# The elements and features of cognitive rehabilitation for stroke and 'mild cognitive impairment' in relation to everyday functioning and quality of life

Chai Chung Han

Thesis submitted in partial fulfilment of the degree of Doctor of Clinical Psychology

University of East Anglia

Faculty of Medicine and Health Sciences

Submission date: 25th May 2021

Candidate Registration Number: 100260763

Thesis portfolio word count: 35495

## Thesis Abstract

**Context:** Stroke and dementia are neuropsychological deficits that impact an individual's quality of life. Computerised cognitive training (CCT) is an intervention aimed to ameliorate the deficits.

**Aim:** The current thesis portfolio aims to provide an updated review on CCT efficacy concerning the quality of life and mild cognitive impairment (MCI). Additionally, the thesis aims to understand better the cognitive domains that best predict the quality of life in stroke individuals.

**Method:** The systematic review examined the efficacy of existing computerised cognitive training at improving everyday functioning in MCI individuals. Additionally, the review aggregated CCT features that are commonly used in the reviewed CCTs. The empirical paper examined the cognitive variables best-predicting quality of life, focusing specifically on functional outcomes.

**Results:** The systematic review showed tentative evidence for CCT at improving everyday functioning in MCI individuals. The review identified preliminary evidence suggesting socio/emotional factors that might contribute to CCT efficacy. The empirical paper found non-spatial attention as a significant contributor to one model of quality of life. However, this significance was only attainable when depression and motivation subscales were removed from the model.

**Conclusion**: The findings provide tentative evidence supporting CCT at improving everyday functioning and identified possible cognitive domains that best predict life quality. Implications of the findings were discussed further in the discussion chapter. More studies are needed before a firm conclusion can be made about CCT efficacy, and the cognitive domains best predict the quality of life.

**Acknowledgement**

First and foremost, I would like to thank my research supervisors, Dr Fergus Gracey and Dr Saber Sami, and Dr Catherine Ford, programme advisor, for the feedback and support from the start to the completion of my thesis portfolio. I want to express my gratitude to the Cognition and Brain Sciences Unit research team for consenting to share their collected data and their contribution in shaping the research question for the empirical paper. Finally, I would like to acknowledge my family and friends. Without their understanding and encouragement, it would have been difficult for me to complete the thesis on top of the clinical training that I had to do.

**Contents**

## List of Tables

## List of Figures

## List of Appendices

# Chapter 1: Introductory Chapter

## Neurological Conditions and the Ageing Population

Life expectancy worldwide has increased from 66.8 years in 2000 to 73.4 years in 2019 (World Health Organisations [WHO], 2021). While the increase in longevity is certainly worth celebrating, it also means more people would reach the age where neurological disorders become more prevalent (Feigin et al., 2017). Examples of age-related neurological disorders are stroke and dementia, which are commonly associated with increased age (Lipnicki et al., 2017; Béjot et al., 2016). Globally, stroke and dementia were considered the second and seventh leading cause of death, respectively (WHO, 2019). It was projected that the prevalence of stroke and dementia would increase in response to the increase in the ageing population (Wolters & Ikram, 2018; Béjot et al., 2019). Therefore, further examination of these age-related neurological disorders is essential in preparation for the future.

## Stroke and Dementia: A Closer Look

The present thesis focused mainly on stroke and MCI. Dementia is an umbrella term for a collection of progressive illnesses impacting memory, thinking, behaviour and the ability to perform everyday activities (Prince et al., 2014). Prevention and timely diagnosis are the primary intervention approaches to dementia (Livingston et al., 2017). Mild cognitive impairment (MCI) represents the precursor stage between normal cognition to dementia (Duara et al., 2011, Roberts & Knopman, 2013).

MCI is described as a stage in which observable changes are detected in an individual or through objective evidence, with impairment in one or more cognitive domains. At the same time, functional abilities are relatively preserved in MCI (Albert et al., 2011). There has been a large focus on MCI as a target to ameliorate the impact of dementia, as evidence has suggested that those with MCI could potentially revert to baseline cognitive state over time (Koepsell & Monsell, 2012).

Therefore, researchers have looked at MCI as a potential target for the treatment of dementia.

Stroke is defined as "a transient episode of neurological dysfunction caused by focal brain, spinal cord or retinal ischaemia, without acute infarction" (Easton et al., 2009). Previous research has also associated stroke with an increased risk of dementia (Tatemichi et al., 1993; Pohjasvaara et al., 1998; Sachdev et al., 2006). The association could be linked by the commonality that both stroke and specific subtypes of dementia are known to be caused by vascular-related deficits (Savva et al., 2009; Vijayan & Reddy, 2016). By extension, vascular risk factors have also been associated with increased risk of MCI among older adults (Wang et al., 2015). Previous research has associated MCI with post-stroke individuals (Sachdev et al., 2009; Pasi et al., 2012), and the potential for reversibility was similarly observed in a percentage of stroke individuals with MCI (Rasquin, Lodder & Verhey, 2005). Hence, MCI status is not exclusive to dementia.

Given the potential to intervene/prevent or reverse the impact of stroke and dementia, researchers have investigated the cause/root of the disorders and the accompanying deficits. Researchers have posited that timely identification and modification of the impaired cognitions could potentially restore the impairment or protect against further deterioration in functioning or quality of life.

**Quality of Life and the Impact of its Reduction due to Stroke and Dementia**

Neurological disorders, including stroke and dementia, impact multiple aspects of an individual's life. Quality of life (QoL) is an essential parameter for measuring the outcome of modern medicine and highly critical in assessing the multifaceted impact of diseases on an individual's life (Salter et al., 2008). Lower health-related qualities of life were also significant predictors of increased short and long-term mortality among older adults (Brown et al., 2015). Research has looked at various predictors of quality of life like demographic (e.g., age and gender), clinical-related (e.g., stroke severity), environmental (e.g., social support and participation) and individual factors (e.g. coping strategies) (Wang and Langhammer, 2018).

Activities of daily living (ADL) is a critical component known to impact the quality of life (Andersen et al., 2004; Haghoo et al., 2013; Imanishi, Tomohisa & Higaki, 2017). Negative associations were found between impairment in ADL with quality of life (QoL) (Edemekongs & Bomgaars, 2018). Cognitive impairment, a common feature of both stroke and dementia (Sun, Tan & Yu, 2014; Gamir-Morralla et al., 2017), negatively affects ADL performance (Claesson et al., 2005; Urwyler et al., 2017). As a result of cognitive impairment, individuals with stroke or dementia are at higher risk of additional physical and mental deficits like loss of mobility (MacIntosh et al., 2017; Borges, Radanovic & Forlenza, 2015) and depression (Robinson & Jorge, 2016; Ma, 2020).

The increased risk of depressive symptoms and mobility loss could have broader implications like social isolation, resulting in further deterioration of an individual's overall quality of life (Fakoya, McCorry & Donnelly, 2020; Montoya-Murillo et al., 2020). Furthermore, the increased risk of late-life depression was predicted to lead to a substantial increase in the risk of dementia (Leyhe et al., 2017). It is posited that the relationship between dementia and stroke with depression could be bidirectional (Del Zotto et al., 2014; Cipriani et al., 2015). The experienced difficulties and bidirectional relationship could create a feedback loop that further perpetuates the disorder and difficulties experienced. Hence, numerous research studies on treatments and interventions have been done over decades in the hope to counter the wide range of detrimental impacts that stroke and dementia have on individuals.

**Interventions: Starting with the Basics**

One core concept of intervention for stroke and dementia is the notion of brain plasticity, defined as the brain's capacity to show structural and functional changes such as reorganisation of brain networks or formation/elimination of synaptic connections (Zatorre, Fields, & Johansen-Berg, 2012). It was posited that areas of the brain related to different functions could be modified by sensory input, experience, and learning (Merzenich et al., 1983; Jenkins & Merzenich, 1987). Plasticity can be induced at any age, but its mechanism could differ depending on age (Merzenich, Van Vleet & Nahum, 2014).

The concept of plasticity was partly formed from the framework proposed by Hebb (1949). He argued that synaptic connections are strengthened when pre- and postsynaptic neurons are co-activated, occurring between singular or clusters of neurons. Neurons separated by lesions could be reconnected if the neurons are simultaneously activated. Since its inception, Hebb's theory has gained strong evidence through the discovery of long-term potentiation (LTP) of synaptic transmission (Bliss & Gardner-Medwin, 1973; Artola & Singer, 1987; Clugnet & LeDoux, 1990; Caporale & Dan, 2008). LTP showed, on a neuronal level, evidence of Hebb's theory that neurons fired together within a critical time window strengthen synaptic transmission between the neurons, which forms the basis of learning and memory (Ito, 2005). In the context of the interventions, the theory has been applied to the basis of motor recovery (Remsik et al., 2016) through cortical reorganisation, potentially through the mechanism of long-term potentiation (Hara et al., 2015).

