velocity of the wrist marker within MT.
		Grasp Kinematics		
Peak Grip Aperture	PGA	mm	Index & thumb	Peak Euclidean distance between the thumb and index finger.
Time to Peak Grip Aperture	tPGA	ms	Index & thumb	Time interval between RT and PGA.
Grip Scaling	Fisher Transformed R^2		Index & thumb	Variables obtained from the linear regression analysis between PGA and object size (also see section 3.2.3).
-	Slope		-	-
-	Intercept		-	-

Every dependent variable (see Table 3.1.) was computed per trial for each of the five grasping repetitions (i.e., five values per trial), but the repetition number within a trial (e.g., grasp repetition one or two) was never explicitly modelled, meaning that grasping repetition was collapsed for analysis. This was comparable to the analysis of the fMRI experiment (i.e., multivariate pattern analysis was performed using blocks of brain activity across the five grasp repetitions). Additionally, performing the analysis in this way maximised statistical power because this allowed a maximum of 35 values for a given exemplar in a condition (e.g., knife atypical grasping was performed across seven blocks with five grasp repetitions per block).

A grand mean was calculated for the PGA and tPGA *grasp kinematics* per exemplar (e.g., knife, knife non-tool, spoon, spoon non-tool, pizzacutter and pizzacutter non-tool) and per grasp direction (i.e., typical/right and atypical/left). This enabled the conditions for each tool exemplar to be matched with non-tool conditions where the grasped portion of the object was of an equivalent size (see *Statistical analysis:* section 3.2.5.). A grand mean was calculated for the RT, MT, PV and tPV *reach kinematics* for the four key conditions (i.e., tool typical, tool atypical, non-tool right and non-tool left) since reach distance was identical between the tools and their paired non-tool exemplars. Finally, additional grip scaling measures were taken to analyse *grasp kinematics* (see next paragraph for the particular variables used). These were computed using a linear regression between object size (i.e., small, medium and large) and the PGA for the *Tool Atypical & Matched Non-tool Conditions* (TA&MNC; see Fig. 3.2A.). These TA&MNC conditions were used because this is where object size increased at an identical rate across both object categories. Note that this analysis could not be performed for typical tool grasping because the *Tool Typical & Matched Non-tool Condition* (TT&MNC; see Fig. 3.2B) all involved grasping identically sized handles meaning that grip would not scale with object size.

The linear regression used to measure the degree of grip scaling resulted in R^2, slope and intercept dependent variables. The R^2 output was normalised with a fisher transformation (Fisher, 1921) for each subject individually (Cohen, 2003; Rossit, McAdam, Mclean, Goodale & Culham, 2013; Keefe & Watt, 2009) and relies on the standard deviation of the MGA, thus removing information about the original units of the variables (Whitwell, Striemer, Nicolle, & Goodale, 2011). These R^2 values 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 (Borchers & Himmelbach, 2012): a slope of 0 indicates no scaling of the MGA to the object and a slope of 1 indicates perfect scaling meaning that higher slopes reflect greater proficiency in grasping (Smeets & Brenner, 1999; Cuijpers, Brenner & Smeets, 2006). 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).

In cases where data needed to be excluded from the analysis for a given grasping repetition (out of the five) within a trial, the data was removed for that specific repetition for every dependent variable. Grasping repetitions within a trial were excluded from the analysis (2.62% datapoints) for the following reasons: index/thumb marker occlusion at the frame following PGA (2.09%), object presentation was incorrect (0.04%), and if the subject reached too late (0.11%) or in the wrong direction (0.38%). A series of one-way RM ANOVAs with all 12 individual grasping conditions per exemplar as factors (see end velocity criteria

ANOVA) and the percentage of these four types of errors as dependent variables (cumulatively or independently), indicated that there was no significant differences between the conditions where these errors occurred (all *p*'s > 0.42).

3.2.5. Statistical analysis

Four types of ANOVAs (three types for grasp kinematics and one type for reach kinematics) were used to meet all the experimental aims. The PGA and tPGA grasp kinematic measures were analysed using two separate types of ANOVA: one type for atypical tool grasping (i.e., 3 x 3 RM ANOVAs with TA&MNC and object size as factors; see top of Fig. 3.2A.) and another type for typical tool grasping (i.e., one-way RM ANOVAs (4 groups) with the TT&MNC as the four groups; see Fig. 3.2B.). Next, the R^2, slope and intercept measures of grip scaling were analysed using *one-way RM ANOVAs (3 groups)* including the TA&MNC (see bottom of Fig. 3.2A.). Lastly, the RT, MT, PV and tPV reach kinematics were examined using *2 x 2 RM ANOVAs* with object category (i.e., tool and non-tool) and typicality (i.e., typical/right and atypical/left) as factors (see Fig. 3.3.).

The first experimental aim (i.e., examining whether PGA changed as a function of object size) was addressed by the *3 x 3 RM ANOVAs* with TA&MNC and object size as factors because a main effect of object size could be tested for here. The second aim (i.e., examining whether grasp and reach kinematics changed across object categories) was addressed by all four types of ANOVA because they allowed comparisons between object categories (i.e., tool versus non-tool). The final aim (i.e., examining whether reach kinematics were altered by the typicality of a tool action) was directly addressed by the *2 x 2 RM ANOVAs* with object category and typicality as factors. A Bonferroni correction was used to control for the problem of multiple comparisons.

3.3. Results

3.3.1. Grasp kinematics

Analysis of PGA and tPGA for the AT&MNC revealed a main effect of object size where PGA was larger ($F(1,28) = 520.2$, $p < 0.001$, $\eta p^2 = 0.96$) and tPGA was later ($F(2,29) = 95.1$, $p < 0.001$, $\eta p^2 = 0.82$) for objects of larger, compared to smaller, sizes (all pairwise comparison p's < 0.006) confirming that participants were able to scale their grip to the object's size regardless of the category of that object (see Table 3.2.).

In this analysis for PGA, there was also a significant interaction between condition and object size ($F(2,51) = 62.74$, $p < 0.001$, $\eta p^2 = 0.75$). Post-hoc comparisons revealed that grasping the bowl of the spoon led to a higher PGA compared to grasping the non-tool spoon exemplar on its left (mean difference [standard error] = 3.9mm [0.6mm]) and right side (mean difference [standard error] = 4.3mm [0.7mm]; all p's < 0.001; see PGA graph in Fig. 3.2A.). Oppositely, grasping the wheel of the pizzacutter of the spoon led to a lower PGA compared to grasping the pizzacutter non-tool on its left (mean difference [standard error] = 3.8mm [0.5mm]) and right side (mean difference [standard error] = 4.9mm [0.6mm]; all p's < 0.001; see PGA graph in Fig. 3.2A.). The same interaction was not significant for tPGA ($p = 0.6$) and, instead, there was a significant main effect of condition ($F(2,42) = 8.6$, $p = 0.001$, $\eta p^2 = 0.29$). Post-hoc comparisons indicate that this effect was driven by differences related to reach direction where the tPGA was achieved later for leftward (i.e., contralateral) relative to rightward (i.e., ipsilateral) grasping: tPGA was significantly later for leftward tool, than rightward non-tool, grasping (mean difference [standard error] = 14.7ms [3.9ms]; $p = 0.004$; see tPGA graph in Fig. 3.2A.) and a similar trend was observed between leftward, relative to rightward, non-tool grasping (mean difference [standard error] = 10.1ms [4ms]; p = 0.058). No other main effects or interactions for these ANOVAs analysing PGA or tPGA for the TA&MNC were significant (all p's > 0.6).

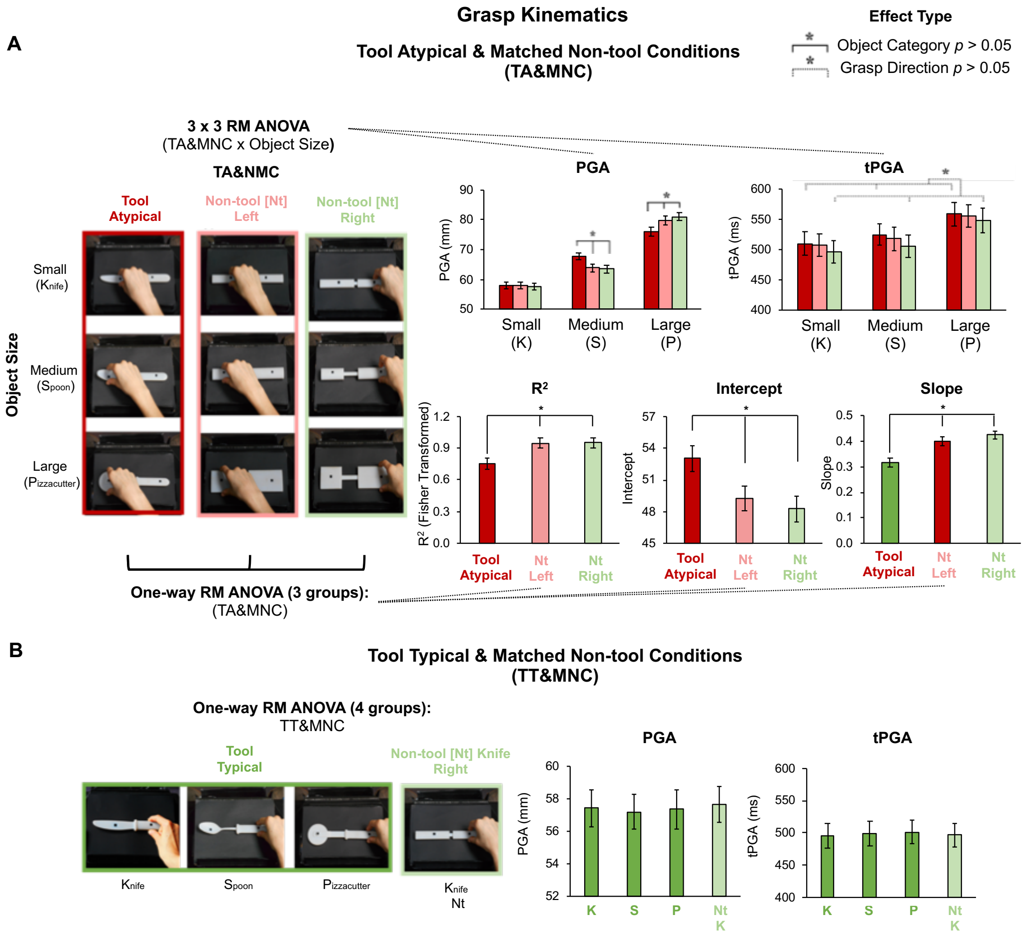

Fig. 3.2. Grasp kinematic analysis and results. (A) Analysis design and results for the *Tool Atypical & Matched Non-tool Conditions* (TA&MNC) (i.e., the tool atypical, non-tool left and non-tool right conditions for each of the three different sized exemplars: small [knife tool/non-tool], medium [spoon tool/non-tool] and large [pizzacutter tool/non-tool]). For PGA and tPGA, the TA&MNC conditions were analysed using RM 3 x 3 ANOVAs (TA&MNC x Object size; see top left of 3.2A.). For the R^2, slope and intercept (i.e., the grip scaling kinematics) the TA&MNC were analysed with one-way RM ANOVAs (see bottom left of 3.2A.). Results are

presented on the right (see dashed lines in Fig. 3.2A.). (B) Analysis and design for the Tool Typical & Matched Non-tool Condition (TT&MNC) (i.e., knife typical, spoon typical, pizzacutter typical and the equivalently sized non-tool knife right condition). For the PGA and tPGA the TT&MNC were analysed using one-way RM ANOVAs involving the four conditions from the TT&MNC as groups. Error bars represent Standard Error of the Mean (SEM).

Table 3.2. Post-hoc pairwise comparisons of the main effect of object size for PGA and tPGA. Acronyms: K = Knife sized stimuli; S = spoon sized stimuli; P = Pizzacutter sized stimuli.

Stimuli size	Mean (standard error)	Pairwise comparison *p* values		
		Small vs. Medium	Medium vs. Large	Small vs. Large
		PGA (mm)		
Small (K)	57.8 (1.1)			
Medium (S)	65.1 (1.2)	< 0.001	< 0.001	< 0.001
Large (P)	78.9 (1.3)			
		tPGA (ms)		
Small (K)	504.7 (18.4)			
Medium (S)	516.2 (18.5)	0.005	< 0.001	< 0.001
Large (P)	554.2 (18.9)			

The grip scaling ANOVAs that compared the R^2, slope and intercept values across the AT&MNC all revealed a main effect of condition which was characterised by the same object category effect: atypical tool grasping was significantly different from the non-tool grasping conditions (see bottom graphs of Fig. 3.2A.). Specifically, analysis of the fisher transformed R^2 revealed a main effect of condition ($F(2,42) = 11.29$, $p < 0.001$, $\eta p^2 = 0.35$) where the extent of grip scaling to object size was significantly lower for atypical tool grasping compared to grasping non-tools on the left (mean difference [standard error] = 0.2 [0.05], $p = 0.001$) or right side (mean difference [standard error] = 0.19 [0.05], $p = 0.003$). Analysis of the intercept found a main effect of condition ($F(2,42) = 51.5$, $p <$ 0..001, $\eta p^2 = 0.71$) where the intercept of the linear regression was significantly higher for tool atypical grasping compared to grasping a non-tool on the left (mean difference [standard error] = 3.8 [0.5], $p < 0.001$) or right side (mean difference [standard error] = 4.7 [0.5], $p < 0.001$). Finally, analysis of the slope of the linear regression revealed a main effect of condition ($F(2,42) = 51.5$, $p <$ 0..001, $\eta p^2 = 0.71$) where the slope was significantly shallower for tool atypical grasping compared to grasping a non-tool on the left (mean difference [standard error] = 0.08 [0.01], $p < 0.001$) or right side (mean difference [standard error] = 0.11 [0.01], $p < 0.001$). No significant differences were observed for the remaining post-hoc tests that compared the two non-tool grasping conditions (all p's > 0.13).

As for the analysis of PGA and tPGA for the typical tool grasping conditions, no significant main effects or interactions were observed between the TT&MNC where the handles of the tools and the matched part of a non-tool were compared (all p's = 0.66; see Fig. 3.2B.).

3.3.2. Reach kinematics

Analysis of RT and MT revealed significant main effects of object category (RT: $F(1,21) = 15$, $p = 0.001$, $\eta p^2 = 0.42$; MT: $F(1,21) = 5.74$, $p = 0.026$, $\eta p^2 = 0.22$) where grasping was slower for grasping tools than non-tools (RT mean difference [standard error] = 9.7ms [2.5ms]; MT mean difference [standard error] = 6ms [2.5ms]; see top graphs of Fig. 3.3.). Reach direction also affected behaviour since there was also a significant main effect of typicality where leftward, relative to rightward, movements were linked to a longer MT (*F*(1,21) = 8.9, $p = 0.007$, $\eta p^2 = 0.3$) and decreased PV (*F*(1,21) = 11.48, $p = .003$, $\eta p^2 = 0.35$) (MT mean difference [standard error] = 14.8ms [5ms]; PV mean difference [standard error] = 34.4ms [10.2ms]; see Fig. 3.3.). No other significant main effects or interactions were observed for the analysis of reach kinematics (all *p*'s > 0.15).

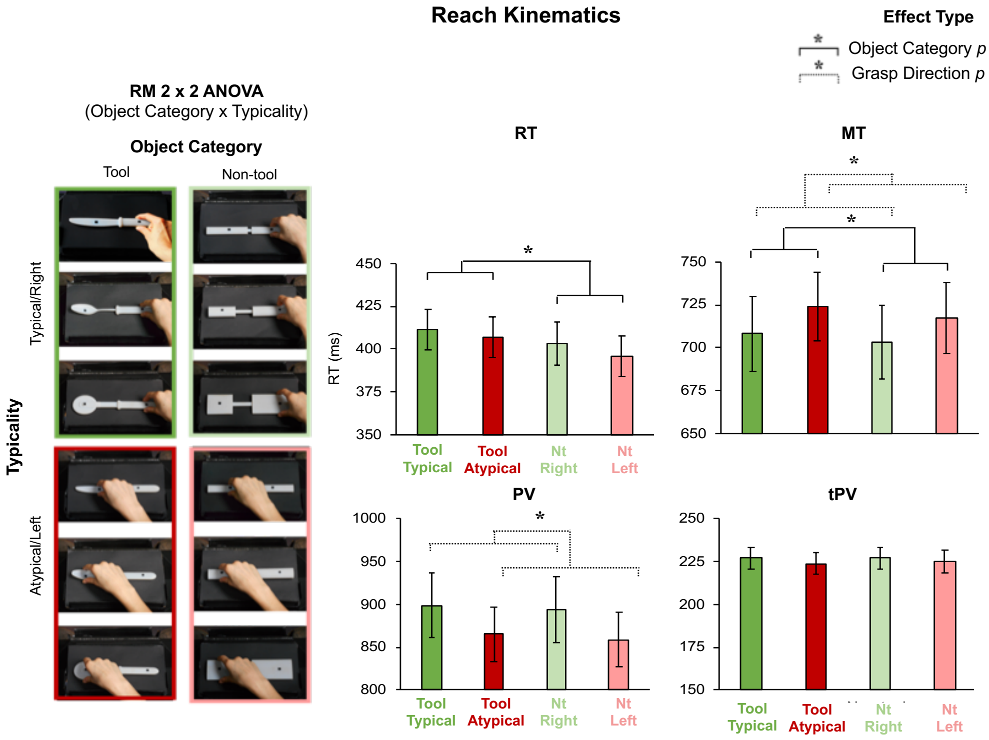

Fig. 3.3. Reach kinematic analysis and results. The conditions examined for all reach kinematics are shown in the left panel and were analysed using a RM 2 x 2 ANOVA with object category and typicality as factors. Graphs for the RT, MT, PV and tPV are presented on the right. Error bars represent SEM.

3.4. Discussion

Despite the highly unconventional setting in which grasping is performed during fMRI (e.g., laying supine), especially for the grasping paradigm used during Project 1 (i.e., grasping five times within a trial), this motion-capture experiment demonstrated that, under similar conditions, participants still demonstrated classic scaling between grip and object size (see Table 3.2. and Fig. 3.2.; Jeannerod, 1984; Gentilucci et al., 1991; Castiello et al., 1992). Rather interestingly, hand kinematics were also revealed to be affected by the category of the object (see *Object category affects hand kinematics;* section 3.4.1.) and, possibly, the typicality of the action (see *Typicality and hand kinematics;* section 3.4.2.) even though many features of these movements (e.g., required grip size, reach distance) were tightly controlled.

3.4.1. Object category affects hand kinematics

As predicted, subtle differences were observed in grasp and reach kinematics when directly comparing tool and non-tool grasping. First, grip aperture size was found to be significantly different between object categories during atypical tool grasping (see Fig. 3.2A.), regardless of whether the comparison simply involved PGA or if these values were transformed into sensitive grip scaling measures (i.e., the R^2, slope and intercept of a regression between object size and PGA). Second, the time taken to initiate (i.e., RT) and perform movements (i.e., MT) was found to be significantly longer when grasping tools, relative to non-tools (see Fig. 3.3.).

From a kinematic perspective, grasping and reaching measures have been extensively studied when changing superficial properties of an object (e.g., its shape or distance away from the hand; Marteniuk, MacKenzie, Jeannerod, Athenes & Dugas, 1987; Roy et al., 2000; Bootsma et al., 1994; Gentilucci et al., 1991; Jakobson & Goodale, 1991; Sartori, Ciani, Bulgherni & Castiello, 2012) or an action (e.g., movement direction or speed; Roy, Paulignan, Meunier & Boussaoud, 2002; Wing, Turton & Fraser, 1986). Related effects were replicated here (e.g., contralaterally directed movements of the right hand were linked to a longer MT and later tPGA; see Connolly & Goodale, 1999; Paulignan et al., 1997), most notably where PGA increased as a function of object size (e.g., Jeannerod, 1984; Jakobson & Goodale, 1991). This suggests that the same hallmark behavioural characteristics may have been exhibited when this paradigm was used during fMRI in Project 1. But the additional findings here showing that object category also affected hand kinematics are particularly interesting because this occurred even after controlling for such superficial properties (e.g., PGA was significantly different between atypical tool and non-tool grasping despite the widths of these object types being matched).

A few behavioural studies indicate that, in line with the evidence here, button-press RTs are faster when processing non-tools than tools. Vingerhoets, Vandamme & Vercammen (2009) found that RTs were faster when simple shapes, relative to tools, were presented as primes in a traditional Stimulus Response Compatibility (SRC) paradigm (i.e., where the handle position does/does not match the responding hand; see *Theory of affordances:* section 1.5.). Likewise, RTs are faster when responding to pictures of natural (e.g., cherry, leaf), relative to man-made, objects (e.g., tweezers, pen) during object categorisation (Borghi, Bonfiglioli, Lugli, Ricciardelli, Rubichi & Nicoletti, 2007). In fact, a portion of the stimuli in those experiments had the same identities to those employed here for both the tools (i.e., knife, spoon; Borghi, Bonfiglioli, Lugli, Ricciardelli, Rubichi & Nicoletti, 2007) and non-tools (i.e., cylinders; Vingerhoets, Vandamme & Vercammen, 2009).

Accounting for this distinction between object categories, Borghi et al., (2007) highlighted that, while both natural and man-made objects are linked to information regarding how to reach and grasp them (e.g., their shape), the latter (i.e., like the tools here) are additionally associated with functional gestures (e.g., how to use them properly; also see Borghi, 2005). Accordingly, perceiving these particular objects was suggested to ‘lead to the simulation not only of the hand gestures required to grasp it, but also of the other gestures required to actually use it’ (Borghi et al., 2007, P. 19). As participants were never instructed to use the tools in this grasping paradigm, the findings here extend this view, implying that the irrelevant use-related actions associated with tools prolong responses even during a real hand-tool interaction. This also fits with Vingerhoets et al., (2009) conclusion that there is a dominance for physical (e.g., shape) rather than functional (e.g., associated actions) action elicitation (also see Rumiati & Humphreys, 1998) because actions initiation was faster if based purely on physical properties (i.e., when grasping non-tools).

Worth highlighting, the opposite pattern of results (i.e., faster RTs for tools than non-tools) could be expected since other detection paradigms have found that RTs are faster for pictures of objects that afford action (e.g., a cup or hammer), relative to other stimuli (e.g., a cactus or animals; Handy et al., 2003; Garrido-Vasquez & Schubo, 2014). However, these effects appear to be restricted to certain parts of visual space (e.g., the right lower visual field; Handy et al., 2003), may be related to object graspability (see Garrido-Vasquez & Schubo, 2014 experiment 2) and often involve object competition displays (i.e., a tool and non-tool are simultaneously presented) that tap into distinctive mechanisms of attentional control (i.e., *between* object attention allocation; see Egly, Driver & Rafal, 1994; Stoll et al., 2015; Buschman & Kastner, 2015). Thus, unlike those findings, grasping a singularly presented tool, relative to a similarly manipulable non-tool, appears to slow RT.

Unique from button-press studies and by virtue of the sensitive motion-capture methods used here, movements were also found to be performed faster when grasping non-tools, relative to tools. Correspondingly, Cicerale et al., (2014) identified a faster MT when grasping a tool for demonstrating its use, rather than if simply for moving, and interpreted this as evidence that more attention was paid to grasping a tool for use. The opposite pattern of results was reported by Valyear et al., (2012), but, in this study, tool-use involved an extensive action sequence (i.e., demonstrate tool-use three times), relative to tool moving (i.e., place the tool once), and led the authors to suggest that this may reflect a compression effect (e.g., grasping is shortened for more elaborate actions; also see Johnson-Frey, McCarty & Keen, 2004). Thus, in line with Cicerale et al.,'s (2014) interpretation, grasping a tool also appears to demand further attention than grasping a non-tool. This more clearly fits with Handy et al.'s (2003) view that tools draw attention and, based on Borghi et al.,'s (2007) suggestion, this could indicate ongoing processing of the functional (yet irrelevant) actions strongly associated with tools.

Again, due to the motion-capture technology utilised here, object category influenced grasp kinematics because PGA and related measures of grip scaling were found to differ between the atypical tool and non-tool actions. Other studies consistently describe how grip components of grasping are affected by semantic properties of an object (e.g., Frak, Croteau, Bourbonnais, Duval, Duclos & Cohen, 2007) particularly when focusing on stored knowledge about objects (e.g., their prototypical appearance) or their associations (e.g., the meaning of an object). For instance, hand pre-shaping is closely linked to the familiar size of an object

(Borchers & Himmelbach, 2012), even if grasping a differently sized replica of that object (McIntosh & Lashley, 2008). Likewise, grip size can be influenced by words (e.g., ‘large’ or ‘small’; Glover & Dixon, 2002) or numbers (a high or low value; Andres, Ostry, Nicol & Paus, 2008) that are printed on, and thus associated with, an object. Here then, the non-superficial properties of an object (i.e., its semantic category) seems to influence both reach (i.e., RT, MT) and grasp kinematics (i.e., PGA and grip scaling; see next sub-section for further discussion about the direction of these effects).

Taken together, these object category effects on reach and grasp kinematics provides evidence that tool-related actions rely on stored knowledge. This converges with previous evidence that tool grasps are slower, with a wider PGA if the action is based on their functional (i.e., for demonstrating tool-use), relative to structural, properties (i.e., for tool-moving; Valyear, Chapman, Gallivan, Mark & Culham, 2011; Cicerale, Ambron, Lingnau & Rumiati, 2014; also see Jax & Buxbaum, 2010). Importantly, the grasping paradigm here demonstrates this even when the conditions that were related to stored knowledge (i.e., tool grasping) or not (i.e., non-tool grasping) are closely matched in terms of movement extent (i.e., a single action is performed) and accuracy demands (i.e., the same grasping action is required; see *Introduction*: section 3.1.). Theoretically, this fits well with many accounts that tool-related actions are achieved via distinctive conceptual (e.g., Arbib, 1981; Rumiati & Humphreys, 1998; Christensen, Sutton & Bicknell, 2019) and neural mechanisms (e.g., Milner & Goodale, 1995; 2006; Buxbaum, 2017; Osiurak et al., 2014; Johnson-Frey, 2003; Johnson-Frey & Grafton, 2003; Young, 2006; Bub, Masson & Cree, 2008).