The two concepts, Hebbian learning and plasticity, play a role in the 'restoration' approach to rehabilitation. Zangwill (1947) defined restoration as the potential for damaged functions to be recovered through training. The prospect of 'restoring' an impaired function to its former state has fundamental clinical implications. However, restoration provides limited clinical applicability in rehabilitation (Zangwill, 1947).

An alternate approach is 'compensation', whereby psychological functions are reorganised to minimise or circumvent the impact of an impairment (Zangwill, 1947). Like restoration, plasticity and Hebbian learning have roles in the compensation approach as well. However, rather than restoring damaged function, this approach would encourage individuals to use learned strategies like landmarks for navigation (van der Kuil et al., 2018) or use mnemonics as memory aids (Goodwin et al., 2020) to offset the difficulties caused by the impairment. This approach to intervention has shown some evidence of efficacy and was recommended for reducing difficulties due to neurological disorders (Cicerone et al., 2011; Cicerone et al., 2019; Goverover et al., 2018). Furthermore, the compensation approach to intervention is more feasible than restoration. This is because neurophysiological deficits of the disorders (e.g., stroke or dementia) are often irreversible or difficult to 'restore' to a pre-disorder state.

**Concept of Near and Far Transfer Effects**

As more interventions are created, the generalisability of the intervention has become more emphasised by researchers (Bonell et al., 2006). Woodworth and Thorndike (1901) posited that the likelihood of transferability relies on the degree to which the trained and untrained domains have in common. The topic of generalisation was further expanded and elaborated into the concept of 'near' and 'far' transfer effects. Barnet and Ceci (2002) distinguished described 'near' transfer as a generalisation of skills across domains similar to what was trained. On the other hand, 'far' transfer referred to the generalisation of domains related indirectly or weakly with the trained domain.

**A Brief Look at Stroke Interventions**

As the survival rate among stroke individuals improve, the number of individuals living with disabilities due to stroke increases (Carod-Artel et al., 2002). Traditionally, stroke interventions have been primarily focused on motor recovery (Pollock et al., 2014) and the indirect impacts of stroke (e.g., depression, anxiety, or sleep) (Hackett et al., 2008; Knapp et al., 2017; Khot & Morgenstern, 2019). These interventions addressing the direct and indirect impacts of stroke often lead to improvement/recovery of quality of life among stroke individuals (Carod-Artel & Egido, 2009). Regarding motor recovery, stroke interventions follow the main principles mentioned above (i.e., Hebbian learning and brain plasticity). These interventions often involve the practice of either simple motor exercises or task-specific training that focuses on functional motor recovery (Takeuchi & Izumi, 2013).

Functional impairments or ADL in stroke individuals have been linked to cognitive impairments like impaired attention and executive dysfunction (Cumming, Marshall & Lazar, 2013). If ADL impairments are the result of cognitive deficits, improvements in those deficits could, in theory, ameliorate the impairment. This is certainly the line of reasoning based on recent advances in stroke rehabilitation, shifting from using conventional motor training to cognitive training to improve ADL and QoL (van de Ven et al., 2016; Gamito et al., 2017; Bo et al., 2019). Various research has posited executive functioning, working memory, sustained attention (Tomaszewski Farias et al., 2009; Vogt et al., 2009; Fortenbaugh, DeGutis & Esterman, 2017) as possible cognitive domains responsible for QoL. There is still a lack of conclusive evidence on which cognitive domains should be targeted for quality-of-life improvement. The empirical paper in the current thesis aims to look at possible cognitive predictors that are responsible for QoL in the hopes to ascertain the relationship between cognition and QoL.

**A Brief Look at MCI (Dementia) Interventions**

As mentioned above, individuals with MCI have a higher risk of developing dementia (Tschanz et al., 2006). There is yet a 'cure' for dementia (Cations et al.,2018). Hence, research has focused primarily on preventing and managing dementia (Livingston et al., 2017). MCI provides an opportunity to prevent or postpone the onset of clinical dementia (Leifer, 2003) as between 14-40% of them return to normal cognitive functions over time (Koepsell and Monsell, 2012).

MCI interventions primarily focused on improving impaired cognitive domains using cognitive training (Belleville, 2008; Hyer et al., 2016). Previous research has shown task improvement in cognitive training for MCI (Hyer et al., 2016; Belleville et al., 2018; Zhang et al., 2019). There have been numerous debates on the evidence and support for cognitive intervention in general. However, the research on cognitive training has not slowed down and has increased in popularity (Zygouris et al., 2017; Mrakic-Sposta et al., 2018; Liao et al., 2019). However, the quality of current evidence supporting the efficacy and generalisability of cognitive training in MCI remained largely lacking (Gates et al., 2011; Butler et al., 2018). While some evidence supports cognitive training with 'near' transfer effects, more conclusive evidence is still needed to support 'far' transfer effects (e.g., improved functional abilities and quality of life).

With the advancement in technology, there has been a rise in the computerisation of cognitive training. However, the issue of generalisability observed in traditional cognitive training, mentioned above, were extended into computerised cognitive training (CCT) as well (Gates et al., 2019). Additionally, the large variations in CCT intervention characteristics (Schubert, Strobach & Karbach, 2014) and small cohort studies (Hampshire, Sandrone & Hellyer, 2019) affected the reliability and validity of the evidence gathered. Hence, the systematic review in the current thesis attempted to 1) to provide an updated review on of the effects of CCT on everyday functioning in MCI individuals through meta-analysis of available randomised controlled trials (RCTs); and 2) identify methodologies and features of CCT that might serve to improve efficacy.

**Summary of Stroke and MCI interventions.**

The present evidence for the efficacy of stroke and MCI cognitive interventions is limited. For cognitive training to be considered effective, the training would need to be generalisable (near and far transfer effects) to similar but untrained tasks related to the trained cognitive domains (Simons et al., 2016; Lindenberger, Wenger & Lövdén., 2017). Bringing the current evidence on stroke and MCI interventions together, both fields face difficulties providing evidence for 'far' transfer effects, specifically how trained tasks could improve untrained tasks that could improve quality of life or ADL.

From a clinical perspective, there is a real need to improve further the current understanding of cognition and methodology of CCT. This need includes further exploration of QoL as an essential outcome measure encompassing various domains such as mood and social functioning. Additionally, considering the broad negative impact stroke and dementia has on QoL, there needs to be a stronger focus on QoL as primary outcomes of interventions and on further improvement in intervention efficacies for stroke and MCI.

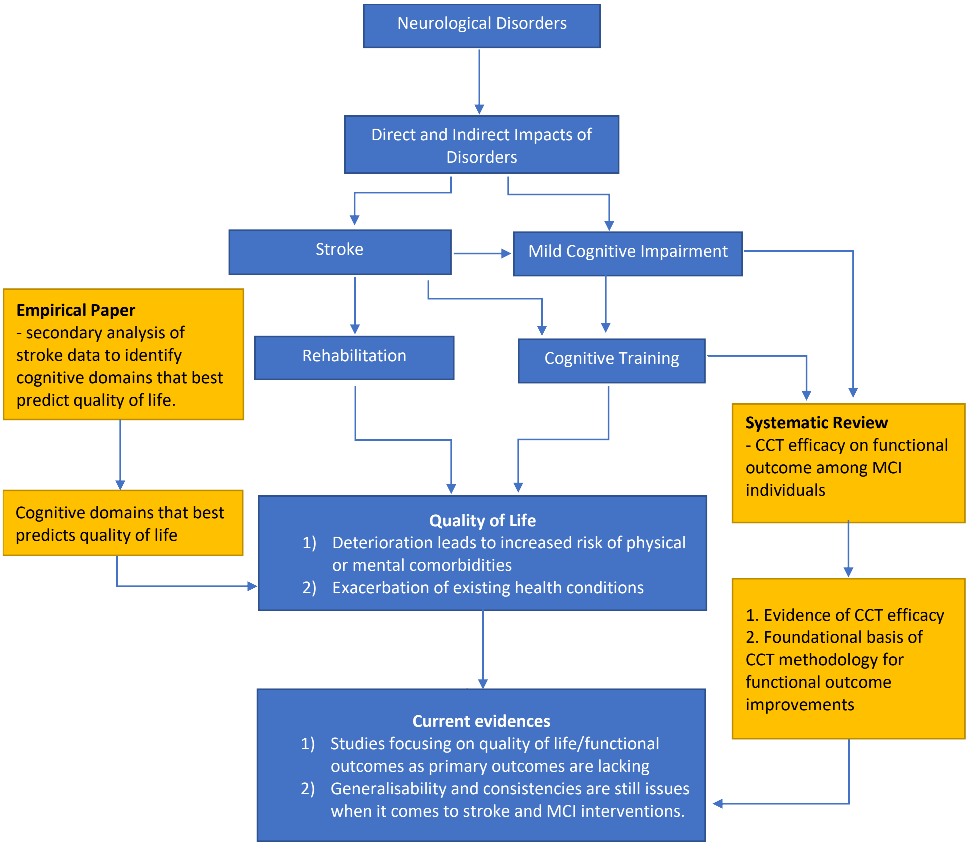
**Thesis Aims and Structure**

The current thesis aims to address two knowledge gaps when it comes to quality of life: 1) provide an updated review on CCT's efficacy concerning QoL and MCI; and 2) gaining a greater understanding of the underlying cognitive domains that best predicts QoL in stroke/MCI individuals. Addressing the gaps could contribute to the field by providing a platform for a stronger focus on QoL with stroke and MCI cognitive interventions. Additionally, this could help identify cognitive domains that would best improve quality of life when targeted.

The thesis is arranged into three main sections: 1) a systematic review discussing the efficacy of CCT for functional outcomes in MCI and the CCT methodologies/characteristics observed in reviewed studies, 2) an empirical paper looking at cognitive predictors of quality of life, focusing specifically on functional outcomes and 3) a discussion and critical appraisal of the results of the two papers as well as considerations for future research. Figure 1 provides a visual representation of how the systematic review and empirical paper could address the gaps within the broader context.

**Figure 1**

Diagram Denoting the Thesis Flow and how the Chapters Fit into the Overall Thesis Portfolio.



# Chapter 2: Systematic Review

## Efficacy of Computerised Cognitive Training on Activities of Daily Living for Older Adults with Mild Cognitive Impairment

Prepared for submission to Neuroscience & Biobehavioral Reviews

## Chapter 2: Systematic Review

# Efficacy of Computerised Cognitive Training on Activities of Daily Living for Older Adults with Mild Cognitive Impairment

Chai Chung Han, Dr Fergus Gracey and Dr Saber Sami

Norwich Medical School, University of East Anglia

Abstract Word Count: 185

Manuscript Word Count: 6197

### Author Note

There is no conflict of interest needed to be disclosed for the current review paper. The review was written as part of the thesis portfolio for the Clinical Psychology Doctorate programme.

Correspondence concerning the review article should be addressed to Chai Chung Han, Norwich Medical School, University of East Anglia, Norwich NR4 7TJ. Email: ccb18zpu@uea.ac.uk

## Abstract

**Background:** Mild Cognitive Impairment (MCI) is a stage before the onset of dementia. Computerised cognitive training (CCT) is used to delay/prevent MCI. However, current evidence supporting CCT's efficacy are lacking. **Objectives**: The present review evaluated CCT efficacy on everyday functioning for MCI and provided a narrative review of the elements fundamental for CCT. **Methods**: Studies with 1) older adults with MCI, 2) CCT interventions, 3) assessed everyday functioning and 4) randomised controlled trials are included. Studies with multidomain tasks that focused primarily on physical interventions were excluded. **Results:** 3618 records were screened against the eligibility criteria, and 128 were selected for full-text screening. 11 studies remained for full-text review. A narrative synthesis was conducted and showed tentative evidence for CCT on improving ADL by focusing on speed of processing. Features like adaptiveness and social groups could contribute to CCT efficacy. **Conclusions:** The findings showed tentative evidence for CCT efficacy in improving ADL among MCI individuals. Social and motivational components could play an integral role in improving ADL in MCI through CCT. More studies are needed before a firm conclusion on CCT efficacy can be reached.

Keyword: *activities of daily living, mild cognitive impairment, computerised, cognitive training, adaptive*

# Efficacy of Computerised Cognitive Training on Activities of Daily Living for Older Adults with Mild Cognitive Impairment

As the number of age-related diseases, such as neurodegenerative disorders (e.g., dementia), increase, more resources would be required to provide adequate treatment and care. Dementia and its associated effects on health and society had been projected to become a significant public health concern as the global number of people living with dementia could increase from 50 million to 152 million in 2050 (Dementia Statistics Hub, 2021). However, there is currently no treatment to cure or significantly slow the condition's progression (Watson et al., 2018).

Mild Cognitive Impairment (MCI) is a transient stage before dementia with one or more cognitive impairments while functional abilities are relatively preserved (Albert et al., 2011). The prevalence of MCI is still debatable due to the variety in classification criteria and setting (Richardson et al., 2019). However, it was suggested that 10 – 20% of individuals over 65 might have MCI (Dementia Statistics Hub, 2018). MCI is associated with an increased risk of dementia (Peterson, 2004). However, 14-40% of MCI individuals' cognition returned to normal over time (Koepsell and Monsell, 2012). Hence, MCI provides an opportunity to prevent or postpone the onset of clinical dementia (Leifer, 2003).

## MCI Interventions

Various forms of interventions have been explored to delay or prevent the progression of MCI. The most recent Cochrane review showed pharmacological interventions as ineffective in slowing MCI progression (Russ & Morling, 2012). Additionally, the review argued that the ineffectiveness and the side effects of those medications do not justify their use. Therefore, non-pharmacological interventions like computerised cognitive training (CCT) have become increasingly popular among researchers as an alternative.

Cognitive training is defined as an intervention consisting of standard tasks that target one or several cognitive domains through repeated and guided practice on standardised exercises (Gate & Valenzuela, 2010). CCT is the computerisation of cognitive training. As more and more people become adept at using technology, CCT provides more avenues to provide care and treatment. CCT enables communication, remote monitoring, and the collection of health data that can be used to deliver optimal and precise care to them (Williams et al., 2017).

Evidence for CCT's efficacy for improving cognition in older adults is mixed. Some reviews provided evidence supporting CCT's efficacy in cognitive improvements among healthy older adults (Lampit, Hallock & Valenzuela, 2014), older adults with MCI (Reijnder, van Heugten & Boxtel, 2013) and those with dementia (Garcia-Casal et al., 2017). However, the quality of available evidence was too low to provide conclusive evidence for CCT's efficacy (Gates et al., 2019a; Gates et al., 2019b). Furthermore, Lampit and colleagues' (2014) review suggested that considerable variation in training design might influence the efficacy of the intervention. Therefore, it might be crucial to consider CCT designs more deeply.

**Different Types of CCT**

Kueider, Parisi, Gross and Rebok (2012) classified CCT into three groups by the type of software used: classic cognitive training tasks, neuropsychological software, and video games. The classic cognitive training focused on improving a specific cognitive domain (e.g., processing speed or attention) through programs delivered by trained professionals personally to either an individual or in a group format (Dunlosky, Kubat-Silman & Hertzog, 2003). Due to the need for qualified individuals to deliver the training, this subtype is not cost-effective. The number of individuals that can be treated is limited to the availability of trained professionals.

Neuropsychological software aimed to improve multiple cognitive domains using various tasks provides real-time feedback and can be adaptive (i.e. allowing individuals to progress at their optimal performance). The software is designed with cognitive enhancement as the central theme. On the other hand, video games focus more on entertainment value than cognitive improvement. Over the last decade, more research has been conducted on approaches to CCT that merged features of neuropsychological software with video games to create an intervention/training that is entertaining and enhances cognition. 'Serious games' describe interventions designed for objectives other than entertainment (Michael & Chen, 2005). Among the many sectors that 'serious games' have been applied, the health sector has used these games to improve individuals' physical or cognitive state (Alvarez & Djaouti, 2012).

**Outcome Measures of Efficacy**

Relevant and sensitive outcome measures are required to demonstrate the efficacy and clinical applicability of CCT (Coster, 2013). The more standard measures of outcome in CCT focused on the cognitive impairment level, looking at an individual's performance in tasks similar to the trained cognitive tasks (Sigmundsdottir et al., 2016). Alternatively, intervention outcomes could also be understood through quality of life (QoL), specifically everyday functioning like activities of daily living (ADL). Edemekong and colleagues (2019) defined ADL as fundamental skills required to independently care for oneself, such as eating, bathing, and mobility. It also included more complex activities (i.e. instrumental ADL) like taking the bus or going grocery shopping independently. ADL could also be understood as participation, defined as an individual's involvement in a life situation (e.g. self-care, domestic life, communication, community, social and civic life). This definition was given by the World Health Organization's International Classification of Functioning, Disability and Health (ICF) (WHO, 2008).

Sood and colleagues' (2019) scoping review of CCT reported that a large proportion of the reported improvements were in performance on tasks similar to the trained cognitive domains. Functional outcomes like ADL or participation were less commonly reported, with only one out of the 17 reviewed studies had assessed ADL. As Sood and colleagues conducted a scoping review, they had not looked at CCT's efficacy.

Traditionally, individuals with MCI were thought not to experience difficulties with ADL (Winbad, Palmer & Kivipelto, 2004; Albert, DeKosky &

Dickson, 2011). However, some evidence suggested that older adults with MCI demonstrated some functional disability compared to controls (Tabert, Albert & Borukhova-Milov, 2002; Pereira et al., 2010). Interestingly, Jefferson and colleagues (2008) compared cognitive healthy older adults with those with MCI. The authors' findings showed no BADL and IADL differences between the two groups through global ADL measures like Lawton and Brody Instrumental Activities of Daily Living and Physical Self-Maintenance Scale. However, there was a strong difference between the two groups when assessed with an informant error-based ADL measure (i.e., Functional Capacities for Activities for Daily Living), which looked at the 'mistakes' an individual made when a task was carried out.