An important consideration is whether these differences between object categories are driven by low level stimulus features. Since actions involving objects with smaller surface areas requires a larger degree of visual feedback (Bootsma, Marteniuk, Mackenzie & Zaal, 1994; Chieffi & Gentilucci, 1993) and, thus, can increase MT (Berthier, Clifton, Gullapalli, McCall & Robin, 1996), perhaps the disadvantage for tools (e.g., poorer grip scaling, slower RT and MT) is a reflection of these actions being, sometimes, directed at smaller parts of an object (i.e., the width of the spoon and pizzacutter handles are smaller than their paired non-tool conditions because these parts of the non-tools match the width of the tools' head, rather than handle; see *Stimuli & apparatus*: section 2.2.1.). Nevertheless, this confound is entirely avoided in the analysis of grasp kinematics (i.e., typical and atypical tool grasping are analysed separately). Further, this kind of effect in the analysis of reach kinematics should contribute to an interaction between object category and typicality where non-tool grasping should be specifically faster than *typical* tool grasping because it is those tool actions where object size is specifically smaller for the tools than the non-tools. In fact, such an interaction was specifically predicted for other theoretical reasons but was not found (see *Introduction:* section 3.1. & *Typicality & hand kinematics*: section 3.4.2.), strongly implying that such low-level changes in size cannot account for the object category effects.

3.4.2. Typicality & hand kinematics

Contrary to predictions, the typicality of tool grasping did not influence RT. Despite the differences in stimulus format in this experiment (i.e., we uniquely used 3D objects) and other behavioural studies that have previously reported how the typicality of a tool-related action affects RT (e.g., Yoon & Humphreys, 2007), these results are rather surprising because the handle of real 3D, but not a pictured 2D, tool provides visual information pertinent to action (e.g., Snow et al., 2011). In fact, Symes, Ellis & Tucker (2007) have systematically shown during a traditional SRC paradigm that the facilitation of RT becomes stronger as 2D objects appear more realistic, three-dimensional and graspable. Nevertheless, there may still be differences that are poorly understood between these types of stimuli that warrant further direct comparison. Indeed, not only does the perceived dimensionality of an object influence the kind of actions that are made towards it (Castiello, Bonfiglioli & Bennet, 1996; Castiello, Bonfiglioli & Bennet, 1998), but fundamental characteristics of grip scaling are also altered when pretending to grasp 2D, relative to 3D, objects (see Holmes & Heath, 2013).

Task differences are another, possibly more likely, source of these unexpected results. Many of the previous behavioural experiments finding that the typicality of an action affected RT involved tasks where there was an explicit need to retrieve tool-related knowledge, such as when naming a tool (Valyear et al., 2011) or judging the category of an object (Kumar, Yoon & Humphreys, 2012). Perhaps the lack of effects of typicality for RT are, thus, related to the context of this grasping paradigm where participants simply grasp an auditorily cued side of an object without needing to recall this information. This view clearly differs from that put forth when interpreting results about object category (e.g., see Borghi et al., 2007), but others have similarly found differences between findings about judgements of object category and typicality (i.e., object category is judged faster than the typicality of a tool action; Yoon, Humphreys, Kumar & Rotshein, 2012).

Clearly, further investigation is needed to determine the conditions under which the typicality of a tool-related action influences processing speed. Indeed, novel task contexts are well known to alter affordance processing (e.g., Tipper et al., 2006; Valyear et al., 2011; Masson, Bub & Breuer, 2011; Kalenine, Shapiro, Flumini, Borghi & Buxbaum, 2014) and even recent traditionally designed SRC paradigms do not always produce expected RT advantages toward the handle of a tool (e.g., Kourtis, Vandemaele & Vingerhoets, 2018; Kourtis & Vingerhoets, 2015; also see Cho & Proctor, 2011; Skiba & Snow, 2016; Pellicano, Iani, Borghi, Rubichi, & Nicoletti, 2010; Vainio, Ellis, & Tucker, 2007). An important next step would be to examine whether RTs are influenced by the typicality of tool-related actions when subsequent actions rely on stored knowledge about these objects. This could be achieved by contrasting hand kinematics across conditions that have, so far, only been utilised during separate experiments, such as between grasping tools for use (e.g., Jax & Buxbaum, 2010; Valyear et al., 2011; Cicerale et al., 2014) and for demonstrating newly learnt actions (e.g., Valyear et al., 2012; Osiurak et al., 2014; Brandi et al., 2014). This would allow a direct test of how learnt tool actions influence processing speed even when suitably controlling for kinematic complexity and when placing similar demands on accuracy.

This said, findings from the grasp kinematic analysis could be taken to suggest that the typicality of an action influences grasping behaviour. When directly compared, grip scaling measures were found to be significantly poorer for atypical tool, relative to non-tool, grasping (see bottom row of Fig 3.2A.). Rather interestingly, this differs from previous studies comparing grasp kinematics between object categories (e.g., familiar and unfamiliar objects; Haffenden & Goodale, 2000; Dijkerman, McIntosh, Schindler, Nijboer & Milner, 2009) because those studies tend to find that object familiarity (e.g., the familiar objects such as tools here) improves the calibration grip size to object size (McIntosh & Lashley, 2008; Borchers & Himmelbach, 2012).

The argument could be made that is the atypical nature of these tool actions (i.e., grasping tools by their head) that led to this detrimental effect on the degree of grip scaling. When viewing tools and their related objects (e.g., a paintbrush and paint-bucket), not only have participants been shown to sparsely gaze at the head of a tool (Natraj, Pella, Borghi &Wheaton, 2015; though see Van Der Linden, Mathot & Vitu, 2015), judging their relationship is slowed if a hand is depicted manipulating the tool in an atypical way (e.g., when holding the bristles of the paintbrush; Borghi, Flumini, Natraj & Wheaton, 2012; also see Natraj, Poole, Mizelle, Flumini, Borghi & Wheaton, 2013). Likewise, distinguishable behavioural characteristics, mostly during button-press responses (though see Anelli, Ranzini, Nicolletti & Borghi, 2013), have been identified when participants avoid responding to affordances related to objects that either afford multiple actions (e.g., a calculator affords clenching and poking; Jax & Buxbaum, 2010), no longer afford an action (e.g., a mug with a broken handle no longer affords grasping; Buccino et al., 2009) or afford dangerous actions (e.g., broken glass; Anelli, Nicoletti, Kalkan, Sahin & Borghi, 2012). Though the underlying processes are debated (e.g., are affordances inhibited or are aversive affordances activated; see Borghi & Riggio, 2015 for review), the nature of these actions are highly similar to the behaviour here where participants had to avoid the learnt action (i.e., grasping the tool by its handle).

Close inspection of the PGA analysis suggests that the disruption of grip scaling associated with atypical tool grasping is driven by actions involving the spoon and pizzacutter tools when each were compared with their equivalently sized non-tools (see Fig. 3.2A. top row). These PGA effects are unlikely to be the result of by a speed-accuracy trade-off (i.e., where tool actions could be more inaccurate due to faster responses) because a similar effect was not seen for tPGA (see Fig. 3.2A.

top row) and MT was generally longer for tools than non-tools (see Fig. 3.3. top row). Oddly, the PGA effects were in opposite directions for the heads of the pizzacutter (i.e., decreased for the tool) and spoon (i.e., increased for the tool; see Fig. 3.2A.) relative to the non-tools. Further study with a variety of tool exemplars that have matching properties (e.g., of the same size and shape) is needed to clarify whether this could be attributed to low level differences in shape that are known to influence kinematics, such as those related to convexity (e.g., the spoon head is more concaved; Sartori, Straulino & Castiello, 2011), edge protrusion (e.g., the spoon head protrudes further toward the hand; Cuijpers, Smeets & Brenner, 2004), overall size (e.g., the spoon head was smaller; McIntosh et al., 2018) or implied texture (e.g., the spoon head is smoother; Fleming, Klatzky & Behrmann, 2002; Flatters, Otten, Tivliet, Henson et al., 2012) as opposed to a higher-level affordance mechanism (e.g., an aversive affordance mechanism activated when grasping a blade; see Borghi & Riggio, 2015).

Regardless, when considering all findings here together (related to object category and typicality), a final important point can be drawn: kinematics during actions involving tools (particularly if they are atypical) and non-tools resemble known distinctions between movements based on moment-to-moment visual information (i.e., on-line actions) and those that are also influenced by stored information (i.e., off-line actions; e.g., Goodale, Jakobson & Keillor, 1994; Thaler & Goodale, 2011; for related reviews see Harvey & Rossit, 2012 and Goodale & Ganel, 2019). According to the DVST, off-line actions (e.g., tool-use, delayed reaching, pantomimed grasping) not only rely on visual processing within the dorsal visual stream, but also that of the ventral pathway since this is linked to memory-based representations of objects (also see Chapter 1), thus, explaining why RT, MT and grip scaling is negatively affected when grasping tools, relative to non-tools. In fact, this view is clearly supported by the fMRI results in the previous chapter where hand-selective cortex of both the visual streams carried information about the typicality of a tool action. Speculation regarding potential brain and behaviour convergence is discussed further in Chapter 5 (*see Hand-selective cortex: From perception to action:* section 5.2.).

3.4.3. Limitations

An important limitation of this experiment is that sensitive grip scaling measures could not be computed for typical tool grasping since the tool handles were of an identical width. This also leaves open the question as to whether grasp kinematics differ between atypical and typical tool grasping, since these conditions could not be directly compared (also see Fig. 5.2.). This said, it is unlikely that the grasp kinematic analysis that *was* performed for the PGA of typical tool grasping (versus non-tool grasping) failed to find a significant effect due to the insensitivity of this analysis because the same analysis for the atypical tool grasping conditions did find significant effects. Extending the stimulus set to include tools with differently sized handles would make this test possible in the future and may even be readily addressable by using a recently available database that includes tool-using motion-capture data across 66 different objects (Roda-Sales, Vergara, Sancho-Bru, Gracia-Ibanez & Jarque-Bou, 2019).

Also, there are other reach and grasp kinematics not computed here that may also have held important insights about how behaviour is influenced by the category of object or typicality of an action. Perhaps most importantly, wrist orientation (Cicerale et al., 2014) and grasp posture (i.e., the orientation between the index finger and thumb; Valyear et al., 2011) are measures previously found to be sensitive to the whether a tool is grasped for use, relative to being grasped for moving. Similar findings could be predicted here based on the grasp kinematic findings (i.e., significant differences between atypical tool and non-tool grasping) and this may help understand differences in PGA when grasping the heads of the spoon and pizzacutter (e.g., perhaps there is more wrist rotation when grasping the pizzacutter head, thus leading to a smaller PGA) as grasp posture is known to change across tool identities (Valyear et al., 2011). Likewise, other novel analysis approaches could be taken such as measuring the force of grip closure (e.g., Dijkerman, McIntosh, Schindler, Nijboer & Milner, 2009) or by investigating individual grip-shaping differences (e.g., Bongers, Zaal & Jeannerod, 2012) as these measures may be sensitive to non-superficial properties of an object too (e.g., Dawson, Buxbaum & Duff, 2010; Chainay, Bruers, Martin & Osiurak, 2014; da Silva, Labrecque, Caromano, Higgins & Frak, 2018).

Finally, like the behavioural control experiments related to many other reaching/grasping fMRI studies (e.g., Begliomini, Caria, Grodd & Castiello, 2007; Bernier & Grafton, 2010; Cavina-Pratesi, Monaco, Fattori, Galletti et al., 2010; Monaco, Cavina-Pratesi, Sedda, Fattori, Galletti & Culham, 2011; Rossit et al., 2013; also see Grol, Majdandzic, Stephan, Verhagen, Dijkerman et al., 2007) motion-capture here was performed in a separate session. This approach has been suggested to validate the approach taken in fMRI (see Bernier & Grafton, 2010) but, ideally, these measures should be taken *during* neuroimaging (e.g., Casellato, Ferrante, Gandolla et al., 2010; also see Maidhof, Kastner & Makkonen, 2014). Brain-behaviour correlations would then be possible within participants (for related approaches using RT measures see Grol, Majdandzic, Stephan, Verhagen, Dijkerman et al., 2007; Tankus & Fried, 2012; Valyear & Frey, 2015) to evidence, for example, that differences in grip scaling (e.g., when grasping tools atypically) is linked to neural representations of typicality (see Chapter 5 for further discussion). Touching on this, the next chapter presents a slow-event related fMRI design that investigated the relationship between hand kinematics and neural representations about the typicality of an action by performing the same analyses as in Project 1 before the action begins (i.e., during pre-movement planning), that is, before differences in hand kinematics can even unfold.

3.4.4. Conclusion

In conjunction with the previous fMRI experiment, so far, it has been shown that the way that tools are grasped is reflected in activity within hand-selective cortex (see Chapter 2) and hand kinematics (this Chapter). Reach and grasp kinematics when interacting with tools even appear to resemble those reported during other types of off-line actions (e.g., pantomimed grasping), and, under the framework of the DVST, clearly fits with the previous fMRI evidence showing that both the dorsal and ventral visual streams carry information about tool-related actions. By using a grasping paradigm where, crucially, there is no intent to use the tools, this motion-capture experiment also implies that the functional actions associated with tools may automatically interfere with motor control during real tool interactions (e.g., Castiello, 1996; Humphreys & Riddoch, 2001; Rafal, Ward & Danziger, 2006; Tucker & Ellis, 1998; Buccino, Sato, Cattaneo, Roda & Riggio, 2009; Naish, Reader, Houston-Price, Bremner & Holmes, 2013; Gentilucci, 2002; Valyear et al., 2011; Jax & Buxbaum, 2010).

Chapter 4

Preparing to grasp tools: A slow event-related fMRI investigation

4.1. Introduction

Voluntary movements are prepared before they are executed (Day et al., 1989, Ghez et al., 1997; Keele, 1968; Kutas & Donchin, 1974; Riehle & Requin, 1989; Rosenbaum, 1980; Sussillo, Churchland, Kaufman & Shenoy, 2013). Most theories of motor control distinguish between this planning phase and a separate execution period (e.g., Kawoto, 1999; Wolpert & Flanagan, 2011; Wolpert, Diedrichsen & Flanagan, 2011), as do many developments in robotic engineering (e.g., Schaal & Schweighofe, 2005; Toussaint & Goerick, 2010; Mainprice, Hayne & Berenson, 2015), even for the act of simply grasping an object (e.g., Toussaint, Plath, Lang & Jetchev, 2010; Galbraith, Guenther & Versace, 2015).

Motor planning, often referred to as movement preparation, can be identified by the correlation between neural responses and future actions (e.g., Li, Daie, Svoboda & Druckman, 2016). This process has been extensively studied with delayed instruction paradigms using non-human primates (for reviews see Graziano, Taylor, Moore & Cooke, 2002; Svoboda & Li, 2018). In these tasks, a delay separates the points in time that a subject receives a ‘plan’ and a ‘go’ cue which, respectively, provide instructions about which movement is to be performed and when. Thus, neural activity about motor preparation and online motor control can be disentangled.

A key finding from monkey neurophysiological recordings, predominantly at the level of the single cell, is that neural activity occurs well before movement onset in motor and premotor cortex (e.g., Weinrich et al., 1984) and that this pre-movement activity can be used to predict whether the upcoming action will be, for example, aimed toward or away from a stimulus (e.g., Zhang & Barash, 2000; Gail & Andersen, 2006). In fact, an early study showed that on the rare trials where the monkey performed the wrong movement (i.e., the one not instructed by the plan cue), the planning activity tended to reflect the future, rather than instructed, movement, strongly characterising this activity as preparatory (Tanji & Evarts, 1976; also see Pearce & Moran, 2012).

Remarkably, Andersen & Buneo (2002) highlighted that the simultaneous firing from as few as 10-15 neurons in the monkey parietal reach region are predictive of which of one, out of eight, trajectories an animal's reach will take, seconds before that movement is even initiated (for similar evidence in terms of voxels during fMRI when human's imagine and observe actions see Filimon, Rieth, Sereno & Cottrell, 2015). Accordingly, preparatory activity in these motor-related regions has since been shown to code various movement parameters like grip-type (Baumann et al., 2009; Fluet et al., 2010; Townsend et al., 2011; Schaffelhofer, Agudelo-Toro & Scherberger, 2015; Schaffelhofer & Scherberger, 2016; Kaufman, Churchland, Ryu & Shenoy, 2014; Michaels, Dann, Intveld & Scherberger, 2018) or wrist orientation (Fattori, Breveglieri, Marzocchi, Filippini, Bosco & Galletti, 2009) and has even been causally linked to reaction times (Churchland et al., 2006; Afshar et al., 2011; Snyder, Batista & Andersen, 1998; Michaels et al., 2015; Churchland & Shenoy, 2007; Gerits et al., 2011), implying that this activity functionally contributes to motor control.

Humans also exhibit preparatory activity prior to movement in regions across bilateral sensorimotor cortex when performing delayed instruction paradigms related to reaching, pointing, looking and/or grasping (e.g. Astafiev et al., 2003; Connolly, Andersen & Goodale, 2003; Tosoni, Galati, Romani & Corbetta, 2008). However, the information that is represented in these regions of the human or macaque brain is contested. Some theories describe how preparatory activity may represent a subthreshold activation or an initial state (e.g., Cisek, 2006) such that efficient movement generation can occur once the action is actually cued (for review see Churchland, Cunningham, Kaufman, Ryu & Shenoy, 2010). Alternatively, this activity may reflect goal processing more abstractly where it is linked to the intentions and action outcomes that occur beyond a set of specified movement kinematics (e.g., Grafton & Hamilton, 2007). Evidence for both views can be drawn from univariate fMRI analyses during instructed delay paradigms. For example, preparatory activity shows some topographical relationship to the sensory stimulation that is linked to the upcoming movement (e.g., reaching and saccading activates distinct parts of the Intraparietal Sulcus [IPS]; Kawashima et al., 1996) suggesting subthreshold motor activation. Yet much of parieto-frontal cortex is also found to be active regardless of which effector is used (e.g., hand or eye), instead suggesting that this activity reflects a higher-level goal, beyond a particular set of kinematics (Beurze, de Lange, Toni & Medendorp, 2009; Hagler, Riecke & Sereno, 2007).

Crucially, when these delayed instruction paradigms with humans have been paired with recently developed fMRI analytic techniques, particularly Multivariate Pattern Analysis (MVPA), richer conclusions can be drawn about what is represented in this preparatory activity (for review see Gallivan & Culham, 2015). Like conventional MVPA classification designs (e.g., Haxby et al., 2001; Kamitani & Tong, 2005; Kriegeskorte et al., 2008; Harrison & Tong, 2009) a test is performed to assess whether a class of conditions in the elicited spatial patterns of fMRI signals can be ‘decoded’ from a given Region of Interest (ROI). But by performing this test using neural activity acquired during a pre-movement delay, it is possible to predict upcoming behaviours, as is normally the case for monkey neurophysiological experiments.

In a number of these studies, the left ventral and dorsal parts of the premotor cortex (PMd; PMv), and/or portions of the IPS (throughout the posterior, medial and anterior IPS; pIPS; mIPS; aIPS) are commonly found to display pre-movement activity patterns that represent distinct qualities of upcoming limb movements, including their direction (Gallivan, McLean, Smith & Culham, 2011; Gallivan, McLean, Flanagan & Culham, 2013; Gallivan, Johnsrude & Flanagan, 2016; Fabbri et al., 2016), grip aperture size (Gallivan, McLean, Valyear, Pettypiece & Culham, 2011), the hand used (Gallivan, McLean, Flanagan & Culham, 2013) or whether a grasping or reaching action is performed (Gallivan, McLean, Flanagan & Culham, 2013). Additionally, preparatory codes for movement intentions have been identified in left PMd, SPL and/or IPS as shown by tasks that either decouple precise kinematics from the goal of a movement (e.g., Krasovsky, Gilron, Yeshurun & Mukamel, 2014; Gertz, Lingnau & Fiehler, 2017) or simply involve imagined actions that require no movement at all (Pilgramm, de Haas, Helm, Zentgraf, Stark, Munzert & Kruger, 2016).

For more complex object directed tasks such as those involving tools, both sensorimotor and occipitotemporal cortex are also found to activate during motor preparation (Johnson-Frey, Newman-Norlund & Grafton, 2005; Fridman et al., 2006; Brandi et al. 2014; Gallivan, Chapman, McLean, Flanagan & Culham, 2013). Across various designs (e.g., instructed delay paradigms or go/no-go paradigms), actions related to tools, regardless of whether their uses are pantomimed (Johnson-Frey, Newman-Norlund & Grafton, 2005; Fridman et al., 2006; Bohlhalter et al., 2009;

Kroliczak & Frey, 2009) or actually executed with a tool in hand (Brandi et al. 2014), lead to both planning and execution related activity within major portions of the left lateralised tool network including the posterior temporal cortex (e.g., Superior Temporal [STG], Middle Temporal [MTG] and fusiform gyri), inferior frontal cortex (e.g., ventral premotor [PMv] cortex and Inferior Frontal Grus [IFG]) as well as the parietal cortex (e.g., anterior Supramarginal Gyrus [aSMG] and IPS).

To my knowledge, only Gallivan, McLean, Valyear & Culham (2013) have combined an MVPA approach with a delayed movement paradigm involving a real tool interaction. This study found that the type of action (i.e., reaching versus grasping) with a pair of tongs, but not if simply performed with the hand, could be decoded from preparatory activity in the left SMG and pMTG. Not only was this pMTG region defined based on its responses to viewing 2D pictures of tools (see *Seeing 2D tools to using 3D tools:* section 1.3.1.), but this pattern of findings across the ventro-dorsal stream areas (e.g., Binkofski & Buxbaum, 2013; see *Two action systems model:* section 1.4.) was unique from other areas that decoded between action types either when using the hand only (i.e., left Superior Occipito-Temporal Cortex; SPOC and Extrastriate Body Area; EBA) or regardless of the effector used (i.e., left aIPS, PMd, PMv, pIPS, mIPS).

However, to what extent might representations in the SMG and pMTG reflect well learnt aspects of tool use? Tools are strongly linked to knowledge-based action routines (e.g., Mahon, Milleville, Negri, Rumiati, Caramazza & Martin, 2007; Mruczek, von Loga & Kastner, 2013; see *What is a tool?:* section 1.2.) where they are associated with typical movements (e.g., grasping the tool by its handle). Based on the findings from Gallivan et al., (2013), it may be predicted that preparatory activity patterns in the left SMG and pMTG would also carry information about the typicality of an action with a tool (e.g., grasping a knife by its handle versus its blade).

Recent evidence shows that parts of the tool processing network (e.g., Garcea & Mahon, 2014; see *A tool processing network:* section 1.6.) are activated (Przybylski & Kroliczak, 2017) when planning to pantomime functional tool grasping, relative to non-tools, and that this can also be decoded from activity patterns throughout the left ventral Lateral Occipital Temporal Cortex and posterior parietal cortex (Buchwald, Przybylski & Kroliczak, 2018). Similarly, recent TMS evidence also shows that interference to the SMG during action planning specifically affects the ability to point a cursor toward the handle of a tool (Potok, Maskiewicz, Kroliczak & Marangon, 2019). Nevertheless, further work is needed to clarify whether conclusions from pantomiming tool-related actions are generalisable to real tool actions (see *Imagining or pantomiming tool-use as a proxy for real action:* section 1.6.1.).

Other MVPA decoding studies hint that object-related actions may be represented in the preparatory activity of the LOTC. First, in a careful grasp-to-lift design, the bilateral area LO and the posterior Fusiform sulcus (pFs), areas which together make up the LOTC (Grill-Spector & Malach, 2004; Grill-Spector, Kushnir, Edelman, Itzchak & Malach, 1999; Malach et al., 1995), have been shown to both contain preparatory activity patterns that can discriminate between heavy and light objects regardless of whether this is based on knowledge that is learned extensively (i.e., cued by texture such that metal is heavier than wood) or only recently (i.e., cued by texture with the opposite mapping but was learnt in a pre-exposure phase; Gallivan, Cant, Goodale & Flanagan, 2014). Similarly, Gallivan, Johnsrude & Flanagan (2016) have shown that preparatory activity within the left LO and right pFs can discriminate between actions within a sequence of object-directed movements (i.e., when having to grasp an object to be held versus placed in a cup on the left/right side). Together, these findings suggest that occipitotemporal circuits are also engaged when having to transform object-related information into complex goal directed movements (Lingnau & Downing, 2015; also see Wurm, Ariani, Greenlee & Lingnau, 2016).

Atleast three reasons highlight the importance of a slow-event related fMRI design investigating pre-movement representations about the typicality of a tool-related action. First, preparing to pantomime tool-use has been shown to preferentially activate several regions (i.e., the left Superior Temporal Gyrus [Johnson-Frey et al., 2005] or caudal Ventral Premotor Cortex [Fridman et al., 2006; but see Kroliczak & Frey, 2009]) but, during real tool-use, no region showed such plan-specific activity (Brandi et al., 2014), indicating that the initial effects could be related to the pantomiming nature of the task (for evidence of STG and PMv activity during hand/tool pantomiming see Lausberg, Kazzaer, Heekeren & Wartenburger, 2015; Krolickzak, Cavina-Pratesi, Goodman & Culham, 2007). Second, movements of large masses (e.g., the shoulder or upper arm) during fMRI can induce artifacts in participant's data (Culham, 2006) but, crucially, they can be avoided if temporally decoupling the preparatory portion of the BOLD signal time course from a reach-and-grasp action (Culham, Danckert, De Souza, Gati, Menon & Goodale, 2003). Thirdly, this approach allows neural processing to be directly linked to intentions or underlying motor representations, rather than simply related to movement kinematics (e.g., Nicholson, Roser & Bach, 2017), suggesting a role of higher-level goal processing in tool-use (e.g., Norman & Shallice, 1986; Hommel, Musseler, Aschersleben & Prinz, 2001; Botvinick, Buxbaum, Bylsma & Jax, 2009; Osiurak, Jarry & Le Gall, 2010; Badets & Osiurak, 2015; Buxbaum, 2017).