Puente and colleagues' (2014) on MCI and ADL suggested that while older adults with MCI experienced decreased ability to complete IADL, it was unlikely to be detected by questionnaires or self-reports. Based on their findings, the authors proposed that older adults with MCI's difficulties with IADL were more likely to be detected using performance-based testing. The findings from Jefferson et al. (2008) and Puente et al. (2014) suggested that ADL assessments for MCI individuals could be approached from a performance-based perspective focusing on assessing the errors made rather than overall ADL capability.

It was shown that individuals with MCI reported lower QoL in the form of difficulties with ADLs, subjective stress, and depression than those who were cognitively healthy (Stites et al., 2018; Leng et al., 2020). The prevalences of some of these QoL difficulties were observed among MCI individuals: depression (32%), apathy (14.7%) and anxiety (31.2%) (Ismail et al., 2017; Di Iulio et al., 2010; Chen et al., 2018). Negative associations had been found between impairments in ADLs and QoL (Edemekongs & Bomgaars, 2017). The increased risks of late-life depression and negatively impacted cognition were associated with reduced QoL (Lin et al., 2014). While individuals with MCI experienced only mild difficulties in complex tasks, combined with the subjective distress and depression, alongside their potential for continued deterioration, meant that early interventions on MCI were warranted to prevent further deterioration of an individual's QoL and subsequent well-being.

In summary, more CCT intervention studies should incorporate ADL/everyday functioning as outcome measures. The present review has two aims. The first was to systematically review the efficacy of CCT on the everyday functioning of MCI individuals. The second aim was to explore the various elements/features implemented in the CCT by those studies to identify common elements fundamental to CCT' efficacy at improving everyday functioning.

# Method

## Searching

The following databases were searched PsycINFO, PSYCARTICLE, MEDLINE Complete, MEDLINE, PUBMED and Web Of Science to identify relevant studies for the review. The databases were accessed in January 2021. These databases were chosen as they were the most common and frequently cited databases. The protocol was accepted by PROSPERO (ID: CRD42021230630, 22/01/2021). The keywords below were entered as search terms:

i. older adults or geriatric or geriatrics or aging or ageing or senior* or older people

   **AND**

ii. subjective cognitive impairment or age-related cognitive decline or mild cognitive impairment or mci or mild dementia or early-stage dementia or pre-dementia or cognitive dysfunction or memory loss or cognitive impairment

   **AND**

iii. video game training or brain gaming or brain training or cognitive training or memory training or cognitive rehabilitation

   **AND**

iv. activit* of daily living or adl or occupational performance or instrument* activit* of daily living or iadl or every* function* or participation or function* *

**AND**

v. randomi* control* trial* or rct

**AND**

vi. prevention or intervention or treatment or program

## Eligibility Criteria

### *Inclusion Criteria*

Articles were included in the review if they focused on the effect of CCT on individuals with MCI. Given the strong association QoL has with ADL, the main outcome of interest was individuals' everyday tasks performance, defined above as either ADL or participation. These are either assessed directly via objective/subjective measures of ADL (e.g., self-reports or objective behavioural assessment of ADL) or indirectly (e.g., questionnaires that assessed global outcome which incorporated general functional abilities and participation in tasks/activities). These measures are often used before and after an intervention. The search was expanded to include studies published post-2000. The use of technology in healthcare gained popularity over the past decade; therefore, the inclusion criteria of 2000 should capture all CCT studies. The review inclusion criteria were, therefore:

1. Studies that looked at the efficacy of CCT on activities of daily living/participation
2. The population of interest are older adults with MCI.
3. Articles published from 2000 onwards.
4. Articles are written in English from any country of origin.

***Exclusion Criteria***

Studies were excluded if the interventions are multidomain (e.g., cognitive and physical training) that are not primarily focused on computerised cognitive training.

Titles and abstracts were screened for inclusion before full-text screening based on the inclusion/exclusion criteria.

**Selection Process, Data Extraction and Quality Assessment**

The present systematic review followed the PRISMA guidelines (Page et al., 2020). Search results were de-duplicated using a reference manager. 20% of the studies were randomly co-assessed by a research supervisor on the eligibility criteria, quality of the study and data extraction. Disparity or disagreements with ratings were discussed and resolved before proceeding to the next step of the review. Data items like outcome measures, intervention targets and characteristics were extracted from the selected studies. The data from the reviewed studies were assessed for their quality. Quality assessment was carried out using the revised Cochrane risk-of-bias tool for randomised trials (Higgins et al., 2011). The entire process was done using the reference manager, EndNote.

**Narrative Synthesis**

Intervention or session characteristics were extracted and tabulated. The findings were presented and reviewed in a narrative format to summarise the various features used by the RCTs.

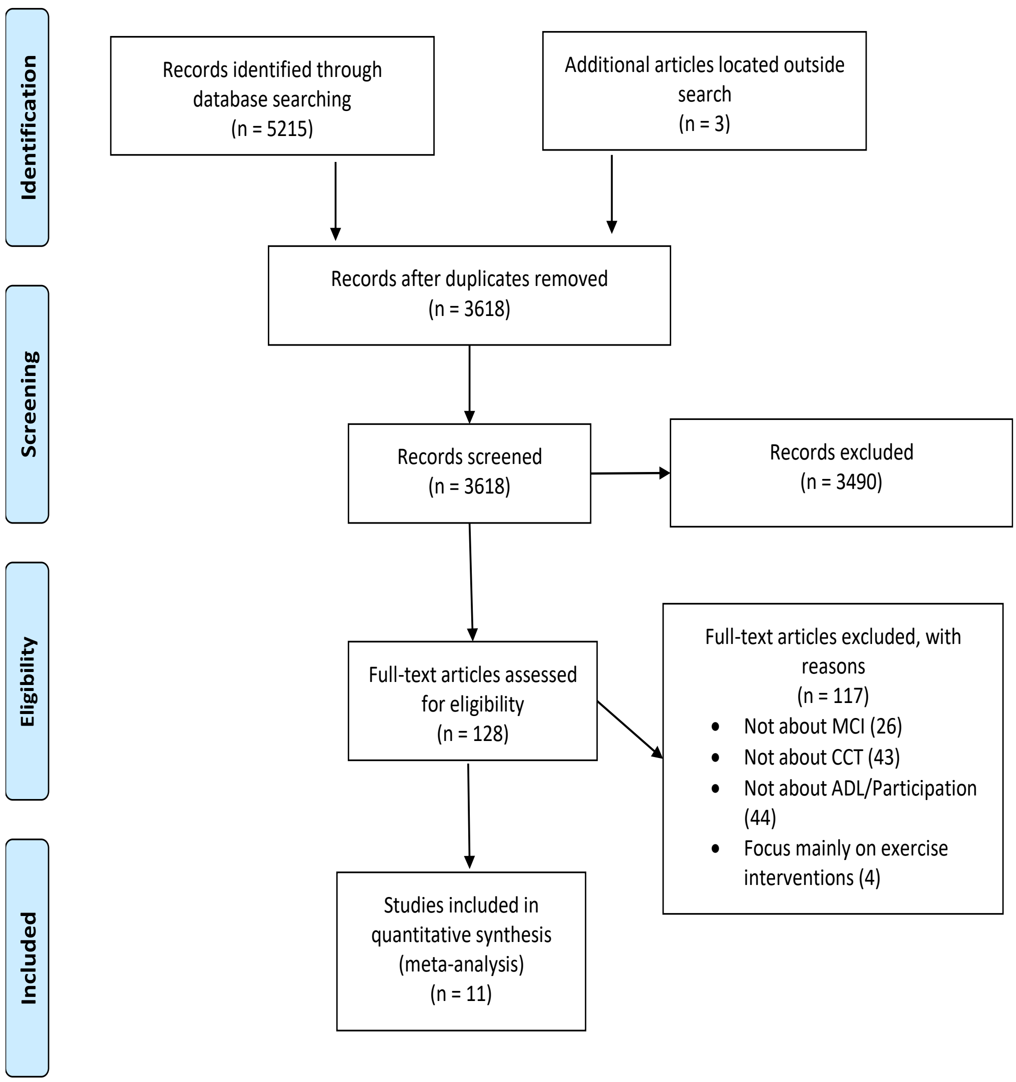
## Results

**Study Selection**

The process of screening and selecting articles for review is summarised in Figure 1 using a "PRISMA" flowchart (Moher et al., 2009). A total of 3618 records were screened against the eligibility criteria, 128 were selected for full-text screening. 11 studies remained for full-text review.

**Figure 1**

*PRISMA flowchart*




## Participant Characteristics

A total of 473 participants were recruited across 11 studies for the present review. Eight of the reviewed studies had a sample size less than 50, the remaining three between 62 and 80 participants. The sample size between intervention and control groups were approximately equal in proportions. The average age for participants was 72.5 years. Gender and sample size proportions were approximately at equal proportion across control and intervention group. The demographic data are shown in Table 1.