Here we were primarily interested in whether preparatory brain activity was sensitive to the learnt aspects of tool-use. The fMRI paradigm reported in Project 1 (Chapter 2) was adapted into a slow-event related fMRI design that included an instructed delay period so that MVPA classification could assess whether preparatory activity patterns predicted the *typicality* of an upcoming tool grasp - as before, this entailed decoding between tool grasps that were considered to be *typical* (i.e., by the tool's handle) versus *atypical* (i.e., by the tool' head) for subsequent use. Again, as a control, we also assessed whether decoding was possible for the *grasp direction* of non-tool grasping - this entailed decoding between non-tool grasps that were located on their *right* versus *left* sides (i.e., the sides of the non-tools that corresponded to the typical and atypical grasping of tools, respectively). The same reasoning was made for the analysis as before: if a region contained representations that were tuned to the learnt aspects of tool-use, then decoding accuracies for typicality were predicted to be significantly higher than (1) chance and (2) the decoding accuracy obtained from the same ROI when discriminating between grasp direction.

This was carried out using the same ROI (i.e., an independent visual localiser design) and searchlight approach as in Project 1 (see Chapter 2 and *Methods*: section 4.2). Ventral visual (e.g., pFs, LOTC), ventro-dorsal stream (e.g., pMTG, SMG) as well as premotor cortex (e.g., PMv) areas were predicted to show the above described pattern of findings because of previous evidence that preparatory activity in them carries information about object- or tool- directed actions (e.g., Gallivan et al., 2013; Gallivan et al., 2014; Gallivan et al., 2016). This may have also been particularly evident in hand-selective parts of the LOTC and IPS (i.e., LOTC-Hand and IPS-Hand) based on the findings that these areas, but not overlapping tool-selective areas, coded for typicality in Project 1 (see *Typicality versus grasp direction decoding results*: section 2.3.1.).

As a secondary objective, there was an interest whether typicality could be decoded during the execution of the movement too (i.e., during the go phase), with results being predicted to converge with those reported in Project 1 (i.e., representations of typicality in the LOTC-Hand and IPS-Hand ROIs [see Fig. 2.5A.] as well as throughout left anterior temporal cortex and right temporo-parietal cortex [see Fig. 2.5B.]). Additionally, the design here allowed neural activity during a preview phase to be isolated where participants passively viewed the different objects (i.e., before they were instructed how to act), much like has been investigated in previous studies where participants view 2D (e.g., Chen et al., 2017) or 3D tools (Macdonald & Culham, 2015). Thus, the ventral visual (e.g., LOTC, pFs) and ventro-dorsal stream (e.g., SMG, pMTG) regions implicated in those studies were expected to show evidence of coding for object category (i.e., tool versus non-tool) and tool identity (i.e., knife versus pizzacutter) during this preview phase.

4.2. Method

4.2.1. Participants

A total of twenty-three right-handed (Edinburgh Handedness Questionnaire; Oldfield, 1971) healthy volunteers were recruited from UEA’s paid participant panel. Three participants were excluded due to excessive head motion during scan sessions and a further three were excluded due to technical errors during data acquisition (see *Data preprocessing:* Section 4.2.6.) leaving a total sample of seventeen participants (9 males, 19-35 years of age; mean [standard deviation] =

24.4 [3.5]). Nine of the participants were naïve to the purpose of the study, while the remaining eight participants had completed the previous fMRI experiment and/or were part of the research team. All had normal or corrected-to-normal vision, no history of motor, psychiatric or neurological disorders and gave informed consent in accordance with the ethical committee at the UEA and National Health Service (NHS). Volunteers received £40 in compensation for their time.

4.2.2. Stimulus & apparatus

Two categories of 3D stimuli were presented during this experiment: tools and non-tools. These were comprised of the knife and pizza-cutter tools and their paired non-tools described in Project 1 (see Fig. 2.1A. and *Stimulus & apparatus:* section 2.2.2.). The decision to remove one stimulus pair (i.e., the spoon tool/non-tool) was based on the constraint to present all exemplars an equal amount of times within a run. Therefore, this decision was made to minimise individual run lengths (i.e., repeating three, rather than two, exemplars per run would have exceeded 10 minutes) whilst maximising the number of condition repetitions (i.e., four conditions repetitions could be achieved by repeating each exemplar once). The decision to exclude the spoon specifically was data-driven: an exploratory univariate analysis from the previous fMRI study identified that the pizzacutter and knife exemplars together revealed the largest cluster of activity selective for typical tool grasping [3*(Tool Typical) > (Tool Atypical + Non-tools Atypical + Non-tools Typical)] in the temporal lobe (see Appendice B). The custom-built turntable apparatus, selected 3D printed models and associated equipment (i.e., headphones, video cameras, Light-Emitting Diodes serving as fixation and illuminators) were setup as in Project 1.

4.2.3. fMRI real action paradigm

To extract the sustained planning response from the visual and motor execution responses, a slow-event related fMRI paradigm was used with the same epoch lengths as in Gallivan, McLean, Smith & Culham (2011). Each trial (34s) consisted of three distinct phases in the following order: ‘preview’, ‘plan’ and ‘go’ (Fig. 4.1.). During the preview phase (6s) the workspace was illuminated revealing the object. The plan phase (12s) was marked by an auditory ‘Left’ or ‘Right’ verbal cue (lasting 0.5s) instructing which side of the object was to be precision grasped in this trial. There were no visual differences between the preview and plan phase, but only during the plan phase did participants have the necessary information to prepare the upcoming movement with the right hand. The go phase (2s) began with a beep sound (lasting 0.5s) which cued the planned movement to be immediately executed with the right hand before returning to the home position. Afterwards the workspace became dark as the illuminator turned off (Inter-Trial Interval; 14s) where the BOLD response was allowed to return to baseline and the next stimulus could be prepared. Actions were completed in closed-loop (i.e., with full visual feedback; Gallivan, McLean, Valyear & Culham, 2013; Gallivan, Chapman, McLean, Flanagan & Culham, 2013; Gallivan, McLean, Valyear, Pettypiece & Culham, 2011; Gallivan, McLean, Smith & Culham, 2011) and, as before, upper fixation was maintained throughout the experiment (measurements to fixation were not recorded).

Functional runs included 16 trials with the two exemplars from both object categories being grasped on the left and right sides twice (i.e., four reps per main condition: tool typical, tool atypical, non-tool right and non-tool left). Except for one participant who completed six runs, all volunteers completed eight runs totalling an average of 128 trials and 32 repetitions per condition. Trials were pseudorandomised so that conditions were never repeated (two-back) and preceded an equal amount of times by other conditions. Including the start and end baseline fixation periods (14s), functional scans lasted 576 seconds (9:36 minutes), making the length of a single session ~1 hour 45 minutes. Before the fMRI experiment, participants were familiarised with the setup and practiced grasping each side of every exemplar in a separate lab session (30 minutes).

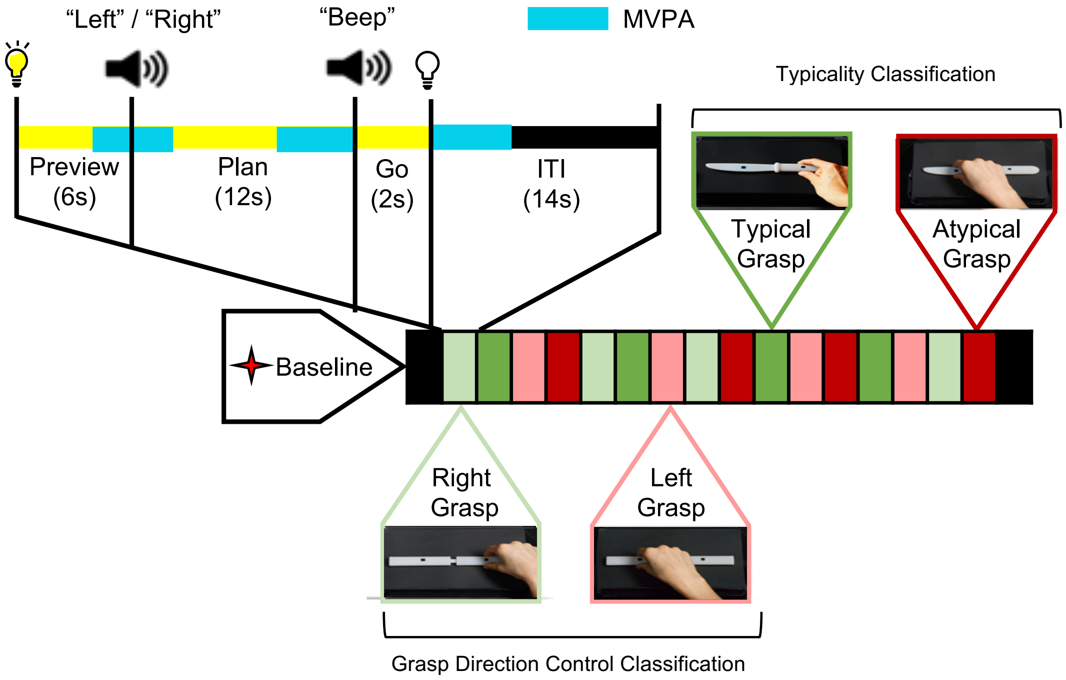

Fig. 4.1. Timing of the fMRI slow event design. A schematic of a single trial is provided (top left). A preview phase begins as the object is first illuminated. A plan phase begins as the auditory instruction is provided about which movement should later be carried out. A go phase begins as another auditory cue signals the movement to be executed in closed loop conditions (i.e., the workspace remains illuminated). The volumes where MVPA was performed (blue blocks) consisted of those during each of the preview, plan and go phases independently. As in Project 1, a classifier received input from the rightward and leftward grasping blocks for both the tool and

non-tools objects independently. For the tools blocks these rightward and leftward movements corresponded to grasping the tool in ways that were typical (i.e., by the handle) and atypical (i.e., by the head) for use, respectively.

4.2.4. fMRI visual localiser paradigm

Following the real action paradigm session, all participants except one (due to recruitment difficulty), returned for a separate Bodies, Objects, Hands and Tools (BOTH) fMRI visual localiser session (Bracci, Iettswaart, Peelen & Cavina-Pratesi, 2010, Bracci, Cavina-Pratesi, Ietswaart, Caramazza & Peelen 2012; Bracci, Cavina-Pratesi, Connolly & Ietswaart, 2016) with the same protocol described in Project 1 (see Fig. 2.2. and *fMRI visual localiser paradigm:* section 2.2.4.). The one participant that did not attend the localiser scans was included in the searchlight analysis only.

4.2.5 Data acquisition

The data acquisition parameters were identical to those described in Project 1 (see *Data acquisition:* section 2.2.5.) except that the amount of T2 scanning volumes for the fMRI grasping paradigm was increased to 288 to account for the increased length of the experimental runs.

4.2.6. Data preprocessing

To ensure that participants performed the grasping paradigm correctly and that they maintained peripheral eye fixation, the recorded videos of the right eye (available of 12 participants due to technical issues) and workspace (available for all participants) were screened. A total of 10 errors were identified after monitoring both hand and eye-related errors which equated to >1% of trials. These types of errors included reaching during the plan phase (2 trials, 2 participants), fumbling with the object (2 trials, 2 participants), reaching in the wrong direction (2 trials, 2 participants) and downward eye saccades (4 trials, 2 participants). A one-way Repeated Measures (RM) ANOVA with 8 groups (i.e., the two exemplars per object category across both grasping conditions) showed that these were equally distributed amongst all trial types when the percentage of errors were compared within an effector (i.e., hand and eye separately) and when collapsed across (all *p*'s > 0.43).

The same preprocessing pipelines for the grasping and visual localiser paradigms were used with the same analysis software as reported in Project 1 (adjusted for the number of volumes; see *Data preprocessing:* Section 2.2.6.). Due to excessive head movements (i.e., x, y & z translation and rotation spikes exceeded 1mm and 1° rotation, respectively), three of the total 23 participants were excluded from the analysis, as well as an additional nine runs (i.e., 6% of runs) from the remaining 20 participants. Additionally, another three of the 20 participants were excluded from further analysis due to poor automated aligning of the functional datasets.

4.2.7. ROI definitions

The same contrast, anatomical guidelines and definitions were used from the previous experiment (see *ROI definitions*: section 2.2.7.) to locate visually defined ROIs in the 16 participants who performed the visual localiser (see Table 4.1.).

Table 4.1. Mean sizes and Talairach coordinates of the ROIs defined from the BOTH visual localiser. Acronyms: SD = Standard deviation.

ROI	Number of Subjects	Mean voxel size (SEM)	Mean peak coordinates (SD)		
			X	Y	Z
EVC	16	125 (7)	-18 (5)	-90 (5)	-11 (5)
LOTC-Object	16	147 (11)	-42 (5)	-76 (5)	-5 (5)
LOTC-Body	13	63 (11)	-46 (2)	-73 (6)	3 (5)
LOTC-Hand	14	104 (9)	-48 (3)	-70 (4)	-2 (6)
LOTC-Tool	16	84 (11)	-49 (5)	-70 (5)	-1 (6)
pMTG	12	102 (16)	-45 (4)	-57 (4)	2 (5)
pFs	16	115 (10)	-38 (6)	-52 (6)	-17 (5)
SMG	14	66 (13)	-52 (6)	-29 (5)	29 (7)
IPS-Hand	15	108 (9)	-37 (6)	-43 (6)	-42 (5)
IPS-Tool	15	88 (12)	-38 (5)	-40 (6)	42 (6)
PMv	12	54 (11)	-46 (7)	-1 (4)	29 (6)
PMd	13	70 (12)	-28 (5)	-12 (5)	52 (4)

4.2.8. ROI MVPA

To prepare the data for spatial pattern classification, the percentage signal change was computed from a windowed average of the time course at a time point of interest (e.g., Preview, Plan or Go) with respect to a windowed average of the time course at a common baseline for each voxel in the ROI (see Fig. 4.2.). The epochs of interest matched those used by Gallivan, McLean, Smith & Culham (2011). Specifically, the baseline window was defined as the average of volumes - 1 and 0 with respect to the start of the trial (i.e., before initiation of the trial). For the Preview phase, we extracted the mean of volumes 3 and 4 (i.e., time points corresponding to the peak of the visual transient response). For the plan phase, we extracted the average of volumes 8 and 9 (i.e., time points corresponding to the sustained activity of a planning response). Finally, the go phase was computed from the mean of volumes 12 and 13 (i.e., time points corresponding to the peak of the motor response). Training and test data, this time in terms of the percentage signal change values, were again normalised using the same procedure as in Project 1 (see *ROI MVPA:* section 2.2.8).

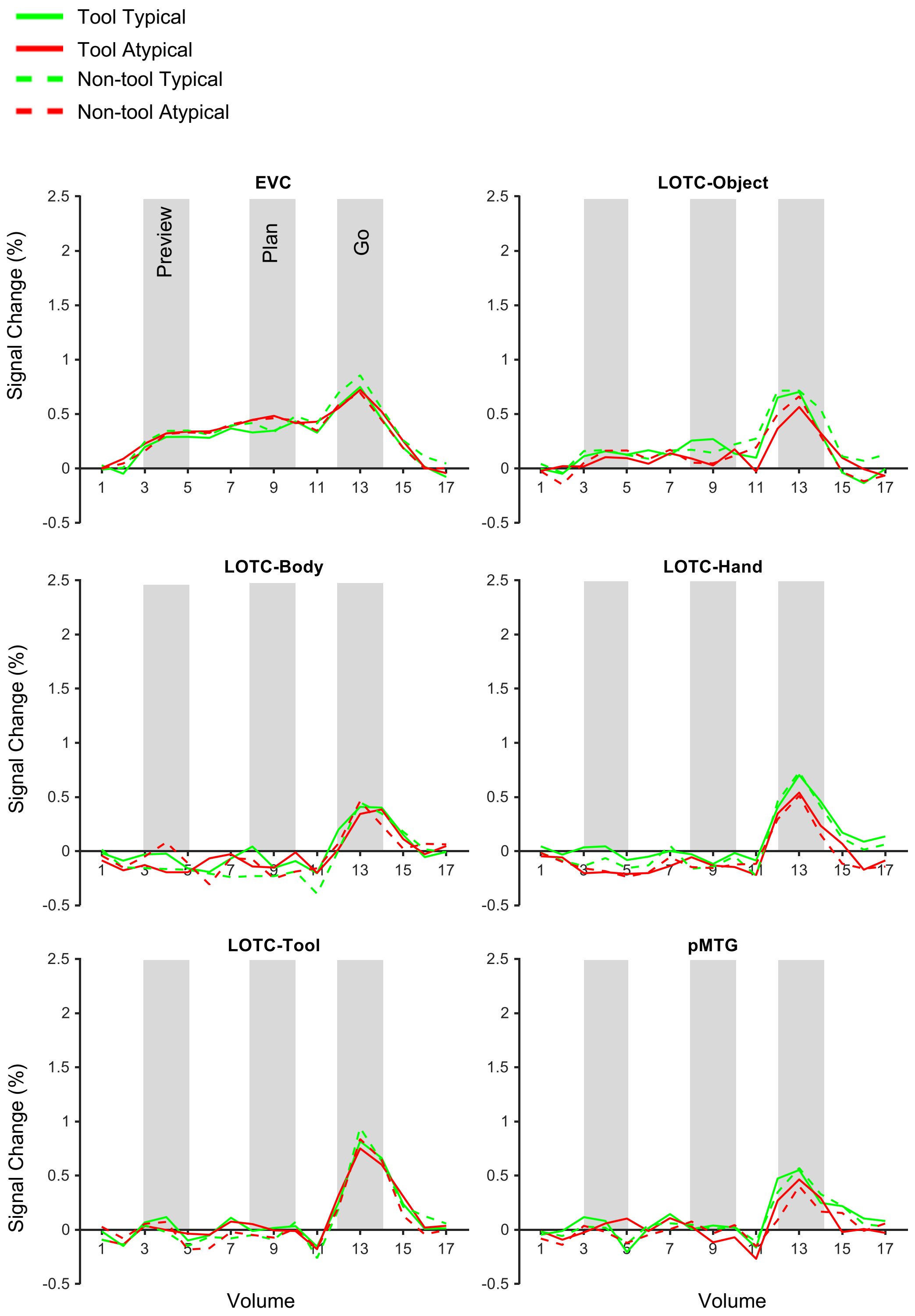

Fig. 4.2. Percentage signal change in localiser ROIs for the main conditions of interest. Grey bars represent the preview, plan and go epochs when MVPA was implemented (also see overleaf).

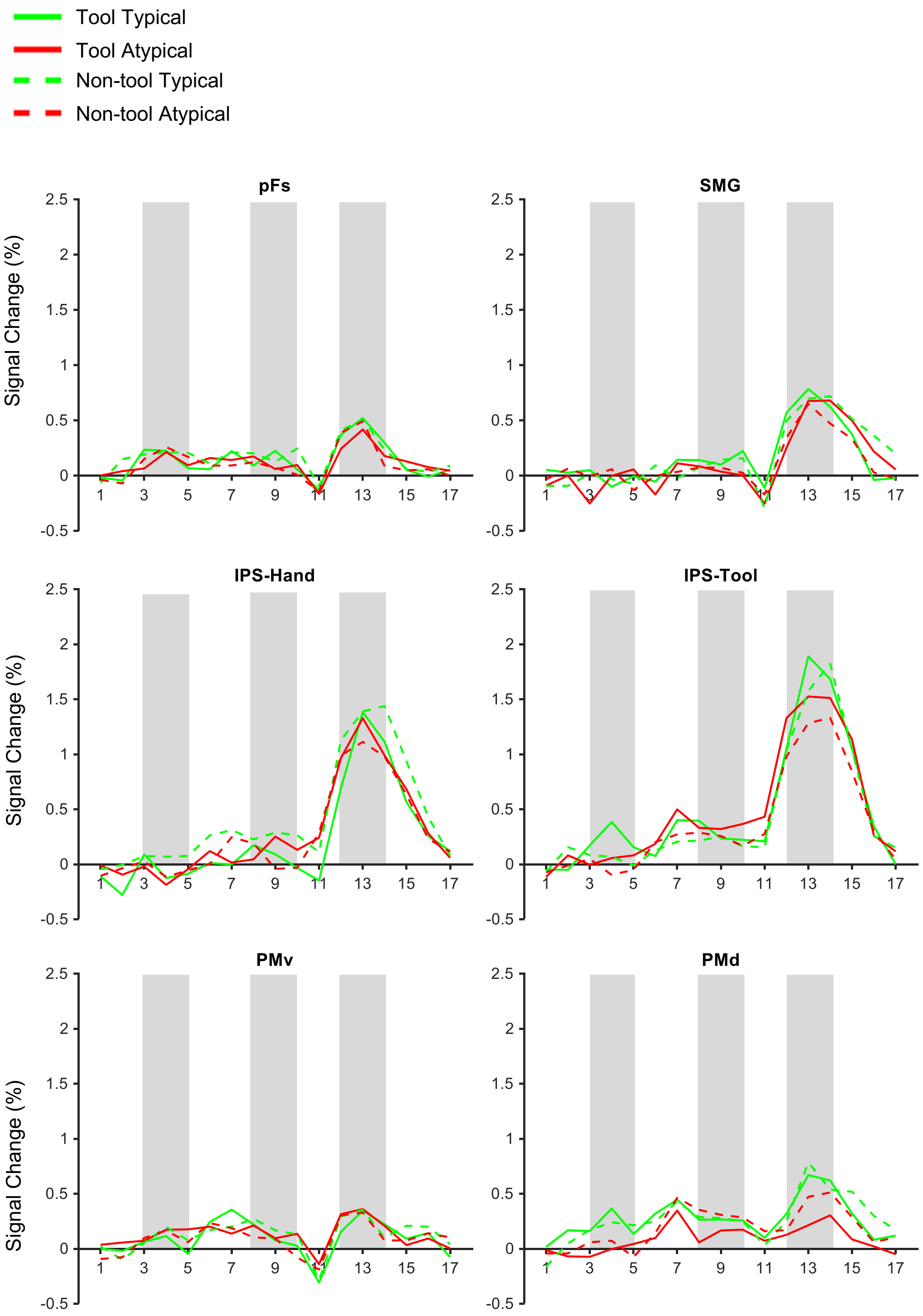

Fig. 4.2. (Continued).

4.2.9. Classification procedure

For every phase (i.e., preview, plan and go) classifications of typicality, reach direction, object size, object category and tool identity were performed in a similar way to those described in Project 1 (see *Classification procedure:* section 4.2.9.). But in this case always using pairwise discrimination because the third spoon tool/non-tool exemplars were not used in this experiment (see Fig. 4.3.). As a result of omitting this stimulus the classification of tool function was also not possible here (i.e., both the knife and pizzacutter tools are strongly associated with the same cutting function).

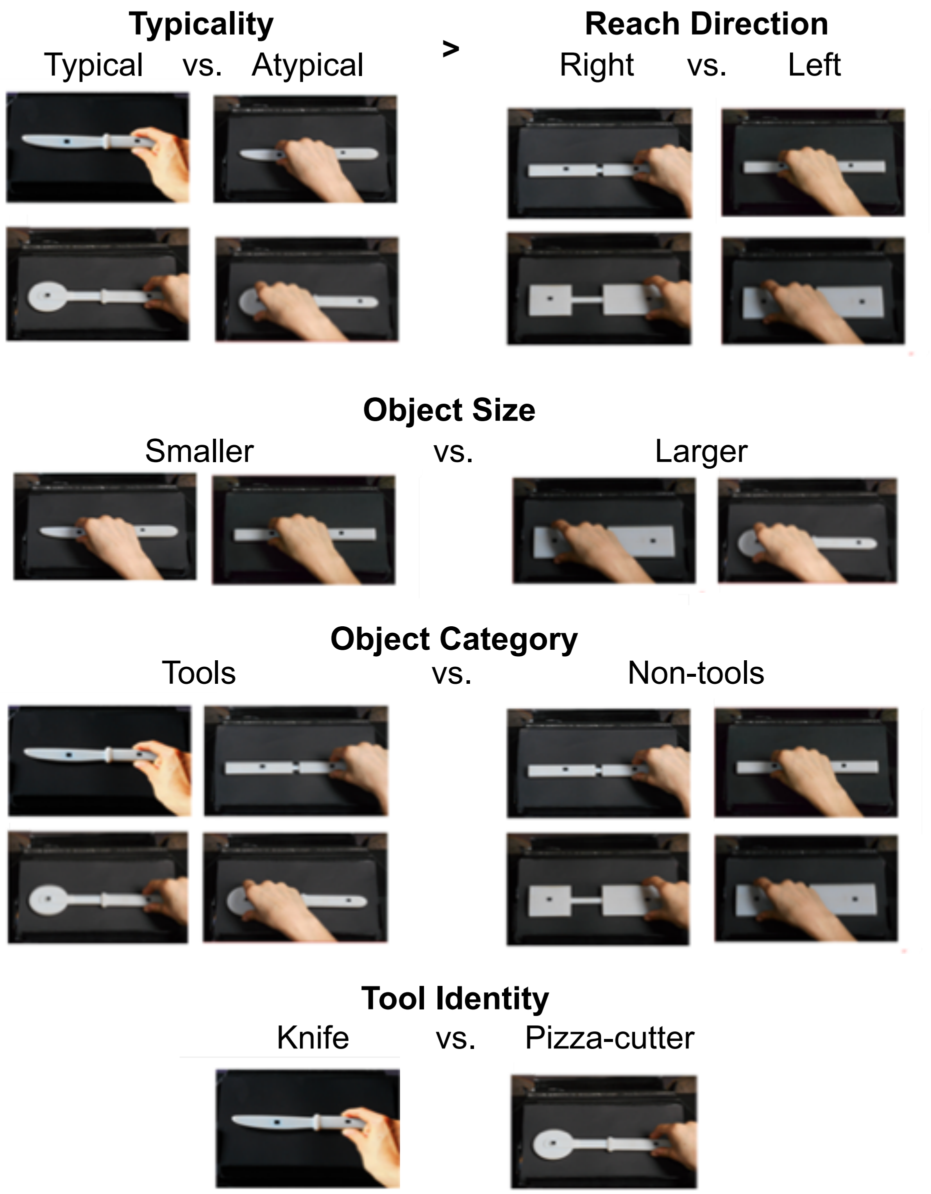

Fig. 4.3. Classification labels for all analyses. As in Project 1, the primary classification of *typicality* and its associated control classification of *grasp direction* (top rows) involved performing independent pairwise classifications of *typical* versus *atypical* for the tool conditions and *right* versus *left* for the non-tool conditions, respectively. The resulting decoding accuracies attained by a given ROI for each of these classifications would then be compared with a paired samples t-test if significant decoding was observed for typicality, but not grasp direction. *Object size* (upper middle rows) classification was a control analysis to ensure typicality

decoding could not be achieved purely because of changes in object size (see *Classification procedure:* section 2.2.9) and was performed using a pairwise discrimination of objects that were *smaller* versus *larger,* regardless of object category. *Object category* (lower middle rows) classification was performed using a pairwise discrimination of objects that were *tools* versus *non-tools*. *Tool identity* (bottom rows) classification was performed using a pairwise discrimination of the *knife* versus *pizzacutter*. Grasp direction for the classifications of object size, object category and tool identity were controlled in the same way as described in Project 1 (see *Classification procedure:* section 2.2.9.).

All statistical tests of decoding accuracy were compared using one-tailed tests as in Project 1 (see Section 2.2.9.). This involved either comparing decoding accuracy against chance (i.e., one sample t-tests) or, in the case of the primary analysis, comparing decoding accuracy between the typicality and grasp direction classifications. The problem of multiple comparisons was overcome using a False Discovery Rate (FDR) correction of $q \leq 0.05$ for all t-tests performed for each ROI per classification and per phase (i.e., preview, plan and go).

4.2.10. Searchlight MVPA

The same classification procedures described in the previous section were used for the searchlight analysis for 17 subjects (i.e., including the participant who did not participate in the BOTH visual localiser). Searchlight MVPA was performed in the same way described during Project 1 (see *Searchlight MVPA:* section 2.2.10.) during the preview, plan and go phases independently.

4.3. Results

All time-locked results from the left hemisphere ROI MVPA are displayed in Fig. 4.5. separated by phase (only results surviving FDR correction are reported in this section). All findings from searchlight MVPA are displayed in Fig. 4.6. with their related cluster sizes reported in Table 4.2.

4.3.1. Typicality & grasp direction decoding

During the plan phase, only the decoding accuracy from the left PMv was found to be significantly higher than chance for the classification of grasp direction (55%, $t(11) = 3.5$, $p < 0.001$, $d = 1.85$). During the go phase, left EVC was the only ROI to demonstrate significantly higher than chance decoding of typicality (59%, $t(15) = 4.16$, $p < 0.001$, $d = 2$ [chance 50%]) and a paired samples t-test showed that this decoding accuracy was also significantly higher for typicality than for grasp direction ($t(15) = 2.38$, $p < 0.016$, $d = 0.57$). Differently, grasp direction was found to be discriminated significantly above chance from the left LOTC-Hand (57%, $t(13) = 3.17$, $p < 0.001$, $d = 1.65$ [chance 50%]) and pFs (58%, $t(15) = 5.66$, $p < 0.001$, $d = 2.83$). As expected, no significant decoding was found during the preview phase after controlling for multiple comparisons (all p's > 0.02) since participants were not yet aware of the direction they would be grasping toward.

For the searchlight, no significant differences were found between decoding accuracies of typicality and grasp direction during the plan phase. For the go phase, however, decoding accuracies were found to be significantly higher for typicality than grasp direction in the vicinity of the cingulate gyrus. The remaining clusters displayed the opposite pattern where accuracy was higher for grasp direction than typicality, which were located in the left PMv, IFG and crus I of the cerebellum, as well as the layer VI of the right cerebellum and within the vicinity of the medial Frontal gyrus (MeFG).

4.3.2. Object size decoding

Activity patterns from no ROIs were found to discriminate object size significantly higher than chance during any of the preview, plan or go phases (all *p*'s > 0.08). The searchlight revealed a cluster in the left insula and middle temporal gyrus that decoded object size significantly higher than chance during the plan phase. During the go phase, a cluster was also identified in the left PMd by the searchlight analysis.

4.3.2. Object category decoding

Activity patterns from no ROIs were found to discriminate object category significantly higher than chance (after controlling for multiple comparisons) during any of the preview, plan or go phases (all *p*'s > 0.047). The searchlight revealed clusters in the left EVC and MeFG that decoded object category significantly higher than chance during the plan phase.

4.3.2. Tool identity decoding

As was the case for the classifications of object size and object category, activity patterns from no ROIs were found to discriminate tool identity significantly higher than chance (after controlling for multiple comparisons) during the preview, plan or go phases (all *p*'s > 0.02). The searchlight revealed clusters decoding tool identity significantly higher than chance in the left Inferior Frontal Gyrus (IFG) and superior temporal gyrus (STG), as well as the right anterior Parahippocampal Gyrus (PHG) during the go phase. During the go and plan phase, overlapping clusters in the crus II of the right cerebellum was found to discriminate tool identity significantly higher than chance. Finally, during the preview phase, a cluster was found to decode tool identity significantly higher than chance in a posterior part of the left PMd.

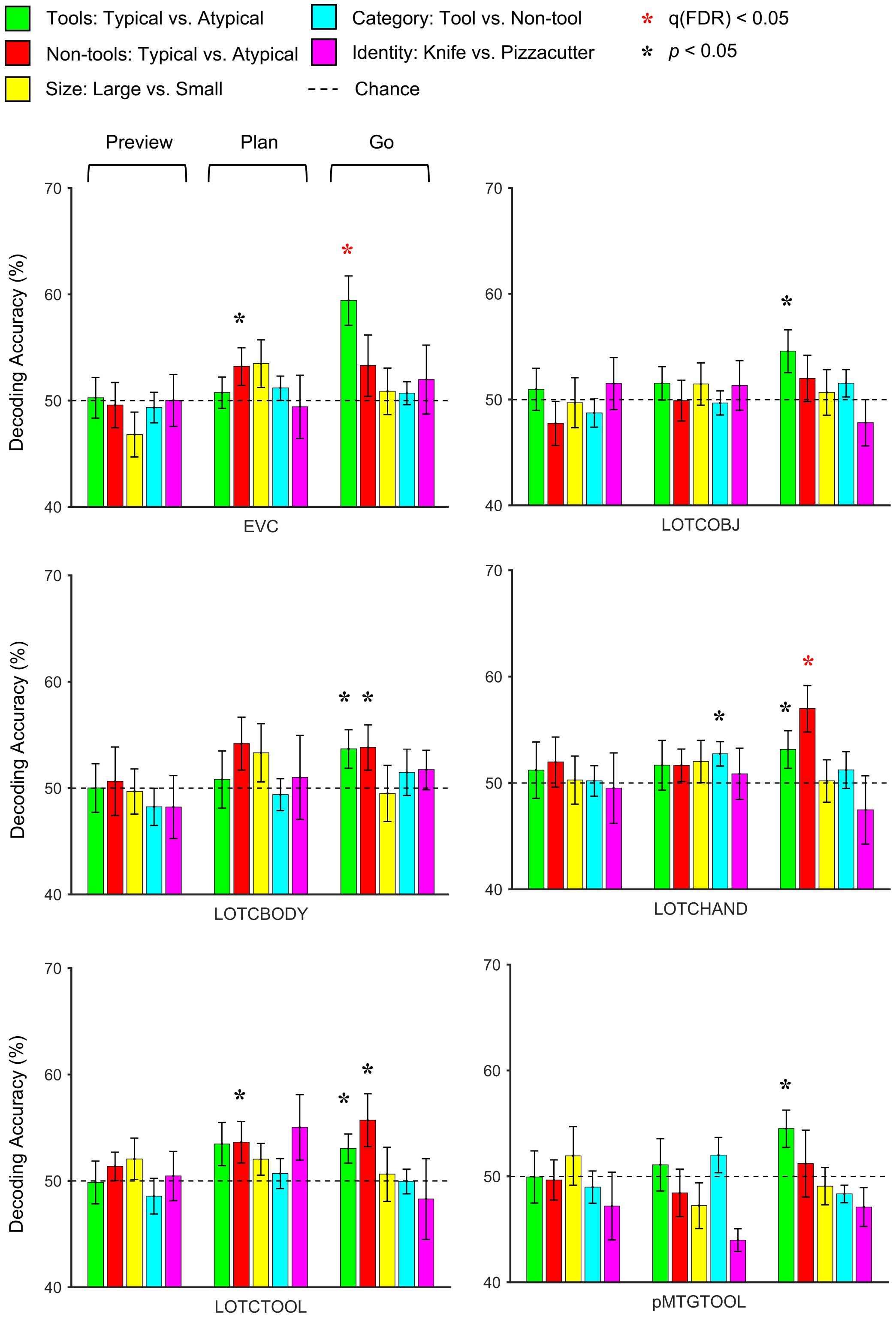

Fig. 4.4. ROI MVPA. Decoding accuracies in left hemisphere ROIs functionally defined from contrasts in an independent visual BOTH localiser. Errors bars represent SEM. (Also see overleaf).

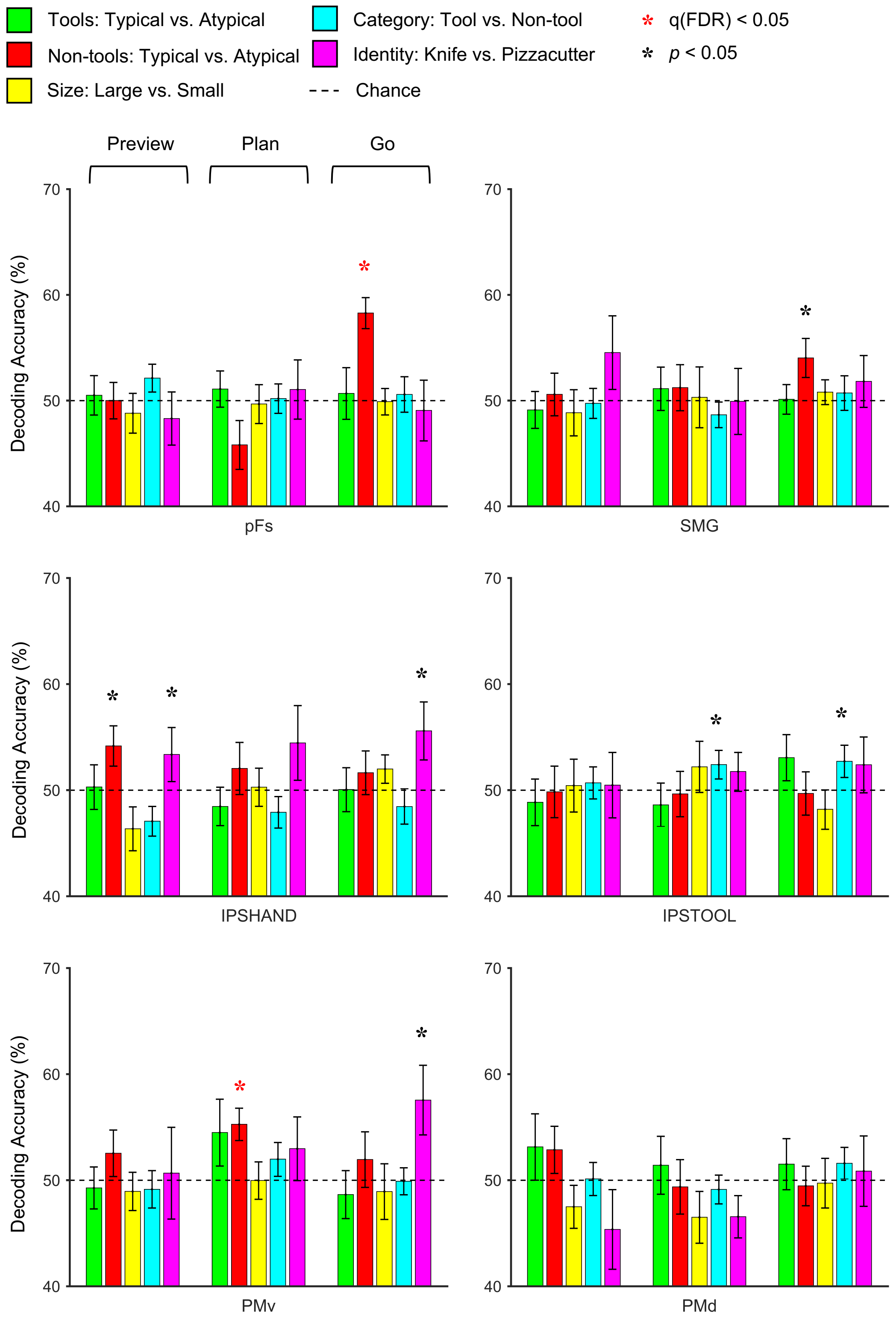

Fig. 4.4. (Continued).

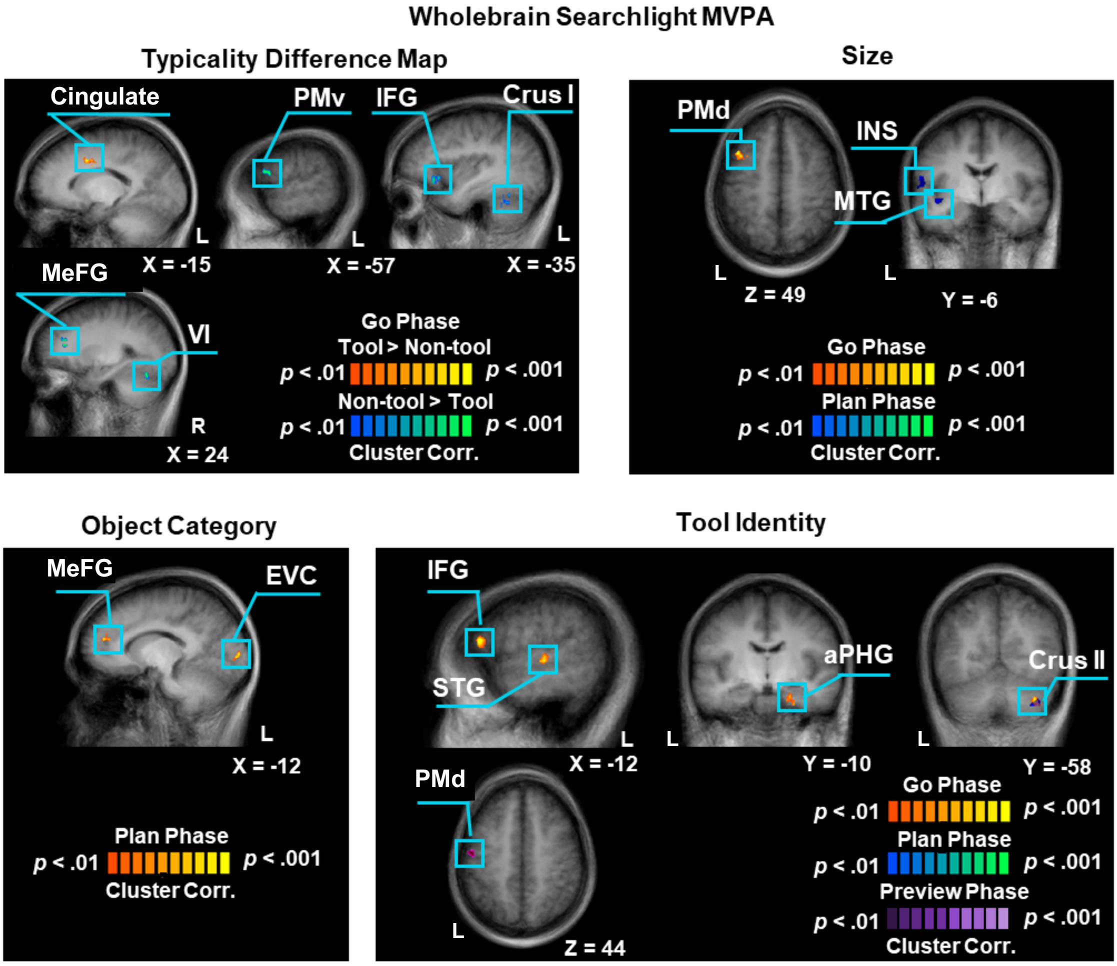

Fig. 4.5. Decoding accuracies from searchlight MVPA. The typicality difference map (top left) is derived from typicality and control grasp direction decoding accuracies that are acquired per voxel independently, where the values from the typicality map was subtracted from the grasp direction map (per participant) - the resulting maps are then tested against zero to reveal where decoding accuracies were significantly higher for tools than non-tools (see section 2.2.10). For the typicality different map decoding accuracies are plotted from the go phase where the red and blue colours represent the decoding accuracies that were significantly higher for typicality and grasp direction, respectively. For the object size classification (top right) the red and blue colours represent significant decoding for the go and plan phase respectively. For the object category classification (bottom left) the red colour

represents significant decoding in the plan phase. Finally, for the classification of tool identity (bottom right) the red, blue and purple colours represent significant decoding in the preview, plan and go phases, respectively.

Table 4.2. Searchlight cluster sizes, peak coordinates (Talairach) & statistical values.

Region of activation	Phase	Cluster voxel size	Peak coordinates			*t*	*p*
			X	Y	Z		
<u>*Typicality Difference Map*</u>							
Tools > Non-tools							
L-Cingulate	Go	236	-15	8	37	4.5	< 0.001
Non-tools > Tools							
L-PMv	Go	244	-57	12	19	-4.3	< 0.001
L-IFG	Go	301	-36	26	-5	-5.6	< 0.001
L-Cerebellar Crus I	Go	374	-33	-43	-32	-4.6	< 0.001
R-MeFG	Go	239	24	33	16	-4.4	< 0.001
R-Cerebellar Lobule VI	Go	300	24	-61	-20	-5.1	< 0.001
<u>*Size*</u>							
L-PMd	Go	258	-39	14	49	4.5	< 0.001
L-INS	Plan	493	-57	-10	16	5.2	< 0.001
L-MTL	Plan	243	-41	-4	-8	5.1	< 0.001
<u>*Object Category*</u>							
L-EVC	Plan	196	-12	-91	4	4.5	< 0.001
L-MeFG	Plan	207	-14	47	16	4.7	< 0.001
<u>*Tool Identity*</u>							
L-IFG	Go	356	-54	26	16	5.8	< 0.001
L-STG	Go	580	-57	-19	1	5.7	< 0.001

R-aPHG	Go	288	18	-13	-20	4.2	< 0.001
R-Cerebellar Crus II	Go	451	36	-52	-38	5.1	< 0.001
R-Cerebellar Crus II	Plan	276	36	-58	-41	4	< 0.001
L-posterior PMd	Prev- iew	190	-51	-10	43	4.5	< 0.001

4.4. Discussion

In this experiment, we were primarily interested in identifying which brain regions coded typicality of tool grasping during a pre-movement phase (i.e., the plan phase), that is, before any action was actually performed. To our surprise, both ROI and searchlight MVPA classification failed to identify a single cortical region whose preparatory activity could be used to predict the typicality of an upcoming action. Findings from MVPA classification during the movement execution (i.e., the go phase) were also surprising since only the left EVC was found to discriminate between typical and atypical tool grasping. Activity patterns from a few regions could, however, be used to discriminate between object category and tool identity when participants passively viewed stimuli at the beginning of a trial (i.e., the preview phase).

4.4.1. Decoding from preparatory epochs

Previously, Gallivan et al., (2013) showed that preparatory activity patterns from canonical ventro-dorsal stream areas (i.e., the pMTG and SMG) can be used to predict the type of upcoming action (i.e., reach versus grasp) performed with a tool. Here, preparatory activity patterns from ROIs in these areas defined based on their selectivity to pictures of tools, were not found to discriminate between typical and atypical tool grasping (Fig. 4.4.). In fact, pre-movement activity patterns could not be used to decode typicality from any ROIs, even though others (e.g., Gallivan, Cant, Goodale & Flanagan, 2014) have previously shown that activity patterns from the ventral visual stream (e.g., left LOTC, pFs) can be used to predict learnt properties about a to be manipulated object (e.g., its weight). Likewise, the type of hand action which is directed at an object, such as whether they involve reaching versus grasping or the left versus right hand, are also known to be decodable from posterior parietal and premotor cortex (e.g., Gallivan, Chapman, McLean, Flanagan & Culham, 2013; Gallivan, McLean, Flanagan & Culham, 2013).

Even the searchlight analysis that covered all voxels found no evidence of a brain region that coded typicality during the plan phase (Fig. 4.5.). This said, the univariate analysis by Brandi et al., (2014) similarly found no area to selectively increase activity when planning to use a tool, relative to other actions that did not rely on stored knowledge about an object (e.g., moving a tool, or acting with non-tools). Taken together with Brandi et al.,'s (2014) results, it may be suggested that no region is specifically relevant to the planning of tool-related actions and, perhaps, previous plan-specific activity during tool pantomime studies (e.g., Johnson-Frey et al., 2005; Fridman et al., 2006) could be linked to their pantomiming nature (e.g., Lausberg, Kazzaer, Heekeren & Wartenburger, 2015). Nevertheless, clearly at odds with the findings here, Brandi et al., (2014) did find a large degree of overlap between brain areas that were active for both the planning and actual execution of tool-use (for similar evidence during pantomiming also see Johnson-Frey et al., 2005; Fridman et al., 2006; Bohlhalter et al., 2009; Kroliczak & Frey, 2009).

While significant decoding evidences different underlying neural representations with respect to different conditions (Norman, Polyn, Detre, & Haxby, 2006), a lack of decoding could have different meanings. Based on the above evidence from both multivariate and univariate approaches, I expect that the lack of decoding does not reflect the fact that the two conditions (i.e., planning typical and atypical grasps) engages all of these areas in (1) a similar manner or (2) not at all. For the same reason, I do not expect that neural pattern differences have simply failed to be identified/utilised by the vector pattern classifier (i.e., a limitation of the methodology; also see Pereira & Botvinick, 2011). This leaves the possibility that these null findings may reflect a limitation of the current dataset.

Exploring this further, an additional post-hoc volume-by-volume ROI MVPA analysis was performed (see Appendice C). The aim being to investigate whether the neural representations about typicality might have been short-lived and were thus not reflected in the activity patterns during the late plan phase epoch (i.e., MVPA was originally performed during the final 2 volumes of the plan phase because previous delayed movement experiments suggest that planning is a sustained neural process that persists throughout the entire delay until the trigger cue; e.g., Chapman et al., 2011; Curtis et al., 2004; Gallivan et al., 2011; Toni et al., 2001). A short-lived representation of typicality would fit well with behavioural and neurophysiological evidence showing that (1) affordance compatibility effects can rapidly diminish (Tucker & Ellis, 2001; Makris et al., 2011; Makris et al., 2013; cf. Phillips & Ward, 2002; Vingerhoets et al., 2009), (2) such representations did not need to be maintained as participants never used the tools and (3) motor planning activity can be transient (Fiehler, Bannert, Bischoff, Blecker, Stark, Vaitl, Franz & Rosler, 2011; Ariani, Oosterhof & Lingnau, 2018).

Nevertheless, significant decoding was never observed after controlling for multiple comparisons when performing ROI MVPA in volume by volume fashion (see Appendice C). This said, it is worth highlighting that even a single volume here lasted two seconds; a period longer than which affordance related effects are demonstrated to peak, regardless of whether they are argued to be long lasting (e.g., 1000-1200m; Phillps & Ward, 2002; Vingerhoets et al., 2009) or short-lived (i.e., around 400ms; Makris et al., 2011; Makris et al., 2013; also see Cohen, Cross, Tunik, Grafton & Culham, 2009 and Kourtis, Vandemaele & Vingerhoets, 2018). Pairing EEG/MEG MVPA classification (e.g., Tucciarelli, Turella, Oosterhof, Weisz & Lingnau, 2015) with the present tool grasping paradigm would be suited to explore the temporal nature of such typicality representations (e.g., sustained versus transient).

Another possibility I considered post-hoc was whether the current study lacked sufficient power to detect the predicted effects. The current sample size (16 and 17 participants were available here for the ROI and searchlight analysis, respectively) seems sufficient given that the effect size for the left LO to decode object weight significantly above chance (see Gallivan, Cant, Goodale & Flanagan, 2014) was considered high (*d* = 0.86; Cohen, 1969) where a power analysis (using Gpower; Erdfelder, Faul & Buchner, 1996) indicated that a total sample of 17 participants would be needed to detect an effect of this size with 95% power (one samples case) with alpha at 0.05. However, the study here had notably fewer repetitions (i.e., on average 32) relative to related fMRI real action decoding studies (i.e., a maximum of either 48 [Gallivan & Flanagan, 2014] or 80 [Gallivan et al., 2013]), particularly if compared with fMRI Project 1 that included an average of 18 experimental blocks per condition with five grasping repetitions within a block (i.e., 90 grasping repetitions).