**MCI Classifications**

Seven of the eleven studies assessed individuals to have MCI based on a set of criteria from previous research (Petersen et al., 1997; Albert et al., 2011). The criteria laid out in the seven studies included ‘some difficulties with complex IADLs (e.g., paying bills or using public transport) but had not impacted on the individual’s ability to function independently. One of seven studies used deficits in executive function to supplement the MCI criteria used. Two of the remaining four studies identified MCI based on psychometric assessment of the individual’s cognitive ability and does not indicate the individual’s functional ability. One study recruited participants with MCI diagnosis based on the International Classification of Diseases-9$^{th}$ Edition for MCI (World Health Organisation, 1978). The last study had not specified any criteria to assess for MCI. Seven of the studies excluded any participants that experienced any mental health disorders. Two studies excluded participants taking medication for their mental health, while the remaining two had not specified mental health as an exclusion criterion. The classification used could be seen in Table 1.

**Outcome Characteristics**

The outcome measures used to assess everyday functioning in the reviewed RCTs varied from objective assessments of ADL to unvalidated questionnaires. The most common and objectively valid outcome measure used was the Timed Instrumental Activity of Daily Living (TimedIADL) (3/11). Two other studies used Lawton's IADL scale and Bristol Activity of Daily Living Scale, which are self-reported measures of ADL. Six other studies used measures that indirectly assessed everyday functioning/ADL (e.g., QoL, attention, memory, or health perspective). The RCTs (Weng et al., 2019) used custom questionnaires that had not been psychometrically validated.

The reviewed studies assessed ADLs as a secondary outcome. Additionally, the quality of evidence gained from the current review could be impacted by the measures used, which varied in reliability and validity. In summary, the variety suggested the need for standardisation of ADL assessment for CCT.

**Risk of Bias**

Table 2 shows the quality of the 11 reviewed studies assessed using Cochrane's Risk of Bias tool (Sterne et al., 2019). Interestingly, even with inclusion criteria for publication date ranging between 2000-2020, the first RCT looking at CCT on ADL on MCI appeared in 2012, but publication only started increasing in frequency post-2016. Of the 11 studies, three studies were rated as having some concerns. For Valdes and colleagues' (2019) study, there was some concern about how the data was handled. The data obtained for the analysis was from a large cross-sectional longitudinal study that collected various physical and cognitive measures and training performance. Park and Park's (2018) study employed carer-based measures which might not reflect accurately participants' perceived experience and improvements.

It is difficult to ascertain if all the reviewed studies followed analysis plans that were set out prior as the current review had no access to the study protocols. Combined with the large variation in study methodology, the overall quality of the reviewed studies was moderate at best. The variation meant that many confounds could not be accurately determined on their specific role in the effectiveness of CCT on ADL. Additionally, most if not all of the reviewed studies did not report sample size calculation. Therefore, the current review does not know if the studies met the required sample size for power, which brings the results into question. Hence, care is needed when interpreting them (Faber & Fonseca, 2014).

**Main Results**

Table 2 showed the Hedges' g of each reviewed study, type of intervention, outcome measures used to assess ADL, and the intervention's characteristics, including the different implemented features. For the reviewed studies, Hedges' g was observed to have a wide range, between -0.172 to 0.3. Heterogeneity was assessed statistically using the Dersimonian-Laird method. The

Q value showed non-significant heterogeneity; $Q(df = 9) = 1.99$, $p = .99$, which indicated that the measures used in the reviewed studies assess a similar construct, i.e. everyday functioning. However, the methodologies and measures used in the reviewed studies varied widely. Therefore, it was determined that a narrative synthesis might be more suitable for the current review than a meta-analysis.

**Table 1**

*Demographic data extracted from reviewed studies*

| Author | Total Sample size (N) | Sample size for intervention (n) | Sample size for control (n) | Mean Age of Sample | Gender proportions (F) (%) [Intervention vs Control] | MCI Classification |
|---|---|---|---|---|---|---|
| Valdés, Andel, Lister, Gamaldo, & Edwards (2019) | 49 | 24 | 25 | 75.18 | 45.8 \| 32 | Cognitive psychometric data |
| Lin, Heffner, Ren, Tivarus, Brasch, Chen, Mapstone, Porsteinsson & Tadin (2016) | 21 | 10 | 11 | 73 | 49.95 \| 55.5 | MCI criteria from Albert et. al., 2011 |
| Djabelkhir, Wu, Vidal, Cristancho-Lacroix, Marlats, Lenoir, Carno & Rigaud (2017) | 19 | 9 | 10 | 76.7 | 70 \| 60 | MCI criteria from Petersen et. al., 1997 |
| Manenti, Gobbi, Baglio, Macis, Ferrari, Pagnoni, Rossetto, Di Tella, Alemanno, Cimino, Binetti, Iannaccone, Bramanti, Cappa & Cotelli (2020) | 49 | 18 | 17 | 76.5 | 27.78 \| 58.82 | MCI criteria from Petersen et al., 1997 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Law, Mok & Yau,(2019) | 29 (but not full total as it includes other intervention) | 15 | 14 | 76 | 58.62 | MCI criteria from Albert et al., 2011 |
| Oh, Seo, Lee, Song & Shin (2018) | 42 | 18 | 16 | 59.435 | 50 \| 56.25 | N/A |
| Hughes, Flatt, Fu, Butters, Chang, & Ganguli (2014) | 20 | 10 | 10 | 77.35 | 80 \| 60 | Cognitive psychometric data |
| Gagnon & Belleville (2012) | 24 | 12 | 12 | 67.71 | N/A | MCI criteria from Petersen et al., 1997 and executive deficits |
| Hagovska & Nagyova (2017) | 80 | 40 | 40 | 67.09 | 45 \| 52.5 | ICD-9 diagnosis of MCI given by clinicians |
| Weng, Liang, Xue, Zhu, Jiang, Wang, & Chen (2019) | 62 | 33 | 29 | 81.27 | 87.88 \| 96.55 | MCI criteria from Albert et al., 2011 |
| Park & Park (2018) | 78 | 39 | 39 | 67.3 | 48.72 \| 43.59 | MCI criteria from Petersen et al., 1997 |

**Table 2**

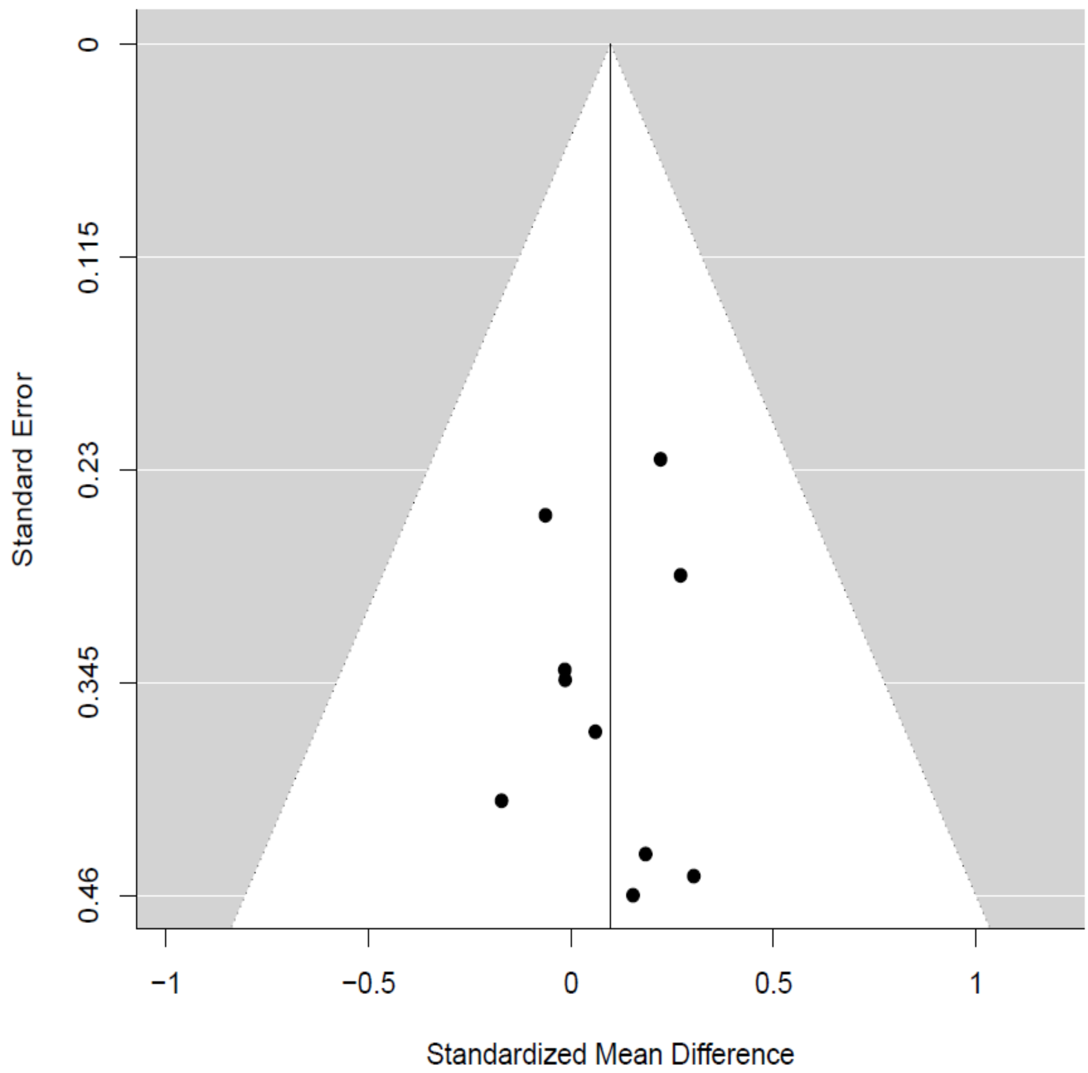
*Level of quality assessment based on Risk of Bias tool by Cochrane*