Another additional exploratory ROI MVPA analysis was performed post-hoc using contralesional motor related ROIs activity patterns (i.e., motor cortex, SPOC, aIPS, pIPS and, as a control the somatosensory cortex; see Gallivan, McLean, Flanagan & Culham, 2013; see Appendice D). This time, to focus on whether statistical power may have contributed to the lack of decoding from preparatory activity patterns. Again, significant decoding of reach direction or grip size was not achieved, despite such effects being commonly reported for comparable behaviours (i.e., when planning to grasp objects that were either presented [Gallivan, McLean, Smith & Culham, 2011] or to be placed [Gallivan, Johnsrude & Flanagan, 2016] on the *left* versus *right,* as well as when grasping a *smaller* versus *larger* object [Galivan, McLean, Valyear, Pettypiece & Culham, 2011]). As a final indication power is an important source of these null findings during planning, a new classification of grasp direction involving more repetitions (i.e., by collapsing across object categories) was even found to boost decoding accuracies in the motor cortex and the aIPS ($p < 0.05$; see Appendice D). Rapid event-related designs may be useful in the future to increase repetitions without prolonging the, already lengthy, participation time (though note that even this leads to additional issues for plan-related decoding designs; see Ariani, Oosterhof & Lingnau, 2018).

Moving on, only in one circumstance was there evidence of decoding during the planning phase from ROI MVPA: activity in the left PMv could be used to predict grasp direction during the control non-tool classification (Fig. 4.4.). Representations of superficial movement kinematics (i.e., left versus right directed movements) in this region fits well with other studies also showing its activity patterns can be used to discriminate between grasping and reaching actions (Turella, Tucciarelli, Ooserhof, Weisz, Rumiati & Lingnau, 2016; Gallivan, McLean, Valyear, Pettypiece & Culham, 2011) and its proposed role in transforming visual information about object features into corresponding grasp-related motor programs (e.g., Jeannerod et al., 1995; Rizzolatti & Luppino, 2001; Vesia & Davare, 2011; Gallivan & Culham, 2015).

As for the searchlight MVPA, preparatory activity patterns from the left insula and MTG were found to successfully decode object size (Fig. 4.5. top right). This finding in the insula is consistent with evidence that it its activity is linked to changes in grip force (e.g., power versus precision squeezing; Ehrsson, Fagergren, Jonsson, Westling, Johansson & Forssberg, 2000; Kuhtz-Buschbeck, Gilster, Wolff, Ulmer, Siebner & Jansen, 2008; King, Rauch, Stein & Brooks, 2014) as well as being selective to object grasping (relative to if it is simply pointing or looked at; Faillenot, Toni, Decety, Gregoire & Jeannerod, 1997), particularly during motor planning, rather than execution (Glover, Wall & Smith, 2012). The fact that the MTG coded object size, however, is more puzzling because this area is normally associated with non-superficial properties of executed or observed object-directed actions (e.g., their meaning or goal; Rizzolatti, Fadiga, Matelli, Bettinardi, Paulesu, Perani & Fazio, 1996; Decety et al., 1997; Grezes, Costes & Decety, 1998; Schubotz, Wurm, Wittmann & von Cramon, 2014). Nevertheless, discrepant results have been reported before (e.g., a cluster in the left inferior and middle temporal gyri has been shown to be more strongly active when imagining to interact with a tool for non-prehensile use, rather than functional grasping; Buxbaum, Kyle, Tang & Detre, 2006), suggesting that whole-brain univariate and multivariate approaches will continue to be useful to clarifying the roles of this area during tool-use.

The last set of findings from the searchlight MVPA during the plan phase were that object category could be decoded from activity patterns taken from the left EVC and MeFG (Fig. 4.5. bottom left). Since the tool and non-tool stimuli inevitably have low-level visual differences (e.g., surface area, luminance), such a finding in the EVC is not surprising (e.g., Boyaci, Fang, Murray & Kersten, 2007; Haynes, Lotto & Rees, 2004). However, why these representations were restricted to the plan phase (i.e., and not the preview phase) is less clear, possibly suggesting that participants paid more attention to the objects once instructed how to act. Such an explanation would be in line with role of the MeFG in shifting visual attention (e.g., Kozasa, Sato, Lacerda, Barreiros et al., 2012), even if only covertly, that is, without moving the eyes (Corbetta et al., 1998; Beauchamp, Petit, Ellmore, Ingeholm & Haxby, 2001; Sali, Courtney & Yantis, 2016).

4.4.2. Decoding from movement execution & passive viewing epochs

Contrary to predictions, activity patterns during the movement execution epoch that were taken from the visually defined hand-selective areas in the left LOTC and IPS (i.e., LOTC-Hand and IPS-Hand) did not evidence representations of typicality (Fig. 4.4.). Neither of the IPS ROIs (IPS-Hand and IPS-Tool) demonstrated any type of decoding that was significantly above chance, probably owing to the lack of statistical power (see *Decoding from preparatory epochs:* section 4.4.1.). Differently, the LOTC-Hand ROI (and left pFs) showed significant decoding of grasp direction during the non-tool control classification, thus, directly contrasting with findings from fMRI project 1 where this area specifically represented typicality (see Fig. 2.5A.). This said, such a finding does fit well with evidence that bilateral LO and pFs activity patterns during movement execution can be used to decode between placing an object on the left versus right (Gallivan, Johnsrude & Flanagan, 2016). Despite not surviving the correction for multiple comparisons, even some of the other LOTC ROIs here (i.e., LOTC-Body, LOTC-Tool) similarly showed some evidence that they may be sensitive to reach direction (Fig. 4.4.).

Perhaps representations in left LOTC-Hand change as a function of visual feedback availability (i.e., visual feedback was provided here but not in Project 1), where, for example, with visual feedback this area is most readily sensitive to the seen direction of the moving hand. Consistently, the LOTC is often argued to play an important role in comparing visual information about an action with afferent sensory information (e.g., Miall & Wolpert, 1996; Seidler, Noll & Theirs, 2004; Gritsenko, Krouchev & Kalaska, 2007; Franklin & Wolpert, 2011; Gallivan, 2014; Gallivan & Culham, 2015) in order to dynamically update limb representations for motor control (e.g., Astafiev et al., 2003; Orlov Makin & Zohary, 2010; Orlov, Porat, Makin & Zohary, 2014; Gallivan, Johnsrude & Flanagan, 2016). An alternative, but not mutually exclusive, possibility is that this area is more actively involved in extracting object features (e.g., the handle of a tool; also see Gallivan, 2014) when visual feedback is withdrawn (i.e., as in Project 1), much like how activity from posterior/inferior parietal areas is modulated by the availability of this visual information during simple reaching, pointing and grasping behaviours (e.g., Inoue, Kawashima, Satoh, Kinomura, Goto et al., 1998; Prado, Clavagnier, Otzenberger, Scheiber, Kennedy & Perenin, 2005; Filimon, Nelson, Huang & Sereno, 2009; Vesia, Prime, Yan, Sergio & Crawford, 2010; for evidence in the monkey see Bosco, Breveglieri, Chinellato, Galletti & Fattori, 2010 and Galletti & Fattori, 2018). Unfortunately, due to other methodological differences between Project 1 and 3 (e.g., number of repetitions), clarification of this would require additional data that directly compares these actions when performed with and without visual feedback.

The finding that the left EVC ROI specifically represented the typicality of an executed action is also likely attributable to the unique availability of visual feedback in this particular experiment. This area may utilise low level visual differences that could be present when grasping the handle or head of a tool such as which parts of the objects are occluded (e.g., Smith & Muckli, 2010; Orlov & Zohary, 2018) and/or subtle changes in hand kinematics (e.g., longer movement times or hand pre-shaping; see Project 2 [Chapter 3]). Another possibility is that activity patterns in this area are indeed modulated by higher level properties of an action, as was the interpretation of some of the regions in Project 1 (i.e., movements were unseen in that experiment, meaning that the observed decoding of typicality cannot be accounted for by simple changes in visual feedback). Growing evidence characterises the EVC in such a way, where its preparatory activity is predictive of action-related object properties (i.e., orientation; Velji-Ibrahim, Crawford, Cattaneo & Monaco, 2018), correlates with other behavioural performance (Williams et al., 2008; Chambers et al., 2013) and is even found to re-activate when reaching to a remembered target (Monaco, Gallivan, Figley, Singhal, & Culham, 2017; Singhal et al., 2013). Notably, however, representations of typicality should be expected elsewhere in the brain (e.g., in LOTC-Hand and IPS-Hand) if appealing to this explanation because such information in EVC is presumed to result from psychophysiological interactions with parts of the dorsal and ventral visual streams (Velji-Ibrahim, Crawford, Cattaneo & Monaco, 2018).

Despite the unexpected findings so far, the searchlight revealed successful decoding of object size during movement execution from the left PMd (Fig. 5.5. top right). This mirrors both human- (Ehrsson, Fagergren & Forssberg, 2001; Monaco, Sedda, Cavina-Pratesi & Culham, 2015) and monkey-based evidence (Raos, Umilta, Gallese & Fogassi, 2004; Stark & Abeles, 2007; Hendrix, Mason & Ebner, 2009; Di Bono, Begliomini, Castiello & Zorzi, 2015) that activation here is affected by different grip sizes or postures and that it has an important role in controlling hand movements (for reviews see Davare, Kraskov, Rothwell & Lemon, 2011; Turella & Lingnau, 2014; also see Rizzolatti, Luppino & Matelli, 1998).

Interestingly, the identity of a tool was also coded in the left PMd (more posteriorly; Fig. 5.5. bottom right) at the beginning of a trial when participants simply viewed these objects. Premotor cortex is well known to activate when simply viewing and/or naming pictures of tools (e.g., Chao & Martin, 2000) with a similar area, though in the right hemisphere, being recently reported to be sensitive to the function of a tool during pantomiming (Chen, Garcea & Mahon, 2016). Such activity in this frontal areas is commonly linked to the visual priming of object-specific motor schemata (e.g., Jeannerod, Arbib, Rizzolatti & Sakata, 1995; Chao & Martin, 2000; Grafton, Fadiga, Arbib & Rizzolatti, 1997; Handy, Grafton, Shroff, Ketay & Gazzaniga, 2003) and is supported by evidence that lesions here cause apraxic symptoms (e.g., difficulty retrieving learnt motor plans; Dovern, Fink, Saliger, Karbe, Koch & Weiss, 2011). Alternatively, it could also be related to the possibility that participants may have silently named the presented tools because such behaviour has been shown to augment PMd activity during 2D tool observation (Grafton, Fadiga, Arbib & Rizzolatti, 1997).

The possible relation of this tool-identity related representations to sub vocalisation (i.e., silent naming) could clearly be extended to the other searchlight results regarding tool identity that were obtained from the movement execution epoch (see red clusters in Fig. 5.5. bottom right). Many of these areas (e.g., STG, left IFG) are well known to be linked to speech and language processing (e.g., Dejerine, 1914; Okada & Hickok, 2006; Karbe et al., 1998; Martin, Naeser, Ho, Doron, Kurland et al., 2009) with some regions (e.g., right medial temporal lobe and pars triangularis of the left IFG) being reported to specifically activate when naming different categories of stimuli (e.g., tools; Chouinard & Goodale, 2010; Shinkareva, Mason, Malave, Wang, Mitchell & Just, 2008; Garn, Allen & Larsen, 2009). In fact, many of the areas here (e.g., medial cerebellum and even the pre-SMA area identified to code tool identity in Project 1; see Fig. 2.9B.) match the regions associated with the semantic-lexical demands of retrieving an object's name or function, rather than merely articulating the word (Kemeny, Xu, Park, Hosey, Wettig & Braun, 2006). Further work focusing on the naming versus the use of real 3D objects would be useful in teasing apart these competing interpretations (i.e., motor versus sub vocalisation). They would also help uncover why there are differences between the brain regions (i.e., the PMd versus the PHG, IFG, STG and cerebellum) that code tool identity between the preview and plan epochs, respectively (e.g., could the PMd transfer information about tool identity to other areas?; for TMS evidence of candidate PMd functional connections see Bestmann, Baudewig, Seibner, Rothwell & Frahm, 2005 and Bestman, Swayne, Blankenburg et al., 2010).

4.4.3. Limitations

Aside from the lack of statistical power (see *Decoding from preparatory epochs:* section 4.4.1.), an important consideration is that pre-movement delays may provoke activation supporting additional cognitive processes (e.g., working memory, anticipation, response inhibition, self-monitoring etc.) that are not needed for natural everyday actions (e.g., Kemeny, Xu, Park, Hosey, Wettig & Braun, 2005). Indeed, motor planning might only truly occur following a go cue (see Ames, Ryu & Shenoy, 2014) with it being action selection that is processed during a delay (Wong, Haith & Krakauer, 2014). Even the go/no-go paradigms dominating this area of study so far (e.g., Kroliczak & Frey, 2009; Brandi et al., 2014) do not necessarily overcome this limitation since they also rely on response inhibition (i.e., when inhibiting a response on a no-go trial) which may influence the BOLD signal that peaks later than when inhibition is cued. To appreciate the extent of this limitation, notice that the only area identified to be selectively active for planning to perform a right handed tool pantomime during Fridman et al.,'s (2006) go/no-go paradigm was the left PMv, and that the same area is responsible for the motor inhibition of contralateral actions (Baumer et al., 2009; Duque & Ivry, 2009; Duque, Labruna, Verset, Olivier & Ivry, 2012; Giboin et al., 2017). As touched on earlier, other methodologies (e.g., EEG/MEG) can overcome such issues by either shortening unnatural delays, taking measures earlier than the time taken for the BOLD signal to peak following a no-go cue (i.e., before inhibition processing contaminates the planned response) or using entirely different approaches (e.g., measuring the readiness potential; for a relevant example see Vogt, Kato, Schneider, Turk & Kanosue, 2017).

Finally, it is worth highlighting that, should evidence of representations about action typicality have been apparent during motor planning here, the specific nature of information during motor planning is heavily debated (see Andersen & Buneo, 2002; Nanay, 2013; Sheahan, Franklin & Wolpert, 2015; Schaffelhofer & Scherberger, 2016; Gilbert & Fung, 2018). Activity during motor planning could be reflective of shifts in spatial attention (e.g., attending to the direction of an impending action; Robinson, Goldberg & Stanton, 1978; Boussaoud, 2003), an intention to act (e.g., a desire to move; Bratman, 1987; Haggard, 2005), a motoric representation of the upcoming movement (e.g., the outcomes and detailed kinematic features of an action; Jeannerod, 1997) or a mixture of these processes. As already discussed, some plan-related findings here may be related to changes in attention (e.g., coding of object category from left EVC and MeFG; see *Decoding from* *movement execution and passive view epochs;* section 4.4.2.), but teasing apart whether the predicted representation of typicality would have reflected motor-related intentions versus representations would have been more challenging (see Butterfill & Sinigaglia, 2014 for a discussion of related philosophy).

4.4.4. Conclusion

Attempting to identify whether representations about learnt tool-related actions are present during motor planning, this fMRI experiment included an instructory delay period prior to the performance of tool grasping. Neural representations about low level sensorimotor information (e.g., reach direction, object size) were identifiable with MVPA during motor planning and execution. Further, abstract properties about tools (i.e., their identity) were also found to be represented during object viewing. However, more statistically powerful designs will be needed (e.g., with more repetitions) to investigate whether plan-based representations exist about the way that tools are typically grasped for subsequent use.

Chapter 5

General Discussion

The principal aim of my thesis was to investigate which brain areas represent learnt information about tools during a real grasping paradigm (Project 1 [Chapter 2] & Project 3 [Chapter 4]) and to explore if this is manifested in the kinematics of these actions (Project 2 [Chapter 3]). I reasoned that this was an important area of study because (1) tools are often defined based on their link to action-related knowledge (e.g., the way in which they are typically manipulated or their typical function) and (2) only very rarely have neuroimaging experiments involved real tool manipulation. To this end, two fMRI and one behavioural motion-capture experiment were carried out using the same paradigm where participants grasped a series of tools and, as a control, a set of non-tools matched for important features including elongation, reach distance and object width.

Findings from each project are first summarised (see *Summary of findings:* section 5.1.) and then a key finding that draws on the projects altogether is discussed (see *Hand-selective cortex: From perception to action:* section 5.2.). Next, the implications of the results are related to theoretical frameworks that were introduced in Chapter 1 (see *Theoretical implications:* section 5.3.) and then considered in relation to other fields beyond cognitive neuroscience (see *Wider implications:* section 5.4.). After, the limitations of my interpretation are emphasised (see *Limitations to interpretation:* section 5.5.) before highlighting which questions in the domain of tool-use I believe to be most deserving of future attention (see *Future directions:* section 5.6.). The chapter ends with concluding remarks that re-iterate the critical contributions of my thesis (see *Concluding remarks:* section 5.7.).

5.1. Summary of findings

In Project 1, the powerful fMRI block-design, analysed using ROI- and searchlight-based Multivariate Pattern Analysis (MVPA), revealed that a number of areas carried information about how to appropriately grasp a tool for its subsequent use (see blue dots in Fig. 5.1.) including hand-selective areas of the left dorsal and ventral visual streams. In addition, there was evidence of representations about object category (i.e., grasping a tool versus non-tool) in left LOTC-Object, whereas tool function (i.e., grasp a tool associated with cutting versus scooping) and/or identity (i.e., grasping a knife versus pizzacutter versus spoon) were found to be represented in various somatomotor regions and the left SMG.

In Project 2, motion-capture was used to record hand kinematics during the same tool and non-tool reach-to-grasp paradigm used in Project 1. Results from this behavioural follow-up experiment first confirmed that participants scaled their grip to the size of the grasped stimuli, even though the block-design task was unusual with respect to everyday life (e.g., grasping objects five times within a block while laying supine). As for differences between the category of the object being grasped, tool grasping was found to be initiated and performed more slowly than non-tool grasping. When directly comparing atypical tool grasping (i.e., grasping the head of the tools) to grasping non-tools on either side (i.e., the conditions where object size was identical), tool grasping was associated with a significantly poorer degree of grip scaling. Contrastingly, no differences in grip size were found when directly comparing typical tool grasping (i.e., grasping the handle of the tools) with grasping an identical part of a non-tool.

In Project 3, a slow event-related version of the fMRI experiment was used that included an instructory delay period in order to examine whether similar representations of action typicality were present during motor planning, that is, before the hand even moves. Efforts to decode abstract information during a plan phase were largely unsuccessful, likely owing to weak experimental power (see bottom of Fig. 5.1.) because, unlike previous reports, grasp direction could not even be decoded using plan-related activity from the contralateral primary motor cortex. The only area where activity patterns during movement execution could successfully decode typical versus atypical grasping was the left Early Visual Cortex (see yellow dot in Fig. 5.1.), probably reflecting methodological differences between Project 1 and 3 (e.g., visual feedback was uniquely available for Project 3; see bottom of Fig. 5.1.). Finally, tool identity (i.e., decoding knife versus pizzacutter grasping) could be decoded from the left PMd when simply viewing tools (i.e., before motor planning) whilst being more widely represented (e.g., across temporal and frontal cortex of both hemispheres) when actually grasping tools.

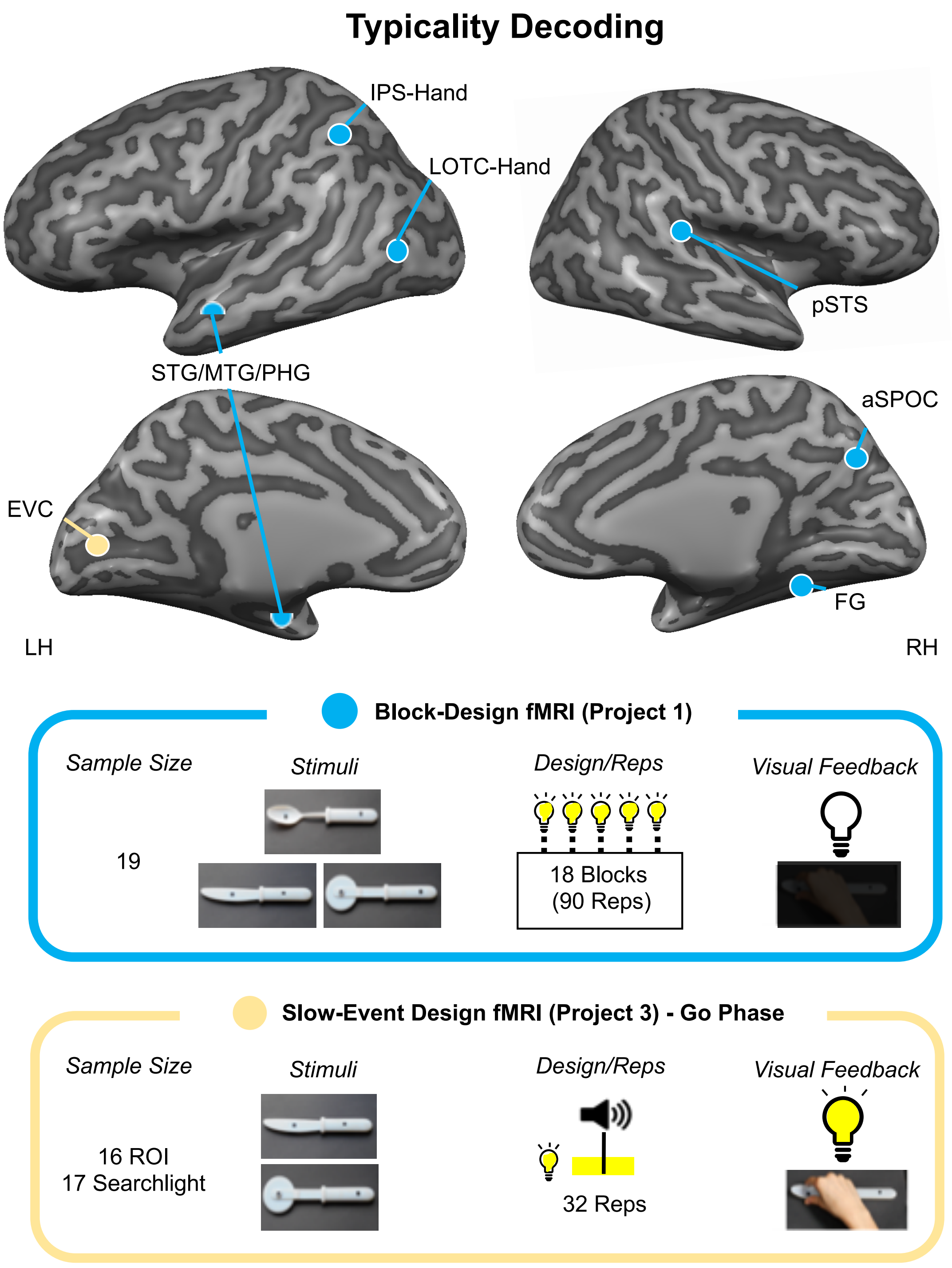

Fig. 5.1. Summary of MVPA typicality decoding from fMRI Project 1 and Project 3. Dots are placed on surface reconstructions from a reference brain (COLIN27 Talairach) available from the neuroElf package (http://neuroelf.net) at approximate locations of ROI peaks or cluster revealed by the searchlights and are coloured blue (Project 1) or yellow (Project 3). As can be seen, Project 1 revealed the coding of

typicality in hand-selective areas of the left LOTC and IPS as well as the areas in the left anterior temporal and right temporal/parietal cortex. For Project 3, the left EVC was the only region to code this information and this was during movement execution. A number of methodological differences between the projects are summarised in the lower boxes. Most notably, Project 3 had weaker statistical power (see *Sample Size* and *Design/Reps* in lower boxes) and uniquely allowed visual feedback during actions. These differences may help explain the null findings during motor planning (see *Decoding from preparatory epochs:* section 4.4.1.) and why EVC decoded typicality (see *Decoding from movement execution & passive viewing epochs:* section 4.4.2.) during Project 3.

5.2. Hand-selective cortex: From perception to action

One of the most remarkable findings in my thesis are drawn from fMRI Project 1: activity patterns from parts of the IPS and LOTC that were selective to 2D pictures of hands (i.e., IPS-Hand and LOTC-Hand) could be used to decode whether a tool was grasped in a way appropriate for its subsequent use or not. The significance of this finding is partly due the failure to perform this same decoding when using activity patterns from overlapping parts of the IPS or LOTC that were instead defined by a selectivity to 2D pictures of tools (i.e., IPS-Tool and LOTC-Tool). In fact, for the LOTC, this decoding of typicality was not possible in additional overlapping regions that were sensitive to pictures of other objects or whole bodies either (i.e., LOTC-Object and LOTC-Body). It seems then, that hand-selectivity in the LOTC and IPS play a unique role in coding the relationships between a hand and a tool (e.g., a knife is typically grasped by the handle, not the blade) during real grasping.

Unlike tool-, body- and object-selectivity that have been heavily investigated (for reviews see Gerlach, 2007; Chouinard & Goodale, 2010; Grill-Spector & Malach, 2004; Lewis, 2006; Kanwisher, 2010, Grill-Spector & Weiner, 2014; Ishibashi et al., 2016; Peelen & Downing, 2017), the cortex that is hand-selective has received far less attention (see Table 5.1.), often being simply described to exhibit functional profiles that are very similar to those in the neighbouring tool-selective regions (e.g., Bracci et al., 2016; Tonin, 2018; Palser & Cavina-Pratesi, 2018). The findings here present new knowledge suggesting that the individual hand- and tool-selective areas do not constitute an entirely common system despite their overlapping voxels (also see Bracci et al., 2012 and Striem-Amit, Vannuscorps & Caramazza, 2017 for a similar consideration). In particular my findings suggest that only hand-selective areas that carry information which may be important for guiding the skilful grasping of tools.