| Author | Randomisation process | Deviations from intended interventions | Missing outcome data | Measurement of the outcome | Selection of the reported result | Overall |
|---|---|---|---|---|---|---|
| Valdes et al. 2019 | Low | Low | Low | Low | Some concerns | Some concerns |
| Lin et al. 2016 | Low | Some concerns | Low | Low | Some concerns | Some concerns |
| Djabelkhir et al., 2017 | Low | Low | Low | Low | Low | Low |
| Manenti et al., 2020 | Low | Low | Low | Low | Low | Low |
| Law et al., 2019 | Low | Low | Low | Low | Low | Low |
| Oh et al., 2016 | Low | Low | Low | Low | Low | Low |
| Hughes et al., 2014 | Low | Low | Low | Low | Low | Low |
| Gagnon and Belleville, 2012 | Low | Low | Low | Low | Low | Low |
| Hagovska et al. 2017 | Low | Low | Low | Some concerns | Low | Low |
| Weng et al., 2019 | Low | Low | Low | Low | Low | Low |
| Park and Park, 2018 | Low | Low | Low | Low | Some concerns | Some concerns |

Note. The quality rating is ranked via levels of risks. In ascending order of risk of bias, the order is Low – Some Concerns – High Concerns.

**Figure 2**

*Funnel plot visualising possible publication bias .*




**Intervention Characteristics**

***Session Characteristics.***

Tables 4 and 5 show the data extracted from the reviewed studies for both CCT and control groups. The number of sessions of CCT ranged from 6 to 40 sessions, with the majority of sessions (6 /11) lasting one hour; two of the studies sessions took 1.5 hours while the remaining three studies were short (i.e., 20-30 minutes). It was observed that between 10 to 30 sessions and spread across several weeks (i.e., sessions were once or twice a week) showed positive Hedges' g compared to interventions with extended sessions (i.e., >40 weeks).

The most common mode for delivering the interventions was via computer and keyboard (7/11) followed by touch screen (2/11). The remaining two studies used the Wii consoles and computer screens with large buttons. There was no discernable pattern in which the mode of delivering the interventions showed better efficacy. Additionally, the session durations varied from 5 to 90 minutes. Similar to the mode of delivery, there was no distinctive pattern that could be observed between session duration and CCT effectiveness.

***Adaptiveness.***

The first common feature present in most reviewed studies was task adaptiveness (6/11), which is the ability to personalise exercises to match the performance of each individual. Hence, tasks get progressively more difficult as the person improves. Three of the six intervention that has adaptive features showed improvement in outcomes compared to the comparison group. Three studies defined the optimal performance set for adaptive training. Valdes and colleagues (2019), Hedges' g = 0.27, defined 75% correct response as optimal performance. However, Hagovska and colleagues (2017), Hedges' g = 0.22, and Lin and colleagues (2016), Hedges' g = 0.18, provided set (e.g., easy, medium, hard) difficulties but not how the parameters were established (e.g., error rate or success rate). Therefore, the set difficulty level might not be fine-tuned to tailor the task to each individual's ability accurately. The remaining three studies did not mention how adaptiveness was promoted (Oh et al., 2018; Manenti et al., 2020; Park & Park, 2018). Interestingly, virtually no differences were observed in the two reviewed studies (Oh et al., 2018; Manenti et al., 2020) that had not specified how adaptiveness was promoted. Hedges' g was not calculated in Park and Park (2018) as the study compared two different CCT groups.

***Cognitive Targets.***

Four studies used single-domain cognition as intervention targets, while the remaining seven focused on multiple cognitive domains. The attentional domain (8/11) was the most common intervention target, followed by memory (i.e., long and short-term memory) (6/11). Visuospatial abilities were cognitive targets in five studies, while executive functions as intervention targets were the least common (3/11). The extracted data suggested that interventions focusing on improving the single cognitive domain 'speed of processing' showed the largest effects (Hedges g = 0.303, 0.271 and 0.184; Hughes et al., 2014; Valdes et al., 2019; Lin et al., 2016) compared to other studies which targeted multiple and other domains.

On the other hand, CCT interventions that targeted cognitive domains like attention or working memory showed minimal improvement or worse performance than the control groups. Hagovska and Nagyova’s (2017) CCT intervention, CogniPlus, was the only exception with Hedges’ g = 0.221 compared to the control group. The study trained other cognitive domains (e.g., executive function and visual-motor coordination) in addition to the two domains specified above. Hence, based on the data extracted, CCT interventions targeting single domain ‘speed of processing’ showed the strongest effects than other single cognitive domain interventions. Only one out of seven (Hagovska & Nagyova, 2017) multi-domain CCT interventions showed an effect at improving ADL. More studies are warranted before any conclusion can be said on effective cognitive targets for CCT intervention.

***Miscellaneous Intervention Characteristics***

Other less common characteristics included guided/feedback by trainer/therapist (4/11) or conducting CCT in group settings (2/11). Guidance from trainer/therapist varied from weekly check-ins with participants (Oh et al., 2018), having the interventions supervised (Valdes et al., 2019; Manenti et al., 2020), to having live feedback (Manenti et al., 2020). Among the reviewed studies that adopted these characteristics, only one study (Valdes et al., 2019) showed a positive effect size, Hedges’ g = 0.27. Out of the four studies that adopted trainer/therapist, only Valdes and colleague's intervention study showed a positive effect, suggesting that the involvement of trainer/therapist in a supervisory role has minimal impact on CCT efficacy.

Two studies adopted group settings as part of the intervention characteristics (Hughes et al., 2014; Djabelkhir et al., 2017). The two studies encouraged participants to interact with each other. In Hughes and colleagues' intervention, participants trained together and competed with other groups, Hedges' g = 0.3. Djabelkhir and colleagues' included feedback and group discussion at the end of each training session, Hedges' g = 0.15. An important distinction between the two studies is the role of social components play in the intervention. Participants in the Djabelkhir and colleagues study had 15 minutes each session for group interaction. In contrast, participants in Hughes and colleagues were constantly interacting with each other within their group and with other groups. Both studies showed small positive effect sizes, suggesting that social components might enhance CCT efficacy at improving ADL/participation.

***Intervention Characteristics Summary***

Based on the data extracted from the reviewed studies, the current findings suggested tentative evidence that CCT interventions that targeted 'speed of processing' yielded the strongest effects in ADL improvement compared to control groups. Based on the reviewed studies, interventions that targeted attention and working memory were not effective cognitive targets. Multi-domain CCT might be more ecologically valid or have higher transferability than single domain CCT. However, more studies were warranted to investigate multi-domain CCT interventions as everyday functions are rarely single-domain tasks. Adaptive training was the most common feature adopted. However, the feature's contribution to CCT efficacy cannot be concluded due to inadequate evidence about the adaptive mechanism. The tentative positive result from two studies suggested that the inclusion of group features might contribute to CCT efficacy. Intervention efficacy was not affected by other intervention characteristics like session duration and mode of delivery.

**Table 3**

*Extracted data from the 11 reviewed studies arranged in descending order of effect size for the CCT group.*

| | | | | | **Computerised Cognitive Training** | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Author** | **Hedges' g (between group)** | **Glass' delta (within group)*** | **Intervention** | **Outcome measures** | **Cognitive Target (e.g. working memory, processing speed)** | **Number of sessions** | **Session duration** | **Interface (e.g. touch screen, eye movement)** | **Features added onto intervention** |
| Hughes, Flatt, Fu, Butters, Chang, & Ganguli (2014) | 0.303 | 0.091 | Nintendo Wii™ gaming console | Timed IADL | Attention, Speed of Processing | 24 session (once a week for 24 weeks) | 90 minutes | Wii Console | Group tournament to promote interest. Split further into various stable groups of 3-4 members. |
| Valdés, Andel, Lister, Gamaldo, & Edwards (2019) | 0.271 | 0.787 | Modified UFOV | Timed IADL | Speed of Processing Test | 10 Sessions | 1 hour: 10-15 minutes of discussion about topics relevant to training + 45-50 minutes of training | Computer and Keyboard | Adaptive (increase difficulty when reaching 75% accuracy)<br><br>Guided by trainer |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Hagovska & Nagyova (2017) | 0.221 | 0.026 | CogniPlus | Bristol activities of daily living scale (BADLS) | Multiple cognitive domains | 20 sessions over 10 weeks | 30 minutes: Each type of cognitive sub-programme lasted for 5–10 min during a single session. During one session, only attention, short-term and long-term memory were trained; Executive functions and visual-motoric coordination were trained at the following session. All of the cognitive functions were trained during each week. | Computer and Keyboard | Adaptive |
| Lin, Heffner, Ren, Tivarus, Brasch, Chen, Mapstone, Porsteinsson & Tadin (2016) | 0.184 | 0.24 | Posit Science included five training tasks: Eye for detail, Peripheral challenge, Visual sweeps, Double decision, and Target tracker. | TimedIADL | Vision-based speed of processing | 24 Sessions (4 days/week for 6 weeks) | 1 hour | Computer and Keyboard | Adaptive |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Djabelkhir, Wu, Vidal, Cristancho-Lacroix, Marlats, Lenoir, Carno & Rigaud (2017) | 0.153 | -0.023 | Computerised cognitive exercises selected from the Institution version of KODRO (Altera-Group, Paris, France). The web-based platform provided several applications tailored to older adults. | Quality of life scale for older French people | Several cognitive domains (not specified which domain) | 12 sessions | 90 minutes | Touch Screen | Group discussion |
| Law, Mok & Yau,(2019) | 0.06 | 0.234 | Computerised Cognitive Training | Lawton IADL | Training of attention, memory, executive function, and visual-perceptual function in a group of 4–6 | Total 12 sessions) supervised by an occupational therapist for a total of 8 weeks. | 1 hour | Computer | N/A |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Oh, Seo, Lee, Song & Shin (2018) | -0.014 | -0.075 | 'SMART' | Multifactorial Memory Questionnaire (MMQ): MMQ-A (Ability), which assesses the frequency of memory-related problems experienced in daily life | Attention and working memory are known to be closely associated with general memory function | 40 (5 days a week for 8 weeks) | (15–20 minutes) | Touch Screen | Variety of levels, but task difficulties increase according to a schedule. Weekly participant check-ins |
| Manenti, Gobbi, Baglio, Macis, Ferrari, Pagnoni, Rossetto, Di Tella, Alemanno, Cimino, Binetti, Iannaccone, Bramanti, Cappa & Cotelli (2020) | -0.015 | -0.42 | Clinical Virtual reality rehabilitation system (Clinic VRRS) versus Home-Based Cognitive VRRS Treatment (Tele@H-VRRS) | Everyday Memory Questionnaire + Quality of Life in Alzheimer's Disease | Memory, visuospatial abilities, attention and executive functions | 12 sessions over 4 weeks + 36 sessions - 3 sessions/ week over 3 month | 60-min sessions: 10 minutes for each six tasks. All exercise tasks will be completed six times | Computer Screen | Feedback performance was given to participants. Progress monitoring by a therapist. Adaptive and tailored to baseline characteristics. Addition of home-based intervention that has similar but different tasks. |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Weng, Liang, Xue, Zhu, Jiang, Wang, & Chen (2019) | -0.063 | 0.142 | A custom program made by Zhejiang University and Nanjing Zhihui Education Technology Company, Limited. | Weng and Huang's Alzheimer's Disease Rating Scale | Working memory | 8 weeks | 2 times/week for 40–60 min | Computer and keyboard | None reported |
| Gagnon & Belleville (2012) | -0.172 | 0.023 | Traditional Computerised Cognitive Training - Variable changes in task rules | Divided Attention Questionnaire (DAQ) | Attention | 6 sessions over two weeks | 1 hour | Keyboard and Computer | Variable Rules (task difficulties changes spontaneously)<br><br>Breaks are given 1/3 and 2/3 into the training<br><br>Supervised |
| Park & Park (2018) | N/A | 0.012 | CoTras program (Netblue, Korea) made for Korean | SF-36 Health Form | Attention, memory, and visual-spatial abilities. | 30 sessions, three days a week for 10 weeks | 30 minutes: 10 minutes on each cognitive domain (i.e. attention, memory and visual-spatial). | Computer Screen with large buttons for ease of use | Adaptive |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Park & Park (2018) | 0.014 | Nintendo Wii™ gaming console | SF-36 Health Form | Attention, memory and visual-spatial | 30 sessions, three days a week for 10 weeks | 30 minutes: 10 minutes on each cognitive domain | Computerised/ VR | Wireless controller |

Note: The effect sizes were not extracted directed from the reviewed RCTs. The effect sizes were derived from the mean, standard deviation, and sample size between intervention and control groups post-intervention. * The column entry is the Glass' delta that looks at pre-post effect size.

**Table 4**

*Extracted data from the 11 reviewed studies arranged in descending order of effect size for control group.*

| | | | **Control** | | | |
|---|---|---|---|---|---|---|
| **Author** | **Control used** | **Cognitive Target (e.g. working memory, processing speed)** | **Number of sessions** | **Session duration** | **Delivery method** | **Interface used (e.g. touch screen, eye movement)** |
| Valdés, Andel, Lister, Gamaldo, & Edwards (2019) | Practice Computer skills such as an introduction to computer hardware, how to use a mouse, how to acquire and use an email account, and how to access and use web pages. | General Cognition | 10 Sessions | 1 hour: 10-15 minutes of discussion about topics relevant to training + 45-50 minutes of training | Computerised | Computer and Keyboard |
| Lin, Heffner, Ren, Tivarus, Brasch, Chen, Mapstone, Porsteinsson & Tadin (2016) | Online crossword, Sudoku, and solitaire games were used. Chosen to: 1) control for computer/online experience and amount of time; 2) simulate participants' everyday mental activities, and 3) entertain participants to prevent dropping out | General Cognition | 24 Sessions (4 days/week for 6 weeks) | 1 hour | Computerised | Computer and Keyboard |

| | | | | | | |
|---|---|---|---|---|---|---|
| Djabelkhir, Wu, Vidal, Cristancho-Lacroix, Marlats, Lenoir, Carno & Rigaud (2017) | Computerised Cognitive Engagement | N/A | 12 sessions | 90 minutes | Computerised | Ipad |
| Manenti, Gobbi, Baglio, Macis, Ferrari, Pagnoni, Rossetto, Di Tella, Alemanno, Cimino, Binetti, Iannaccone, Bramanti, Cappa & Cotelli (2020) | (Clinic-TAU) - Group Cognitive stimulation group | Learning cognitive strategies and use external aids. Reality orientation therapy, reminiscence therapy, paper and pencil exercises and metacognitive training | 12 sessions over 4 weeks. | 60 minutes | N/A | Group sessions led by mental health professionals |
| Law, Mok & Yau,(2019) | Waitlist | N/A | N/A | N/A | N/A | N/A |

| | | | | | | |
|---|---|---|---|---|---|---|
| Oh, Seo, Lee, Song & Shin (2018) | FitBrains or Waitlist (unsure) | Concentration, Speed, Memory, Visual, Logic | 40 (5 days a week for 8 weeks) - Participants are asked to complete each task twice due to the task being shorter than SMART. | (15–20 minutes) | Computerised but Smartphone | Touch Screen |
| Hughes, Flatt, Fu, Butters, Chang, & Ganguli (2014) | Healthy Aging Education Program (HAEP) + Jeopardy tournament to match Wii Group | | | | Group-based. | |
| Gagnon & Belleville (2012) | Traditional Computerised Cognitive Training with a fixed rule | Attention | 6 sessions over two weeks | 1 hour | Computerised | Keyboard and Computer |
| Hagovska & Nagyova (2017) | Physical activity only which is provided to the intervention group as well. | | Daily for 10 weeks | 30 minutes | Supervised | |
| Weng, Liang, Xue, Zhu, Jiang, Wang, & Chen (2019) | Mental leisure activities (MLA) | Simulate participants' everyday mental activities | 8 weeks | 2 times/week for 40–60 min | Researchers or community workers conduct activities | Face to Face |

Note: The effect sizes were not extracted directed from the reviewed RCTs. The effect sizes were derived from the mean, standard deviation, and sample size between intervention and control groups post-intervention.

## Discussion

The initial plan for the review was to conduct a meta-analysis to ascertain the efficacy of CCT interventions on improving ADLs among MCI individuals. Statistically, the reviewed studies showed strong homogeneity. However, due to large variations in the assessments used, the intervention methodologies and characteristics, it was determined that a narrative synthesis might be a more appropriate approach to answering the two aims.