An important arising question is: why would hand-selective cortex uniquely code this information? I hypothesise that, despite being visually selective brain areas, these specific regions have particularly important roles in generating and/or monitoring hand actions, behaviours by which they come to represent the learnt relationship between hands and tools. Not only have similar proposals been made regarding the function of body-selective cortex (e.g., the Extrastriate Body Area; Di Nota, Levkov, Bar & DeSouza, 2016; Orlov, Porat, Makin & Zohary, 2014), results from the motion-capture experiment (Project 2) could be interpreted as support for this particular hypothesis: subtle changes in grasp kinematics were identified when directly comparing *atypical* tool and non-tool grasping, but not when directly comparing *typical* tool and non-tool grasping. Speculatively then, decoding between atypical and typical tool grasping in hand-selective cortex could be linked to potential differences in the control of hand movements (see Fig. 5.2.). Worth noting, Project 3 was designed to shed further light on the link between hand kinematics and decoding of typicality by using the same MVPA procedures during a motor planning phase. However, due to a number of limitations (see Fig. 5.1. and *Decoding from preparatory epochs:* section 4.4.1.) no brain area could be used to successfully decode such a property when using activity patterns prior to movement onset. Aside from addressing the limitations in Project 2, an important test of this hypothesis could also be achieved in the future by directly comparing grasp kinematics when grasping the handles and heads of tools that are of identical sizes (see *black arrow* in Fig. 5.2; though for another approach see *Limitations:* section 3.4.3.).

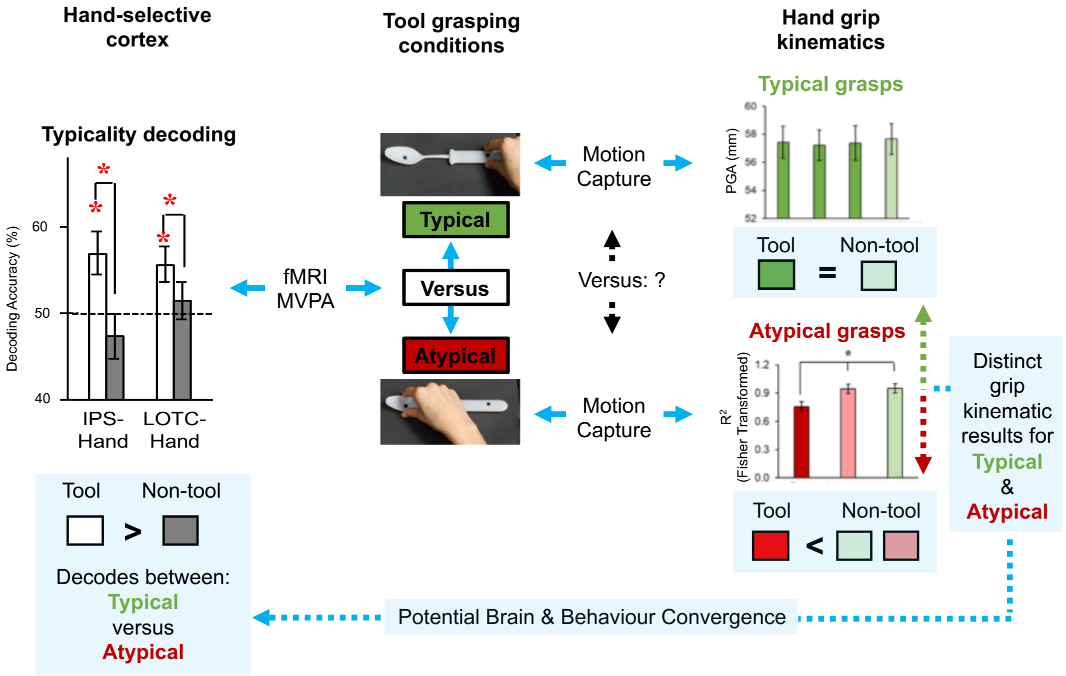

Fig. 5.2. Background to the hypothesis that hand-selective cortex is involved in generating and/or monitoring hand actions. Example grasping movements for the typical and atypical tool grasping conditions are displayed in the *Middle*. Project 1 results from fMRI MVPA hand-selective ROIs are shown on the *Left:* decoding accuracies associated with the left IPS-Hand and LOTC-Hand were found to be

significantly stronger when classifying typicality during tool grasping (i.e., typical versus atypical) relative to the control classification of grasp direction during non-tool grasping (i.e., right versus left). Project 2 grasp kinematic results are shown on the *Right:* no differences were found between typical tool and non-tool grasping (*Top)* whereas measures were found to significantly differ between atypical tool and non-tool grasping (*Bottom).* I predict that the sensitivity of hand-selective cortex to typicality is interrelated with distinct grasp kinematics that could occur when grasping tools by their handle versus their head (*see Bottom: Potential Brain & Behaviour convergence arrows).*

Consistent with this, many picture viewing studies have identified properties reflecting action processing in hand-selective areas of the left LOTC and IPS (see Table. 5.1.). The left LOTC-Hand is sensitive to retrieving tool-related actions from long-term memory (Perini et al., 2014; Tonin, 2018) or whether a viewed object is a tool (Bracci et al., 2010; Bracci et al., 2012; Bracci & Peelen, 2013; Bracci & Op de Beeck, 2016; Bracci et al., 2016) and even codes their unique identities (Tonin, 2018). Likewise, this region's activity adapts when viewing consecutive pairs of semantically related stimuli (Palser & Cavina-Pratesi, 2018) and represents the type of a seen action-related hand posture (Bracci et al., 2018). Though less extensively studied, the left IPS-Hand has similarly been reported to be sensitive to the category of an object (Bracci & Op de Beeck, 2016) and codes for the identity and action-related information of a seen tool (Tonin, 2018).

Table 5.1. Properties of left LOTC-Hand and IPS-Hand areas interpreted from fMRI studies. In the conditions column, italicised text refers to an *example stimulus*. In the properties column, bold text indicates the **property** of the left LOTC- or IPS-Hand region and bracketed text indicates the (related result). The results from my thesis are presented in the rows highlighted grey. Acronyms: Exp.# = Experiment number; V. Picture = View Pictures; Panto. = Pantomime.

Study (Exp.#)		**Task type**	**Conditions**	**Properties of hand-selective area**
			Left LOTC-Hand	
Bracci, et al., (2010)	Exp.#1	V. picture: Univariate	View hands, whole bodies, body parts, tools & chairs.	**Hand preference** (hands > all) with **tool preference** (tools > chairs).
	Exp.#2		View human hands, fingers, body parts, feet & robotic hands.	**Hand preference** (human hands > all except robotic hands).
Bracci, et al., (2012)	Exp.#1		View hands, tools, animals & scenes.	**Hand preference** (hands > all) and **tool preference** (tools > scenes & animals).
	Exp.#2	V. picture: Univariate	View hands, tools, chairs, whole bodies & body parts.	**Hand preference** (hands > all others).
Bracci & Peelen (2013)	Exp.#1		View tools (*hammer*) & objects that are acted-with/-on (*comb/door knob*) or of high/low graspability (*book/clock*).	**Tool preference** (tools + act-with objects > act-on or high/low graspability objects) with a **sensitivity to graspability** (high > low graspability).
	Exp.#2	V. picture: Univariate	View tools, small/large music instruments (*guitar/piano*) & small/large objects (*alarm-clock/blackboard*).	**Tool preference** (tools > instruments) & **insensitive to size** (small object = large object**).**
	Exp.#3		View sports act-with objects (*racquet*), sports-related objects (*ball*), animals & vehicles.	**Tool preference** (sports act-with > sports-related objects) and **insensitive to animacy** (animals = vehicles)

Perini et al., (2014)	Judge picture: Univariate	Judge a tool's related action (*rotate/squeeze)* & location (*kitchen/garage*).	**Action-retrieval preference** (action > location).
Bracci & Op de Beeck (2016)	V. picture: MVPA	View tools, sports equipment, musical instruments, fruit/veg, animals & minerals.	**Codes shape** & **category of stimulus** (activity patterns & behaviour ratings correlate).
Bracci et al., (2016)	V. picture: MVPA	View tools, nonmanipulable objects, hands, bodies & scrambled objects	**Hand preference** (hands > all) with **body** (body > tools) **& tool preferences** (tool > nonmanipulable objects).
Palser & Cavina-Pratesi (2018)	V. Picture: fMRI adaptation	View tools, hands with a tool-related/-unrelated posture (*power grasp/pointing*) & semantically pairable stimuli (*mouse/cheese*).	**Sensitive to semantically pairable stimuli** (adaptation for mouse/cheese but not tools/hands regardless of posture).
van den Heiligenberg et al., (2018)	V. picture: Univariate & functional connectivity	One-handed participants viewed hands, active- or cosmetic-hand prosthetics and objects.	**Modified by visuomotor experience** ([1] One-handers activity & connectivity with somatomotor cortex > controls. [2] One-handers correlation with daily usage > controls correlation with observing prosthetics).
Tonin (2018)	Panto. & V. picture: MVPA	Pantomime/view tools with different functional (*rotate/squeeze*) & structural (*power/precision grasp*) actions.	**Codes functional & structural-action retrieval** with a **functional-preference** (functional > structural). Codes **tool identity.** No differences across task (pantomime = view).
Bracci, et al., (2018)	V. picture: MVPA	View hand postures for action & communication (*grasp/thumbs-up*) from differing viewpoints.	**Codes hand postures invariant of viewpoint** (activity pattern correlations of same viewpoint > different viewpoint).
Project 1	Grasping: MVPA	Grasp 3D tools and non-tools by their handle or head.	**Codes typicality of tool grasping** ([typical vs. atypical tool grasping] > [right vs. left non-tool grasping])
Project 3	Grasping: MVPA	Plan and grasp 3D tools and non-tools by their handle or head.	**Codes grasp direction** ([right vs. left non-tool grasping] > chance) during action execution.

Left IPS-Hand

Bracci & Op de Beeck (2016)	V. picture: MVPA	See above.	Codes **category of stimulus** (activity patterns & behaviour ratings correlate).
Bracci et al., (2016)	V. picture: Univariate	See above.	**Hand preference** (hands > all).
Tonin (2018)	Panto. & V. picture: MVPA	See above.	Codes **structural-action properties when pantomiming.** Codes **functional-action properties across tasks** with a **functional-** (function > structural) & **pantomime-preference** (pantomime > view). Codes **tool identity** with a **view-preference** (view > pantomime).
Project 1	Grasping: MVPA	See above.	**Codes typicality of tool grasping** ([typical vs. atypical tool grasping] > [right vs. left non-tool grasping]).

Only cautiously, however, should findings from picture viewing paradigms be generalised to behaviours involving actual visuomotor control (e.g., grasping 3D tools). Despite picture viewing experiments being sensible (i.e., LOTC-Hand and IPS-Hand are defined based on their sensitivity to 2D pictures of hands), there is strong support for the claim that the systems for visually-based perception and action are, atleast partly, divisible (see *Dual Visual Stream Theory:* Section 5.3.1.) and a growing number of both behavioural (e.g., Snow, Skiba, Coleman & Berryhill, 2014; Kithu, Saccone, Crewther, Goodale & Chouinard, 2019) and neural studies (e.g., Freud et al., 2016; Snow et al., 2011) imply that 3D objects are processed differently to those of pictured 2D objects. If excluding Project 1 and Project 3, to my knowledge, only Tonin (2018) has investigated the roles of IPS-Hand and LOTC-Hand during actual movement (i.e., when pantomiming the action of a pictured tool) and found, for the IPS, that the coding of tool function and identity are indeed altered across tasks concerning perception (i.e., picture viewing) versus action (i.e., pantomiming; see Table 5.1.).

Accordingly, further experiments involving real tool-related actions are needed to address the hypothesis that hand-selective cortex is important for controlling hand movements. Examining if LOTC-Hand and IPS-Hand share a similar neural code for behaviours involving acting with and perceiving tools (e.g., by using cross-task decoding designs; see Chen, Garcea, Jacobs & Mahon, 2017 for evidence of such in the IPL and ventral temporal cortex across perceiving tools and pantomiming their use) would also advance this issue because this would imply that properties found during tool perception would be readily apparent during tool-related actions. Nevertheless, so far, classifiers trained on activity patterns from these areas during tool perception have not been generalisable to tool-use pantomiming (or vice-versa; Tonin, 2018), indicating that a shared neural code may be unlikely and, consequently, why further tool-related action studies are important.

5.3. Theoretical implications

The theoretical questions raised during the General Introduction (Chapter 1), are next considered in light of the results from Projects 1-3.

5.3.1. Dual Visual Stream Theory (DVST)

A key aim of my thesis was to test the claim that tool-use relies on an interplay of processing between the ventral and dorsal visual pathways (e.g., Milner & Goodale, 1995; 2006). Support for this view can be taken from the results of Project 1 in the sense that areas canonically described to be parts of either stream coded information about the relationship between a hand and tool during grasping (i.e., left LOTC-Hand, right FG, left IPS-Hand and right aSPOC). This is a particularly novel finding because the ventral visual stream was not implicated in previous neuroimaging studies of learnt hand tool interactions (Valyear et al., 2012; Brandi et al., 2014). Prior to this project, the closest evidence linking ventral visual stream activity to processing learnt knowledge about tool-related actions comes from pantomiming studies (e.g., Buchwald et al., 2018; Tonin, 2018) whose interpretations are limited because the ventral stream activity might be influenced by the non-goal-directed nature of pantomiming (e.g., Krolickzak, Cavina-Pratesi, Goodman & Culham, 2007; Cohen, Cross, Tunik, Grafton & Culham, 2009; Singhal, Monaco, Kaufman & Culham, 2013; Tonin, Romei, Lambert, Bester, Saada & Rossit, 2017; Lausberg, Kazzaer, Heekeren & Wartenburger, 2015; also see *Imagining or pantomiming tool-use as a proxy for real action:* section 1.6.1.).

The motion-capture results from Project 2 showing that reaching was slower and that grasping was performed more poorly for tool than non-tool actions, might also be interpreted, atleast indirectly, as evidence that tool-related actions require input from the ventral visual stream. Like the tool-related actions here, slower and more inaccurate hand movements are also known to occur for other actions previous argued to not rely purely on real-time dorsal visual stream processing (e.g., when acting toward a target versus a remapped target or after a delay; Thaler & Goodale, 2011; Goodale, Jakobson & Keillor, 1994) and, thus, require input from the ventral visual stream (e.g., Manzone & Heath, 2018). Such a view converges with additional evidence from Project 1 showing that a part of the ventral visual pathway (i.e., LOTC-Object; see Fig. 2.7.) was specifically sensitive to the category of the object being grasped (though an experiment with more than three tool stimuli is needed to verify the reliability of this particular finding).

Nevertheless, the strict functional division of labour that the DVST proposes to exist between the dorsal and ventral visual streams has been frequently challenged (e.g., Franz, Hesse & Kollath, 2009; Schenk & McIntosh, 2010; Farivar, 2009; also see Vaziri-Pashkam, & Xu, 2018) and the data presented here further question the claim that these streams exclusively process visual information for the roles of action and perception, respectively. In the case of dorsal visual stream areas, successful decoding of typicality and tool-function was observed (e.g., within IPS-Hand Fig. 2.5A. and SPOC Fig. 2.8B.) and is not explainable if assuming that this pathway has no access to information other than that which is provided in real-time (or if it rapidly decays; e.g., Jax & Rosenbaum, 2009). As for the ventral visual stream, successful decoding was possible about the size of a grasped object (e.g., superior portion of the LOTC; Fig. 2.6B.) or direction of a grasp (e.g., pFs; Fig. 2.5A. and Fig. 4.4.) which is normally related to the dorsal visual stream and the premotor cortex that it projects to (e.g., Monaco, Sedda, Cavina-Pratesi & Culham, 2015; Fabbri, Caramazza & Lingnau, 2010). Thus, the results here somewhat contradict the traditional views of the dorsal and ventral visual streams, suggesting that they are each sensitive to action-related information regardless of whether these are based on stored knowledge or acquired in real-time (for recent similar views see Lingnau & Downing, 2015; Freud, Plaut & Behrmann, 2016).

The major outstanding question then, concerns how information is transferred between the ventral and dorsal visual streams (e.g., Mahon & Caramazza, 2011; Cloutman, 2013; van Polanen & Davare 2015; Milner 2017). Xu (2018) has recently highlighted that, although tool-related information may be represented in the posterior parietal cortex, it does not necessarily originate from there (though see Mahon, Milleville, Negri, Rumiati, Caramazza & Martin, 2007) because the representation of action information is only present in this area when it is task relevant (Bracci et al., 2017; though note that this is different from Project 1 where this typicality was irrelevant to the task). Findings from fMRI experiments capitalising on the fact that the two streams have unique links to visual awareness support this view (see Darcy, Sterzer & Hesselmann, 2019; Almeida, Fintzi & Mahon, 2013; Mahon, Kumar & Almeida, 2013; Kristensen, Garcea, Mahon & Almeida, 2016), as do voxel-based lesion symptom mapping results showing that impaired access to tool-use knowledge is associated with lesions of posterior temporal, not posterior parietal, cortex (Buxbaum et al., 2014).

Approaches to functional connectivity that utilise Dynamic Causal Modelling (DCM) are well suited to deepen our understanding of how the visual streams interact to support tool-use (e.g., Chen, Snow, Culham & Goodale, 2017). This technique can reveal the direction of communication between the LOTC and IPS that has already been established by traditional functional connectivity measures when viewing tools (Bracci et al., 2012; Garcea & Mahon, 2014) or if simply at rest (Hutchison, Culham, Everling, Flanagan & Gallivan, 2014; also see Hutchison, Culham, Flanagan, Everling & Gallivan, 2015). The datasets collected here enable such an investigation where it could be examined, for example, if left hand-selective cortex (but not body-, object- or tool-selective cortex) in the LOTC exerts an influence on activity in IPS-Hand during tool grasping. This predicted finding would be in line with recent functional connectivity evidence revealing that another area selective to pictures of the body in occipital cortex (i.e., the Extrastriate Body Area), but not object-selective area LO, connects with parietal areas during object-directed action (e.g., grasping/reaching; Hutchison & Gallivan, 2018). In fact, DCM also enables testing of sophisticated architectures that could answer questions related to additional models such as whether activation in left anterior temporal cortex influences ventral visual stream activity in a bidirectional manner (as proposed by hub-and-spoke theory; Lambon Ralph, Jefferies, Patterson & Rogers, 2017) or if ventral visual stream activity influences left SMG processing for the resolution of affordance competition (as proposed by the two-action systems model; Buxbaum, 2017).

As a final point, results here also question the long-standing interpretation that visual form agnosia patient D.F.'s inability to grasp visually presented tools by their handle is primarily due to her ventral visual stream damage (Carey, Harvey & Milner, 1996; see *Dual visual stream theory:* section 1.3. and *Introduction:* section 2.1.). The assumption that the ventral visual stream was responsible for her tool grasping deficit is not so clear-cut given that the dorsal visual stream was shown here carry information about how to grasp a tool for its subsequent use. This point is worth considering given that more recent examinations of D.F.'s aetiology have revealed cortical thinning in the parieto-occipital cortex (Bridge, Thomas, Minini, Cavina-Pratesi, Milner & Parker, 2013; also see Whitwell, Milner & Goodale, 2014) as well as misreaching deficits conventionally taken as evidence of optic ataxia (i.e., a disorder commonly associated with the dorsal visual stream; Hesse, Ball & Schenk, 2012; Hesse, Ball & Schenk, 2014; Rossit et al., 2018). A motion-capture paradigm like that presented in Project 2 paired with TMS to either the LOTC or IPS would be appropriate for studying this issue as it could indicate whether one, or both, of these visual streams have a causal role in tool grasping (see Tonin, 2018 and Cohen, Cross, Tunik, Grafton & Culham, 2009 for related approaches during pantomimed grasping). Though perhaps less feasible, testing whether optic ataxia patients suffer from D.F.'s reported tool-grasping deficit could also highlight whether dorsal visual stream damage is responsible for this behaviour, and thus causally linked to humans' unique ability to use tools.

5.3.2. Two-action systems model

Another key aim of my thesis was to test the claim that the ventro-dorsal stream supports tool-use through its processing of manipulation knowledge (i.e., multisensory and motor memories about objects; Binkofski & Buxbaum, 2013; Buxbaum, 2017). Generally, the finding that left LOTC-Hand decoded the typicality of tool grasping actions is highly consistent with this because, in its most recent account, the two-action systems model describes how 'the *posterior temporal lobe* encodes information about hand-tool relationships' (Buxbaum, 2017).

However, it is the left pMTG area that is usually taken as evidence in favour of the ventro-dorsal stream's role in tool-use (e.g., Martin et al., 1995; Martin et al., 1996; Chao et al., 1990; Damasio et al., 2001) and this area was not found to house such abstract tool-related representations even after being carefully isolated in the ROI MVPA approaches. Surprisingly, these projects also failed to find that the IPL, another traditionally described ventro-dorsal stream area, coded the relationship between the hand and tool, despite a wealth of previous research implicating this area for similar tool knowledge retrieval or tool-action tasks (for review see Vingerhoets, 2014). Further work is needed to test the possibility that it is particularly taxing tool-use tasks (i.e., beyond grasping a tool) that recruits these brain areas because the pMTG was, like here, not identified if participants simply demonstrated tool-use (Valyear et al., 2012), but has been when actually using a tool on a real object (Brandi et al., 2014; also see Randerath et al., 2010 for evidence of different left hemisphere brain lesions associated with tool grasping and tool-use deficits). In light of the results here (i.e., typicality representations in LOTC-Hand specifically), such new investigations would benefit from carefully dissociating characteristic ventro-dorsal stream areas (e.g., pMTG, SMG) from other category-selective parts of temporal cortex (e.g., Valyear & Culham, 2010; Perini et al., 2014).

In line with the *reasoning-based approach* (e.g., Osiurak, 2014), the largely null evidence throughout canonical ventro-dorsal stream areas might reflect the possibility that these areas are normally implicated in the study of tool-use because of their involvement in reasoning about the physical properties of objects: since tool-use was not required in the grasping paradigm, no technical/mechanical reasoning was necessary, thus, explaining the lack of successful decoding from these areas. Taken this way, the findings fit with the three-action pathways model's (Osiurak, Rossetti & Badets, 2017) claim that it is the ventral visual stream that stores contextual relationships between hands and objects (e.g., LOTC-Hand) while the ventro-dorsal stream is needed to understand mechanical actions (e.g., SMG, pMTG).

Supporting this possibility, after a careful examination of the brain regions sensitive to the understanding of physical laws (e.g., the outward direction of colliding objects), Fischer, Mikhael, Tenebaum & Kanwisher (2016) remarked that the implicated areas were similar to those normally identified during tool-use and motor planning (e.g., bilateral SPL and left IPL; also see Schwettmann, Fischer, Tenebaum & Kanwisher, 2018 and Frey, Hansen & Marchal, 2015). Likewise, much of the left frontoparietal network usually linked to tool knowledge, has recently been shown to be recruited when processing movement-related information regardless of whether they were semantically linked to stimuli considered to be tools (e.g., a saw), non-tools (e.g., windmill) or animals (e.g., flapping wings; Borghesani, Riello, Gesierich, Brentari, Monti & Gorno-Tempini, 2019). Nevertheless, whether the ventro-dorsal stream is truly agnostic to learnt knowledge, as is argued by the reasoning-based approach (e.g., Osiurak, 2014), is yet to be determined (see for example Leshinskaya & Caramazza, 2015); after all, tool-use could be supported by abilities that draw on learnt knowledge as well as online reasoning (see Buxbaum, 2017) and might be expected given the extensive connectivity between the left IPL across the brain (Zhang & Li, 2014).

Hybrid models that discuss how tool-use is not only based on learnt knowledge but can also be adapted in the case of novel contexts will continue to be informative (see for example Mizelle & Wheaton, 2010 and Fausto & Valentina, 2017). In terms of their verification, tasks already designed to tap in to the generation of hypothetical novel tool-related uses (e.g., Tobia & Madan, 2017; Benedek et al., 2018) should be adapted for compatibility with real action-based fMRI experiments. Likewise, tool selection tasks will be critical (e.g., choosing between a pair of knives where one is too flimsy for a required slicing) since they can uncover whether ventro-dorsal areas contain representations about other physical properties (e.g., rigidity; see Yildirim, Wu, Kanwisher & Tenebaum, 2019) that would be important for successful tool-use.

As a last point, the same regions were never found to code both the typicality of an action as well as other abstract information about tools (e.g., tool identity or tool function). This fits with the view that there is segregated processing of knowledge about how to manipulate a tool and functional knowledge (e.g., Ochipa, Rothi, & Heilman, 1989; Buxbaum et al., 2000). Rather interestingly, however, left anterior temporal cortex was found to code typicality (also see Chen, Garcea & Mahon, 2016 for similar evidence during pantomime actions) despite the ATL normally being shown to be dedicated to processing the function of a seen tool, rather than how it should be manipulated (e.g., Ishibashi et al., 2011; Lambon Ralph et al., 2008; also see Clarke & Tyler, 2014). Perhaps the lack of tool function coding here reflects the small number of tools used and should be addressed with larger stimulus sets in the future; but as it stands, this evidence suggests that even the segregation of processing between manipulation- and function-related knowledge in that ATL is not clear-cut (also see Campanella & Shallice, 2011). The significance of this point lies in the fact that, while the SMG and pMTG have commonly been shown to contain information about both types of knowledge (e.g., Gallivan et al., 2013; Martin et al., 2016; Chen et al. 2016; Watson & Buxbaum, 2015), the ATL previously seemed to abide by this segregation as it processes knowledge about tool function (e.g., Laura-Grotto, Piccini & Shallice, 1997) that dissociates from that linked to their manipulation (e.g., Martin, et al., 2016; Ishibashi et al., 2011; Lambon Ralph et al., 2008).

5.3.3. Theory of affordances

Originally, the concept of affordances was used to capture the relationship between an object and actor where objects are perceived in terms of the actions that they *afford* (Gibson, 1979), but most neuroimaging studies on this topic present 2D pictures of objects that afford no genuine possibility for action (though see Gallivan et al., 2009, 2011). Project 1 found that a number of left and right hemisphere brain regions coded the typicality of a grasp for real 3D tools (see Fig. 5.1.) even though participants were simply required to arbitrarily grasp the instructed side of the object. Likewise, the fact that various regions also coded tool identity and function (e.g., left PMd, SMG) in Project 1 and/or 3 further supports this point as there was no explicit need to process these properties either. In fact, throughout all projects, most participants were entirely naïve about the focus on typicality or tools as the experiments were simply described to concern the grasping of 3D objects.

This coding of typicality across both hemispheres fits well with the priming study by Valyear et al., (2012) showing that responses in select parieto-frontal areas (e.g., left aIPS, right SPL) when demonstrating well learnt tool-use (e.g., cutting with a knife) were suppressed if the same tool had been viewed earlier in the same trial. In that study, the control task was to perform a newly learnt tool-use demonstration whereas in the projects here the control task was to grasp non-tool objects on their different sides. Thus, with these different control tasks, these studies provide converging evidence that the functional action afforded by tools (e.g., grasp a knife by the handle) may be automatically processed (particularly around the left IPS that was implicated here and by Valyear et al., 2012), even in absence of an intention to use these objects.

Such a conclusion would be strengthened by behavioural evidence showing that this neural activity indeed reflects the preparation of these learnt motor programs. In a modified behavioural-version of the priming experiment just highlighted, Valyear, Chapman, Gallivan, Mark & Culham (2011) have complementarily identified faster RTs when participants grasped tools for use (relative to moving) if the viewed prime and grasped tool matched in terms of their identity (see their experiment 1). A similar RT advantage for actions consistent with the tools functional affordance was not, however, observed in Project 2 here (i.e., RTs were equal between typical and atypical grasping; for further discussion of this discrepancy see *Typicality & hand kinematics;* section 3.4.2.). Additional work therefore seems necessary to highlight whether perceiving a tool really reflects automatic motor planning with a focus on clarifying whether the fMRI repetition suppression reported by Valyear et al., (2012) co-occurs with faster RTs (e.g., as shown during other non-tool action related paradigms; Valyear & Frey, 2015) or that these effects are abolished following interference to their processing by using TMS (e.g., as shown for affordances evoked by images; Xu, Humphreys, Mevorach & Heinke, 2017).

Evidence merging these neural and behavioural approaches will be critical for supporting various models building on the principle of affordances to suggest that the representation of skilled actions depend on the same mechanics contributing to both action comprehension and production, including the common coding hypothesis (Hommel et al., 2001; Prinz, 1997; also see Johnson-Frey, 2004), affordance matching hypothesis (Bach, Nicholson & Hudson, 2014) and affordance competition hypothesis (Cisek, 2007; also see Buxbaum, 2017). For example, MR-compatible motion-capture equipment could enable the test of whether the distinctive grasp kinematics linked to atypical tool grasping (see bottom right of Fig. 5.2.) correlates with decoding accuracies of typicality in hand-selective cortex. Such a finding would go some way in suggesting that motor control is influenced by action comprehension because these movements involve the specific avoidance of responding to affordances (see *Typicality & hand kinematics;* section 3.4.2.). This approach would even enable a clear test of the earlier made hypothesis that hand-selective regions have a role in generating and/or monitoring hand actions.

Even separate neuroimaging and behavioural approaches that make use of previously examined tasks would be useful in clarifying whether tool-related actions are automatically planned when perceiving a tool. For example, the neural (e.g., decoding of typicality) and behavioural (e.g., slower RT and MT for tools than non-tools) should be expected to disappear under circumstance previously described to violate affordances such as when the tool is broken (see Buccino et al., 2009 and Wulff & Humphreys, 2015) or if the afforded action cannot physically be realised (e.g., with an arthritic or immobilised hand; see Kuhn, Werner, Lindenberger & Verrel, 2014 and Bassolino, Bove, Jacono, Fadiga & Pozzo, 2012). Innovative designs (e.g., virtual reality) may even allow the incorporation of other factors known to influence affordance processing such as that of reachability (e.g., presenting extrapersonal space; see Gallivan et al., 2009; 2011) or danger (e.g., presenting painful objects; see Garrido-Vasquez & Schubo, 2014) by overcoming the fact that movements in such experiments would be impossible or unethical.

5.3.4. The tool processing network

A final major aim of my thesis was to assess which of the regions in the tool processing network carry information relevant to performing learnt tool-related actions. In comparison to relevant pantomiming work which also involved performing learnt actions about tools (e.g., Tonin, 2018; Garcea et al., 2019; Buchwald et al., 2018), the performance of multivariate decoding when using activity patterns during real actions appeared rather poor. In fact, if considering the tool-selective ROIs (e.g., PMd, PMv, SMG, pMTG, LOTC-Tool, IPS-Tool), there was no evidence (after controlling for multiple comparisons) that these areas showed above-chance decoding for abstract principles related to grasping tools (i.e., tool-function, tool-identity, object category, typicality).

Importantly, these findings may be influenced by the fact that the ROIs here were visually defined based on contrasts when viewing different categories of 2D pictures. Indeed, this may help explain why even low-level kinematic property (e.g., grasp direction and object size) were only rarely decoded (e.g., sometimes from premotor ROIs; see Fig. 2.5A. and Fig. 4.4.) despite parieto-frontal cortex ROIs (e.g., IPS, premotor cortex) defined based on action-related contrasts (e.g., all actions > baseline) previously being shown to code such properties during movement execution and planning (e.g., Gallivan et al., 2011; 2016). Fitting this explanation, the searchlight MVPA approach did identify markedly more areas for low-level action properties (e.g., object size; see Fig. 2.6B. and top right Fig. 4.5.). As a consequence, the results here showing that 2D tool-selective ROIs were notably poor at reflecting action properties regardless of whether they were about abstract tool properties or simple movement kinematics (also see Valyear et al., 2007; but see Gallivan et al., 2013), imply that proxy tasks involving 2D tool perception may not be best suited for inferring about the brain areas need to perform tool-related actions (for similar views about stimulus format in general; see Snow et al., 2011; Kithu, Saccone, Crewther, Goodale & Chouinard, 2019).

This said, the searchlight analysis still could have implicated abstract representations (e.g., tool identity, tool function) in the IPL and frontal cortex (e.g., PMd, PMv) as has been the case for other pantomiming studies (e.g., Chen et al., 2017; Ogawa & Imai, 2016), but even this only occurred in select frontal cortex (e.g., IFG). Nevertheless, the pantomime of tool-use requires cognitive processes not necessarily needed for real tool use (e.g., Sperber, Chistensen, Ilg, Giese & Karnath, 2018; Lewis, 2006) which may explain why others have similarly found (e.g., Jacobs, Danielmeier & Frey, 2010) no neural differences between hand and tool-related actions if required to actually use a tool. Unfortunately, due to other important differences between this paradigm and pantomiming experiments (e.g., stimulus format: Macdonald & Culham (2015) also failed to find affordance effects during fMRI when viewing real 3D tools too) further study that separately controls for these factors (i.e., pantomiming and stimulus format) are required to tease apart which factors led to the sparse decoding effects here.

Nonetheless, the only perceptual ROIs that reliably decoded typicality were those based on 2D pictures of hands. Perhaps it is these regions, rather than tool-selective ROIs, that may be particularly important for tool-related actions (but see Gallivan et al., 2013). Indeed, based on their evidence that activity responses are higher for hands than tools in the IPS and LOTC, Bracci, Cavina-Pratesi, Connolly & Ietswaart (2016) have recently suggested 'that the purported well-accepted definition of a "tool" network should now be refined to take into account that these areas respond first and foremost to hands'. As previously noted, perhaps these regions were implicated in particular here because these experiments examined hand, rather than tool, movements, but further study is required to test this (for a suggestion on how see *Hand-selective cortex and learnt actions:* section 2.4.1.).

Interestingly, some patches of the tool processing network, aside from the LOTC and IPS, are known to include other areas selective to the pictures of hands (see meta-analysis in Grosbras, Beaton & Eickhoff, 2012). Though their properties remain hugely unexplored, those in the hand-tool overlapping area in the left Ventral Temporo-Occipital Cortex (VOTC) have received slightly more attention: Bracci et al., (2016) showed that this area primarily encodes the category of a pictured object (i.e., animacy) which is different from the properties encoded in hand-tool selective parts of the left IPS (i.e., action-related properties) and LOTC (i.e., category- and action-related properties). Therefore, given the insensitivity of this area in the left VOTC to action-related properties (i.e., hand and tool responses did not cluster together), it could be predicted that VOTC-Hand would not display the same results as in LOTC-Hand and IPS-Hand here. As a whole then, it may be that hand-selective cortex (atleast in the LOTC and IPS) is particularly important for hand-based tool actions, whilst the role of the tool-processing network requires further investigation (e.g., with tool-, rather than hand-related movements).

A final aspect often discussed regarding the tool-processing network is its left hemisphere lateralisation (e.g., does it follow the lateralisation of language representations; see Kroliczak, Piper & Frey, 2011). Only studies that experimentally manipulate the acting hand are able to ascertain whether left lateralisation occurs irrespective of the hand used (Brandi et al., 2014; Kroliczak & Frey, 2009). Nevertheless, the lateralisation of some areas here does fit with prior research since left anterior temporal cortex has shown similar results during semantic categorisation (e.g., Brambati, Benoit, Monetta, Belleville & Joubert, 2010) as well as the fact that apraxics with left hemisphere damage are impaired when using either side (Goldenberg et al., 2003). Even connectivity measures of LO are known to be much more extensive from a seed in the left, relative to the right, hemisphere (Hutchison & Gallivan, 2018). Regarding the right hemisphere activation found here (e.g., pSTS) other innovative paradigms have found bilateral activation (e.g., SPL, SMG) such as during real (Brandi et al., 2014) or virtual reality-based tool-use tasks (Rallis, Fercho, Bosch & Baugh, 2018).

5.4. Wider implications

Thus far, I have focused on cognitive neuroscience models of human behaviour and brain function. Nonetheless, implications can also be drawn from these findings further afield, most evidently in clinical (see *Clinical implications*: section 5.4.1.) and robotic domains (see *Robotics implications:* section 5.4.2.).

5.4.1. Clinical implications

Apraxic impairments following left hemisphere stroke have been estimated to occur in 30-50% of patients (see Geusgens, Heugten, Cooijmans, Jolles & van den Heuvel, 2007) with such symptoms (e.g., difficulty performing pantomimed and/or real tool-use; Goldenberg, 2013) having long lasting consequences (e.g., Donkervoort, Dekker & Deelman, 2006; Hanna-Pladdy, Heilman & Foundas, 2003). Various approaches to rehabilitation are being developed (for review see Worthington, 2016) including those that rely on occupational health programmes (e.g., using pictures showing the correct order of task performance or natural action therapy; van Heugten, Dekker, Deelman, van Dijk, Stehmann-Saris & Kinebanian, 1998; Buchman et al., 2019) as well as those related to neural modulation techniques (e.g., transcranial direct current stimulation [tDCS]; Bianchi, Cosseddu, Cotelli et al., 2015). However, further evidence is required to show that any of these approaches provide effective rehabilitation that transfers to activities of daily life (Buxbaum, Haaland, Hallet, Wheaton, Heilman, Rodriguez & Rothi, 2008; Park, 2017; Buxbaum & Randerath, 2018).

Usually, impairments related to the actual performance/pantomiming of tool-use are specifically linked to left inferior frontal (e.g., IFG) and parietal lesions (e.g., IPL; Goldenberg & Spatt, 2009; Dressing, Nitschke et al., 2016). Yet, here even temporal areas (e.g., left LOTC-Hand and anterior temporal cortex as well as right pSTS) were found to be sensitive to the first step of actual tool-use, that is, grasping the object by its handle. Thus, extending other evidence that temporal lesions impair abilities to retrieve knowledge about the purpose of a tool (e.g., Hodges et al., 2000), the findings here suggest that these areas are also important for carrying out such behaviour.

Finding such a link between temporal cortex and tool grasping is highly consistent with lesion symptom mapping evidence showing that deficits specific to the grasping of tools, rather than those related to tool-use, is associated with damage to occipito-temporal cortex (Randerath et al., 2010). Skilled motor performance of the left hand (e.g., lifting objects with a spoon) in ideomotor apraxia patients has already been shown to improve following tDCS delivered to the left PPC (Bolognini, Convento et al., 2015). The results here indicate that, perhaps, temporal areas may also be useful sites for such therapy, atleast for problems with tool grasping. This fits with the view that different patterns of apraxic performance emerge from lesions to different areas across the tool-processing network (e.g., Goldeberg & Spatt, 2009; Manuel, Radman, Mesot et al., 2012) as well as the position that rehabilitation procedures can be improved based on a better understanding of the neuroanatomical correlates of human tool-use (Randerath & Buxbaum, 2018).

5.4.2. Robotics implications

Designing and implementing Brain Machine Interfaces (BMI) lies at the forefront of the wider implications related to movement-related neuroscience. A clear goal being to successfully utilise movement-based neural signals to control a machine, such as a Cognitive Neural Prosthetic (CNP) for a person with a sensorimotor disability. Consisting of an array of electrodes, a decoding algorithm, and an external device controlled by the processed signal (Andersen, Burdick, Musallam, Pesaran & Cham, 2004), CNPs could feasibly be controlled by signals related to a range of cognitive processes including intention, motor imagery, decision making, forward estimation, executive function, attention and multi-effector movement planning (for review see Andersen, Hwang & Mulliken, 2010).

Most forms of BMIs or CNPs rely on activity from primary motor cortex (e.g., Carmena et al., 2003; Fetz, 1969; Serruya et al., 2002) which is rather sensible given that this region is a main source of cortical output to the spinal cord during reach-to-grasp movements (e.g., Saleh, Takahashi & Hatsopoulos, 2012; Mollazadeh et al., 2011). However, as recognised before (e.g., Kobler et al., 2019), other regions known to be critical for carrying out these actions (e.g., posterior parietal cortex; Begliomini et al., 2014), will likely generate useful activity decodable by these technologies. In fact, Andersen & Buneo (2002) highlighted that, since different areas of the sensory-motor pathway provide different types of information, multi-area-based prosthetics will be vital for more sophisticated machinery.

Therefore, in the case of technology that would be able to facilitate human-like tool-use (e.g., performing a grasp that is use-appropriate) the results here indicating that this property is decodable in a part of the IPS clearly highlights the posterior parietal cortex as a site for such endeavours. This evidence is particularly important since most research of BMI decoding models are based on non-human primate models (Andersen, Hwang & Mulliken, 2010), yet these animals lack the sophisticated cognitive capacities that humans do when engaging tools.

5.5. Limitations to interpretation

Different to the *limitation* sections in previous experimental chapters, this section focuses on broader limitations that impact my interpretations. These stem from the fact that I used MVPA throughout Projects 1 and 3 (see *Multivariate approaches:* section 5.5.1.) and how I have interpreted the decoding of typicality (see *Representing the typicality of a grasp:* section 5.5.2.).

5.5.1. Multivariate approaches

The decision to use an MVPA technique throughout my thesis was influenced by the findings that voxel-wise analysis and MVPA differ in their sensitivity to psychological or physical dimensions underlying task processing (e.g., Davis et al., 2015; for a recent example see Fuelscher et al., 2019; though see Bhandari, Gagne & Badre, 2017). Based on this justification, many highly relevant fMRI studies have also focused exclusively on multivariate approaches (e.g., Wurm & Lingnau, 2015; Chen, Garcea & Mahon, 2015; Bracci, Peelen & Caramazza, 2018; Buchwald et al., 2018) including many of those examining real object-directed actions (e.g., Ariani, Wurm & Lingnau, 2015; Gallivan et al., 2013; Gallivan, McLean, Flanagan & Culham, 2013; Gallivan, Chapman, McLean, Flanagan & Culham, 2013). In fact, this strategy is now widely, and often solely, adopted across many research domains (e.g., working memory, arithmetic, language; Pinheiro-Chagas, Piazza & Dehaene, 2019; Albers, Kok, Toni, Dijkerman & de Lange, 2013; Sheikh, Carreiras & Soto, 2019), regardless of the neuroimaging technique used (e.g., MEG, EEG; Kaiser, Azzalini & Peelen, 2018; Mai, Grootswagers & Carlson, 2019). This may even be reflected in my results given that, the results here uniquely implicated left anterior temporal cortex, while this area was not identified by other highly relevant studies which did not utilise MVPA (i.e., Vayear et al., 2012; Brandi et al., 2014).

However, valuable insights about the preferential responses of an area are only available to univariate analyses (e.g., Naselaris & Kay, 2016). To use a relevant example, Valyear & Culham's (2010) activation measures found preferential responses in the bilateral LOTC and left pMTG when participants viewed typical, relative to atypical, grasping. The MVPA techniques used in my thesis cannot make this same inference, instead showing that the activity patterns in, for example, left

LOTC-Hand could be used to decode between the performance of these two movement types (a point that is particularly useful to BMI development; see *Robotics implications:* section 5.4.2.). Presenting both MVPA and activation measures will be useful in the future (for the introduction of such an approach see Leone, Heed, Toni & Medendorp, 2014), though it should be highlighted that simply identifying brain regions where uni-and multi-variate findings converge/deviate cannot offer conclusions about the nature of the neural code and instead requires further computational testing (see Davis, LaRocque, Mumford, Norman, Wagner & Poldrack, 2014).

A final important point concerns what exactly does above-chance decoding mean about the qualities of a brain region? Commonly, decoding is described to reflect a *neural representation* of the related phenomena (e.g., a representation of how to appropriately grasp a tool) and is simply based on a pattern of BOLD signals across a series of voxels. I have been careful not to state that the information decoded from patterns of neural activity is necessarily what information those patterns represent (i.e., the decoder's dictum; see Ritchie et al., 2017) - for example, successful decoding of typicality does not mean that the brain explicitly reads out this information in a similar way (e.g., where one movement is considered more or less typical than another). Instead successful decoding is treated to mean that information was available in the latent neural patterns, and, as such, the given brain region is sensitive to differences between the experimental conditions (e.g., grasping an object in a way that appropriate for its learnt use or not). Understanding what a representation is remains a key question in cognitive science (e.g., Ritchie, Kaplan, & Klein, 2017; Shay, Chen, Garcea & Mahon, 2018) and combining classifier analyses with other behavioural measures (e.g., ratings [Bracci & Op de Beeck, 2016] or hand kinematics [as in Project 2]) using representational dissimilarity matrices can further capture their nature (e.g., their geometry; Kriegeskorte & Kievit, 2013) as well as if the brain is likely to read-out information in the way that is experimentally operationalised (Grootswagers, Cichy & Carlson, 2018).

5.5.2. Representing the typicality of a grasp

When participants grasped the tools by their handles versus their heads, I have used the term *typicality* to capture this difference where the former movements were considered to be typical to the learnt use of tools. However, this kind of manipulation has been referred to in various ways. Valyear & Culham (2010) have described how related findings reflect a ‘sensitivity to learned contextual and/or semantic associations’, while a related study describing these findings (Kumar, Humphreys & Yoon, 2012) specifically wrote how they relate to ‘grasp typicality’. Johnson-Frey et al., (2003) described how this experimental manipulation could ‘determine whether these responses were modulated by familiarity’ and Mizelle, Kelly & Wheaton (2013) described how these types of movements can be used to study ‘correct’ or ‘incorrect’ movements (though in this case tools were presented with receptive target objects). Regardless of the particular description used, my view is that this approach can tap into the processing relevant for understanding which brain regions are sensitive to learnt knowledge about tool-use.

Nevertheless, I also appreciate that typicality, as I have referred to it, can dissociated from familiarity because knowing how a tool should be typically grasped is possible even if unfamiliar with that particular object (e.g., understanding the typical way chopsticks are held despite having never used them). An explanation based on familiarity, rather than typicality, could be relevant for some of the findings here. For example, interpreting the successful decoding between handle and blade grasping in the left anterior temporal cortex would fit with other results showing that activity in this area is modulated by the familiarity of a face (e.g., Gainotti, 2007; Snowden, Thompson & Neary, 2012). To return to the decoder's dictum, it could be that the information read out by the brain is actually related to familiarity, rather than typicality, per se. Worth highlighting, the non-tools used in these projects were able to control for familiarity to some extent (i.e., despite the tools resembling familiar kitchen utensils, all stimuli were in fact novel), but further study with equally familiar objects (e.g., a set of tools, a set of non-tools that have been trained for use and a final set of non-tools not trained for use; for further discussion on tool training interventions see *Future directions:* section 5.6.) would be required to tease apart these largely interrelated explanations of familiarity and typicality (e.g., if results are specifically explainable by familiarity then effects should be replicated for the tool, but not either of the non-tool sets).

5.6. Future directions

The role of knowledge, as well as the process of learning, is clearly critical to tool-use (e.g., Mizelle & Wheaton, 2010; Johnson-Frey, 2004), as emphasised from the outset (see *What is a tool:* section 1.2.), where I considered tools to be objects associated with learnt action routines and functions (e.g., Johnson-Frey, 2007; Mahon, Milleville, Negri, Rumiati, Caramazza & Martin, 2007; Mruczek, von Loga & Kastner, 2013). Even proponents of the reasoning-based approach concur that the ventral visual stream stores functional knowledge about tools (e.g., Osiurak, Rossetti & Badets, 2017). A better understanding of how these object-associations are learnt would advance the neuroscience that underpins human tool-use.

Tool training paradigms (e.g., Weisberg et al., 2007; also see Roy & Park, 2010) where, between neuroimaging sessions, participants learn to use a set of novel objects as tools, offer an effective way to tap into this learning process. When viewing a tool whose function has been learnt through visual training, activity increases have been observed in areas like the left pMTG (Weisberg et al., 2007; Bellebaum, Tettamanti et al., 2013) whereas learning-related changes for objects that have been manipulated, or atleast watched be manipulated, is linked more strongly to activity changes in the left IPL (Bellebaum, Tettamanti et al., 2013; Ruther, Brown, Klepp & Belle, 2014; for similar evidence during learnt knot-tying see Cross, Cohen, Hamilton, Ramsey, Wolford & Grafton, 2012). Generally, modality and task type (e.g., visual, auditory, sensorimotor, haptics) is well known to influence object representations during learning (e.g., Oliver, Geiger, Lewandowsk & Thompson-Schill, 2009; Butler & James, 2013; Song, Hu, Li, Li & Liu, 2010; van der Linden, Wegman & Fernandez, 2014; van der Linden, van Turennout & Fernandez, 2011; Clarke, Pell & Ranganath & Tyler, 2016; Chrysikou, Casasanto & Thompson-Schill, 2017), but it remains unexplored how interventions would affect neural activity related to actual tool manipulation during neuroimaging. For example, do visual and manipulation training interventions equally lead to typicality representations in hand-selective cortex during grasping, or are these generated more efficiently through manipulation training (e.g., as is the case in the IPL for learning about object category; Bellebaum, Tettamanti et al., 2013; Ruther, Brown, Klepp & Belle, 2014). In fact, such paradigms can even overcome the limitation that tools and non-tools have low level differences (see for example *Object category affects hand kinematics:* section 3.4.1.) because identical stimuli are used pre- and post-training.

Ambitiously, it would also be useful to track the neural characteristics of this learning process over development, as has been the case for responses to other stimulus categories (e.g., Pelphrey, Lopez & Morris, 2009; Peelen, Glaser, Vuilleumier & Eliez, 2009; Cohen, Dilks, Koldewyn et al., 2019; Ashby & Maddox 2005). While face-, scene- and body-selective activity has been reported to occur in an adult-like fashion from as early as 4-6 months of age (Deen et al., 2017), it is unclear when this is the case for tool-selective activity. If there is overlap between the ages by when there is maturing of skills related to physical object reasoning (e.g., Remigereau, Roy, Costini, Osiurak, Jarry & Le Gall, 2016) and tool-use (e.g., van Leeuwen, Smitsman & van Leeuwen, 1994; Barrett, Davis & Needham, 2007), then this would correspond with the view that neural processing during tool-use is largely supported by technical reasoning abilities (Oisurak, Rossetti & Badets, 2017).

Lastly, by combining the novel tool grasping paradigm here with neuroimaging measures other than fMRI, it would become possible to better understand the temporal nature of these representations about typicality. Recent EEG studies have characterised small, yet reliable, time-course differences when reasoning about object attributes (e.g., their typically associated actions [Lee, Huang, Federmeier & Buxbaum, 2018] or locations [Kaiser, Moeskops & Cichy, 2018]) which may also be detectable during real tool manipulation. Relative to fMRI, such techniques would also be easier to implement with cutting-edge motion-capture techniques (e.g., cyber glove; see Agashe & Contreras-Vidal, 2013; Roda-Sales, Vergara, Sancho-Bru, Gracia-Ibanez & Jarque-Bou, 2019) in order to combine neuroimaging and behavioural measures within the same session (see *Limitations:* section 3.4.3.), thus, allowing critical links to be drawn between brain and behaviour (see Fig. 5.2.).

5.7. Concluding remarks

A major goal in cognitive neuroscience is to understand how knowledge about objects is represented and organised in the brain. For objects described to be tools, these representations are linked to our knowledge of their associated actions and functions. By utilising state-of-the-art brain decoding techniques during a novel tool grasping paradigm, I have shown that the left hand-selective areas of the dorsal and ventral visual pathways, as well as left anterior temporal cortex and right parietal/temporal cortex, carried information about whether a grasp was consistent with the way the tool would be held for subsequent use (i.e., by the handle; Project 1). Likewise, various somatomotor areas across both hemispheres (e.g., left PMd, SMG, right PHG) were found to code the identity and/or function of the tools being grasped (Project 1) or simply viewed (Project 3).

These findings in the ventral and dorsal visual pathways conform to a major prediction by the DVST (Milner & Goodale, 1995; 2006) that both visual streams support tool-use; however, they also question the traditional view that it is the ventral, rather than dorsal, visual stream that is sensitive to the learnt aspects of tool-use. As for accounts that identify an additional ventro-dorsal stream (e.g., two-action systems model [Binkofski & Buxbaum, 2013]; reasoning-based approach [Osiurak & Badets, 2014]), the results revealed that its canonical areas (i.e., left SMG and pMTG) are not sensitive to stored knowledge about how to grasp a tool, possibly implying that these areas have roles in technical reasoning processes (Osiurak & Badets, 2014]) or, for the SMG, affordance competition resolution (Buxbaum, 2017). Since the grasping paradigm never required an intention to use the tools, or even process their identities, the findings also reflect the view that object affordances are automatically perceived (Gibson, 1979). Finally, with regard to the tool processing network identified by many neuroimaging experiments that contrast pictures of tools with other categories of objects, none of these regions were found to be specifically sensitive to the performance (Project 1) or planning (Project 3) of use-appropriate tool grasping. Instead, these findings were restricted to hand-selective areas of the left LOTC and IPS, which, remarkably, even overlapped with the tool-selective areas in these same areas. Based on distinct hand kinematic findings during motion-capture of the same typical and atypical tool grasping movements (Project 2), I suspect that these hand-selective regions play an important role in motor control which links them to humans’ intelligent use of tools.

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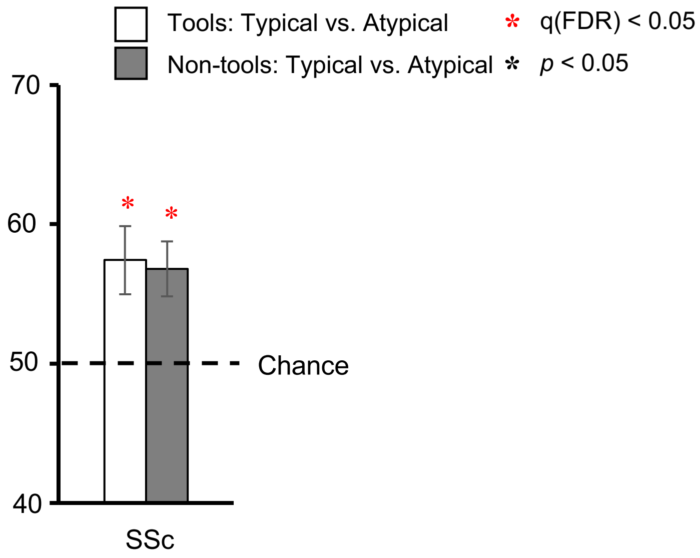
Appendix

Appendix A - Somatosensory Cortex decoding in fMRI Project 1

To test whether the decoding accuracies that were found to be significantly above chance for typicality (i.e., decoding typical versus atypical tool grasping), but not for the control classification of reach direction (i.e., decoding right versus left non-tool grasping) in fMRI project 1 could be attributed to somatosensory differences that occur in the tool, but not non-tool, conditions, I repeated these analyses with an ROI in the primary somatosensory cortex (SSc). The SSc ROIs (mean Talairach coordinates: $x = -47$ $y = -26$ $z = 49$) were defined using functional activations for each participant from the real action experiment with a contrast that avoided circularity (all actions > baseline; Fabbri et al., 2014) and by selecting the peak voxel in the postcentral gyrus and sulcus (Fabbri et al., 2016). Decoding accuracies were significantly higher than chance in the SSc for both typicality (57%, $t(18) = 3.04$, $p = 0.004$, $d = 0.7$ [chance 50%]) and reach direction (57%, $t(18) = 3.45$, $p = 0.001$, $d = 0.79$ [chance 50%]; Appendix A: Fig. 1.).

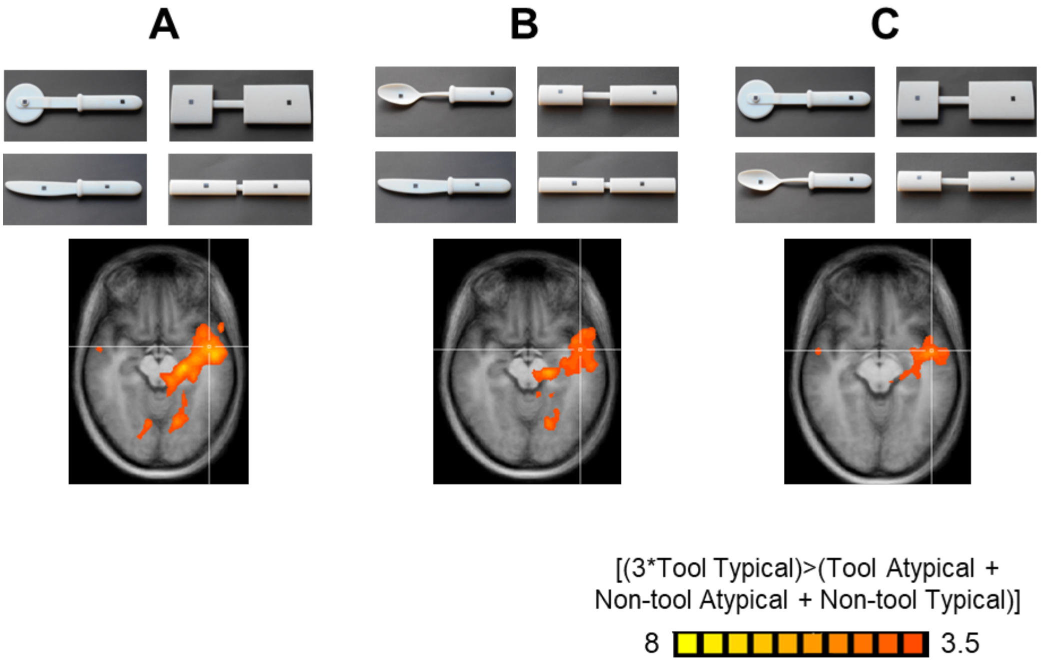


Appendix A: Fig. 1. Decoding accuracies when classifying typicality and reach direction in somatosensory cortex ROIs. Error bars represent SEM.

If decoding of typicality in the left LOTC-Hand and IPS-Hand during the first project was driven purely by differences in somatosensation (e.g., tool handles are different than tool heads) then the same results should be expected in somatosensory cortex. However, this was not the case, highlighting that a somatosensory explanation could not fully account for the results discussed in Project 1 (Chapter 2).

Appendix B - Data-driven selection of stimuli for fMRI Project 2

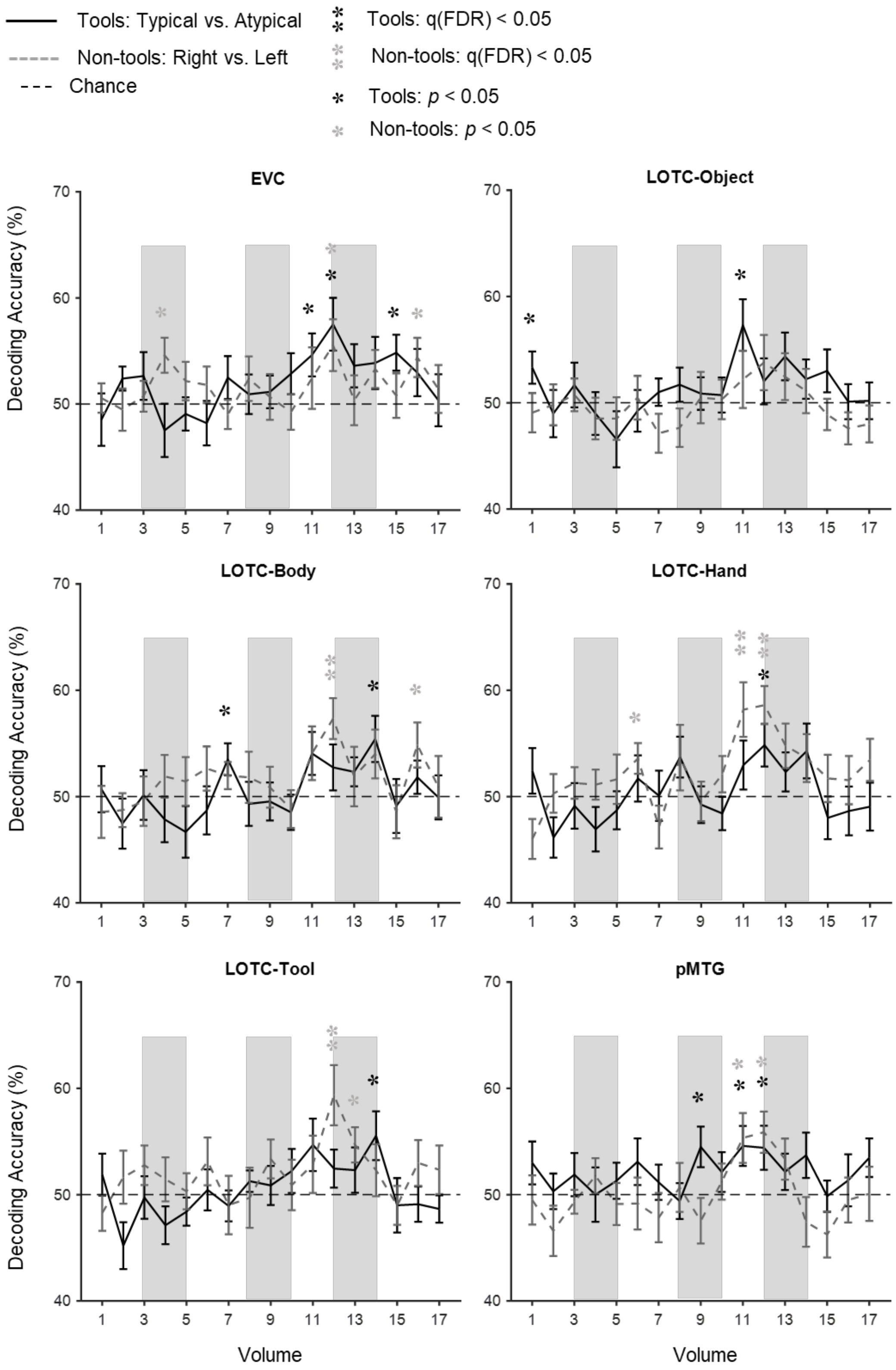
To choose which of the two stimuli should be used in the second fMRI project I used an exploratory univariate approach to visually check which combination of two stimuli led to the greater activation within the temporal lobe when contrasting grasping tools typically with grasping tools atypically and the non-tools by either side (see contrast in Appendix B: Fig. 1.). Activation was clearly stronger in the case of the pizzacutter and knife tools (see section A of Appendix B: Fig. 1.) than when either of these objects was paired with the spoon (see section B and C of Fig. 1.: Appendix B). The decision to focus on the temporal lobe was based on the view that the ventral visual stream is highly theoretically relevant to tool based interactions (see *Dual Visual Stream Theory*: section 1.4.) and the interesting findings in Project 1 showing that the left anterior temporal cortex also represents this information (see section 2.4.2.).



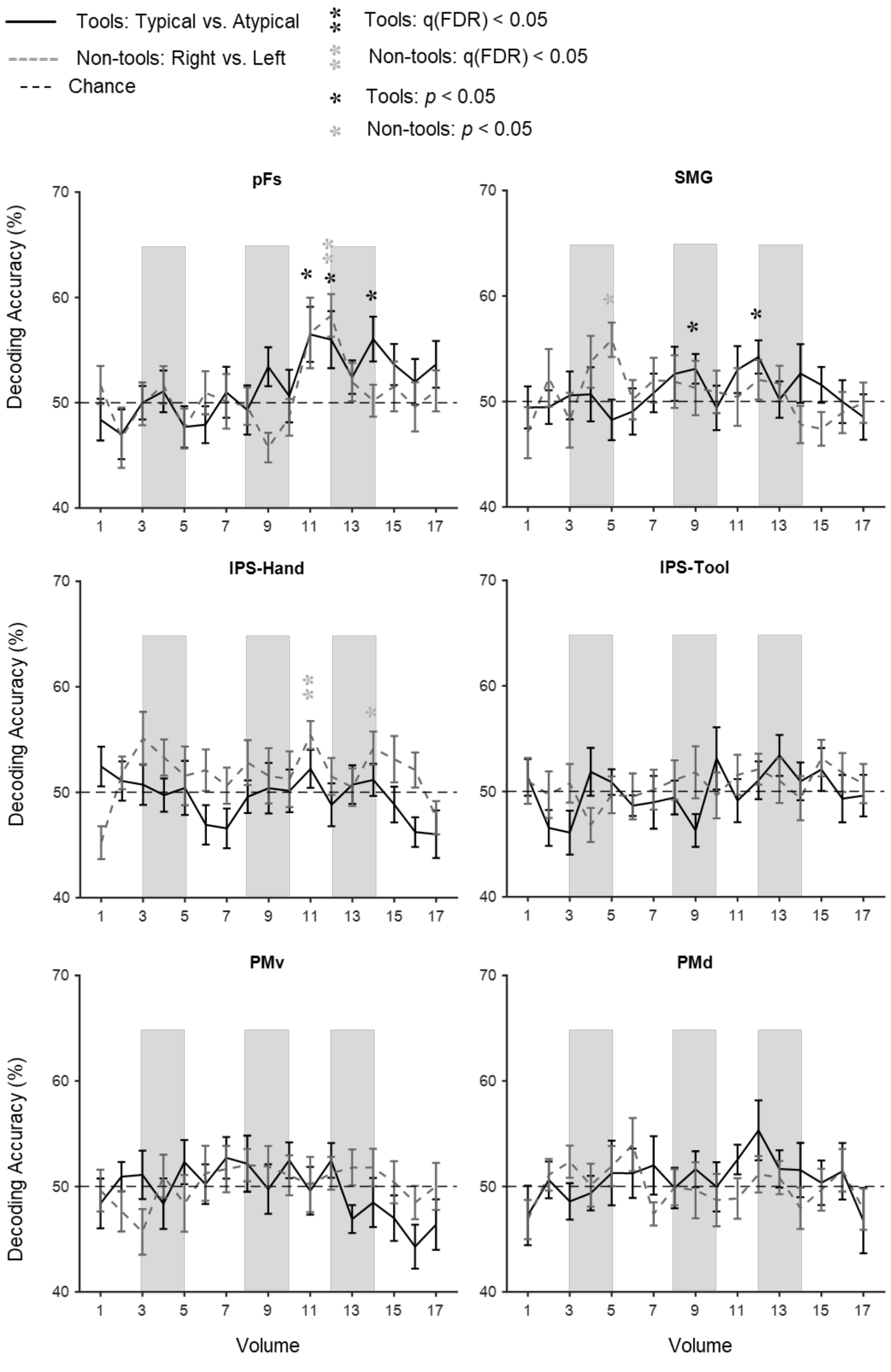
Appendix B: Fig. 1. A random effects general linear model was applied to the dataset from the real action experiment in the first project. Individual regressors were assigned for each of the exemplars per the two grasping conditions (e.g., knife typical, knife atypical, knife non-tool left, knife non-tool right etc.) and convolved with a two gamma Boynton hemodynamic response function (HRF). A boxcar HRF was aligned to the onset of the stimulus block with the same duration as block length. The OFF-block epochs and the baseline epochs at the beginning and end of the experiment were excluded from the model, and therefore, all regression coefficients (betas) were defined relative to this baseline activity. Finally, the results for the contrast used to determine the activity that was stronger for tool typical grasping is displayed above when using different combinations of the stimuli including the knife and pizzacutter (A), spoon and knife (B) and spoon and pizzacutter (C).

Appendix C - Volume by Volume decoding in Localiser ROIs in fMRI Project 2

To assess if another plan-related decoding was possible from an epoch other than volumes 12 and 13 (i.e., as were chosen in Project 3), I repeated the same ROI MVPA analysis in a volume by volume fashion (Appendix C: Fig. 1.).



Appendix C: Fig. 1. Volume by volume decoding in left hemisphere localiser ROIs.



Appendix C: Fig. 1. (Continued).

Appendix D - Motor ROI decoding in fMRI Project 2

Results for the decoding of left hemisphere ROIs based on all actions > baseline are presented here in order to try and replicate commonly decoding effects found in human studies examining representational content of pre-movement activity patterns (e.g., Gallivan et al. 2011). I defined these and repeated the same decoding analyses as in fMRI project 2. This was in order to validate the MVPA approach I had taken since there was very little evidence of any succesful decoding during the plan epoch from visually defined ROIs (i.e., from the Bodies, Objects, Tools and Hands fMRI localiser). The percentage signal change plots of the ROIs are presented in Appendix D: Fig. 1. and the decoding results in Appendix D: Fig. 2.

The chosen regions were functionally defined based on the same GLM as presented in Appendice B (except with three times the regressors for each of the preview, plan and go phases), with a contrast avoiding circularity (Plan & Go all actions > Preview) using the following anatomical guidelines:

- *Motor Cortex* (Mc) – defined by selecting voxels around the left “hand knob” landmark in the central sulcus (Yousry et al., 1997) (mean [standard deviation] Talairach coordinates: x = -36 [6] y = -27 [5] z = 55 [7]).

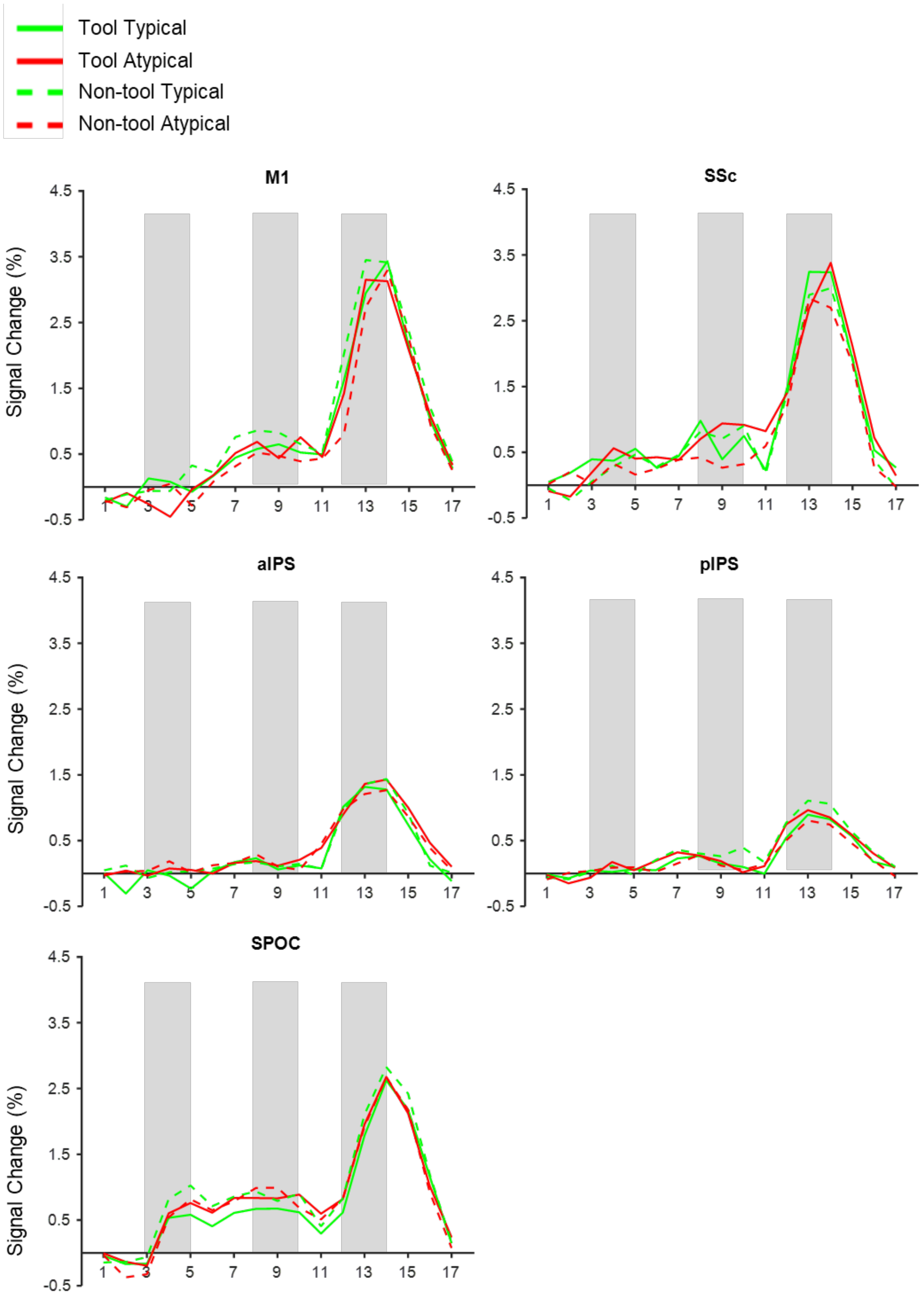
Somatosensory Cortex (SSc) - defined by selecting the peak voxel in the postcentral gyrus and sulcus (Fabbri et al., 2016) (mean Talairach coordinates: x = -37 [7] y = -35 [5] z = 45 [6]).

Anterior Intraparietal Sulcus (aIPS) - defined by selecting voxels at the junction the IPS and post-central sulcus (Culham et al., 2003) (mean Talairach coordinates: x = -37 [5] y = -38 [5] z = 33 [5]).

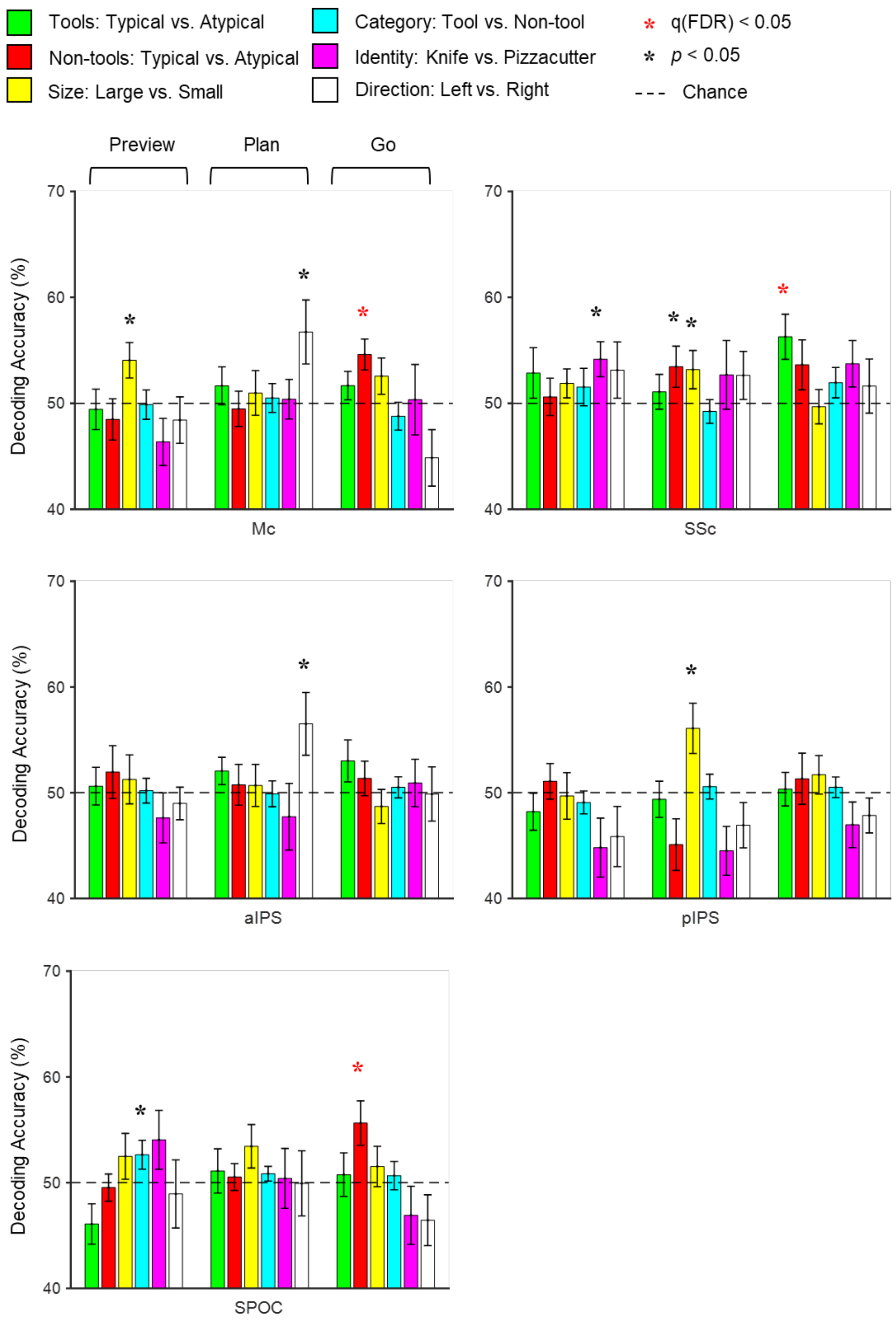
Posterior Intraparietal Sulcus (pIPS) - defined by selecting activity at the caudal end of the IPS (Beurze et al., 2009) (mean Talairach coordinates: x = -28 [4] y = -69 [6] z = 44 [4]).

Superior Parieto-Occipital Cortex (SPOC) – defined by selecting voxels located medially and directly anterior to the parieto-occipital sulcus (Gallivan et al., 2009) (mean Talairach coordinates: -8 [5] -83 [5] 32 [6]).

See Chapter 4 for discussion of the results.



Appendix D: Fig. 1. Percentage signal change in motor ROIs. Grey bars represent the preview, plan and go epochs (see section 4.2. for further details).



Appendix D: Fig. 2. Decoding results in motor ROIs. All of the classifications performed are described in section 4.2. However, uniquely here, I performed an additional left versus right classification that collapsed across object category (white bars) to closely match previous studies (this is all left versus right trials except the pizzacutter tool to remove the grip change).