The review's key findings suggested that single-domain interventions focused on ‘speed of processing’ showed the biggest improvement in ADLs compared to controls. The review also showed tentative evidence of strong effect size for multi-domain CCT interventions. However, the amount of evidence (one of out seven studies) from the review warranted further research before a conclusion could be made. The adaptiveness of intervention was most common, but more studies were warranted before any conclusion could be made on the feature’s contribution to CCT efficacy. Finally, preliminary evidence suggested group features within CCT intervention could enhance CCT efficacy at improving ADL among MCI individuals. All the reviewed studies looked at ADLs secondary outcomes and were measured using a variety of ADL assessments. The following section served to further elaborate on the findings observed from the synthesis.

## Findings of the Narrative Synthesis

### *Target Cognitive Domains*

The reviewed studies showed that the three studies that aimed to improve processing speed showed positive effect sizes compared to other cognitive domains such as attention or executive functioning. Targeting speed of processing could improve global cognition as suggested by the 'speed of processing theory', which posited that the generalised slowing of cognition is the fundamental reason for cognitive decline (Birren, 1974). Additionally, improvement in processing speed has been associated with ADL (Ball, Edwards & Ross, 2007).

On the other hand, CCTs targeting executive functioning and attention showed poor efficacy compared to the control groups. There is a lack of evidence examining CCTs targeting executive functioning/attention to improving ADL/participation. Interestingly, previous research has linked attention with processing speed (Tunnerman, Petersen & Scharlau, 2015). In their CCT study, Burge and colleagues' (2013) showed that processing speed training improved the attentional domain. This could suggest interventions that target processing speed could also be training attention. Hence, the poor efficacy of attentional training in the current review does not suggest that attention does not improve ADL/participation. Furthermore, Peers and colleagues (2018) study suggested that both spatial and non-spatial aspects of attention could benefit functional recovery in stroke rehabilitation. Additionally, EF has been closely associated with attention. Hence, more studies are still warranted regarding attention and EF as viable targets for CCT intervention effects on ADL/participation measures.

***Adaptiveness***

As for the second aim, task adaptiveness was a common characteristic used in many reviewed RCTs. Adaptive learning ensures continuous and optimal performance for individuals by minimising the difference between actual and target performance (Shute, Ke & Wang, 2017). Six studies adopted adaptive features, but only three studies showed positive effects of CCT with improving ADL/participation. Various studies have shown the effectiveness of adaptive training programs, either in education or neurorehabilitation, over non-adaptive programs (Smith et al., 2009; Pedulla et al., 2016; Hooshyar, Yousefi & Lim, 2017).

On the other hand, one study argued against adaptive learning' efficacy. Colom and colleagues' (2013) study stated that the adaptive working memory task does not improve fluid intelligence, on a psychological construct level, significantly. Previous research showed a strong association between working memory and fluid intelligence (Fukuda et al., 2010). However, it could be argued that the ineffectiveness of adaptive training in Colom and colleagues study could be due to the lack of generalisation of the trained tasks to fluid intelligence.

In the context of the present review, if implementing adaptive learning increases the effectiveness of an intervention, there should not be sizeable observable variability in CCT efficacy. Granted, other confounds like intervention type or measures used in the reviewed studies could explain the variable efficacy.

The variability in efficacy could also be due to how adaptiveness was defined. Wilson and colleagues (2019) posited 85% as the optimal training accuracy to facilitate training based on their results from machine learning. The 85% accuracy for optimal learning was known in Psychology and Cognitive Science, with experiments commonly designed to produce the same level of accuracy (Garca-Perez, 1998; Kumar, Packer & Koller, 2010). Arbitrary difficulty level (e.g., easy, medium and hard) could not capture optimal performance for individuals that Wilson and colleagues posited. On the other hand, this fine level of adaptiveness might not be necessary for CCT. Lin and colleagues' study observed a relatively strong positive effect size in improvement in ADL/participation using Posit Science, which employed set difficulties. Future studies comparing the different types of adaptiveness mentioned could be interesting and helpful to distinguish their effectiveness as a CCT element.

### ***Social Components***

Two reviewed RCTs that included social components showed a small to medium positive effect size for CCT compared to a control group. However, the social components were encouraged differently in these studies. Hughes and colleagues (2014) used group learning and competition, while Djabelkhir and colleagues (2019) used feedback and group discussion at the end of each training session. The findings are consistent with previous research that suggests the lack of social contacts among older adults is a significant modifiable factor influencing ADL deterioration and QoL (Chang et al., 2017; Cintra et al., 2017; Ćwirlej-Sozańska et al., 2019). A cross-sectional study supported the notion that social participation in recreational activities could delay the onset of ADL deterioration associated with ageing (Rubio, Lazaro & Sanchez-Sanchez, 2009). Yates and colleagues (2017) suggested that poorer social functioning mediated increased depression and the rate of MCI conversion to dementia among older adults.

Given the quality and a small number of studies that had social components, the findings are tentative. Hence, more research is needed to ascertain the causal and mediating relationship between social functioning, depression, ADL and MCI. In the context of intervention, it is essential to clarify the roles of each factor to allow researchers to create a more focused and effective intervention.

***Motivation***

The social component implemented by Hughes and colleagues' study could also serve a secondary purpose, motivation. In stroke rehabilitation, higher degrees of motivation were associated with better ADL performance among individuals with stroke and increased

QoL (Lee & Kim, 2014; Haghgoo et al., 2013). As mentioned previously, a negative association was observed between ADL impairment with QoL (Edemekong & Bomgaars, 2017), increasing the risk of late-life depression (Lin et al., 2014). Older adults with depressive symptoms often exhibit difficulties with motivation, retaining interest and generalised fatigue when participating in physical activities (Knapen et al., 2009). Participants in Hughes and colleagues' study played interactive games in groups of 3-4 members, and the groups competed in a 'Wii tournament' every ten weeks. The set-up aimed to promote social interaction between participants. However, it could also enhance motivation and interest via competition.

Anderson-Hanley and colleagues' (2011) study on exergaming showed a significant group effect for levels of competitiveness. The authors suggested that participant competitiveness served as a moderating factor that maximises participation effort (i.e., motivation). The competitive element could address the motivation and interest issue individuals with MCI may encounter due to ADL deterioration. Therefore, inference can be made that increased motivation through competitive elements could also promote intervention adherence. This could lead to increased ADL participation and thereby increasing the QoL among individuals with MCI. Hence, future research could consider the promotion of motivation among older adults as an additional factor in CCT intervention.

**Outcome Measures used**

Current methodological structure and outcome measures used in CCT studies have focused on assessing cognitive outcomes using domain-specific cognitive measures. Specific cognitive measures like verbal fluency and digit span tasks (Sood et al., 2019) were commonly used in CCT and might be more sensitive at showing any cognitive gains from the intervention. Therefore, a more specific ADL measure like the Timed IADL might be more sensitive to possible functional gains from CCT.

The present review showed reviewed studies that employed more ecologically valid measures of ADL/participation (e.g., TimedIADL or Bristol Activities of Daily Living Scale) reported higher CCT efficacy. Indirect but validated measures like the one used by Djabelkhir and colleagues might not accurately assess the outcome of interest. However, the findings of the review are tentative at best due to the large variability. Nonetheless, future research could consider using more 'direct' and specific measures of ADL/participation in CCT.

**Interpreting the Low Effect Size Observed**

Two aspects need to be considered when interpreting the low effect size observed in the reviewed studies. The first being that MCI individuals typically do not have gross difficulties with living independently. The impairment in ADLs was typically in the realm of complex ADLs like paying bills, taking medication or using public transports (Tabert, Albert & Borukhova-Milov, 2002; Pereira et al., 2010). This could potentially cause a ‘ceiling effect’ when basic ADLs were assessed, leading to small or no effect size observed.

Secondly, MCI individuals might not be aware of any ADL difficulties. This could be in relation to the reason stated above (i.e., do not experience gross difficulties with independent functioning). Alternatively, researchers had also suggested that MCI individuals have a tendency to overestimate their cognitive ability and were unaware of their impairments in everyday functioning (Fragkiadaki et al., 2016; Steward, Bull & Wadley, 2019). Therefore, it could be hypothesised that they would be less aware of any errors made when during complex tasks, which could be reflected in possible inflated self-reports of IADL functioning. Hence, any improvement or reduction in ADL performance might be difficult using self-reports.

Taking the two points mentioned above, future studies on CCT could implement more objective, performance-based measures of ADLs like ‘TimedIADL’ or informant-based measures like the ‘Functional Capacities for Activities for Daily Living Scale’. Future studies comparing these measures with self-report measures used among MCI and cognitively healthy older adults might provide further evidence on the most appropriate measures to detect IADL changes post-intervention. Alternative, a proxy task like the Multiple Errands Test (Shallice and Burgess, 1991) that measured executive functioning, could be used as the cognitive process has been intrinsically linked to IADL (Nguyen et al., 2020). This could be a crucial aspect that needed to be considered before CCT interventions could be assessed for their efficacy.

**Strengths and Limitations**

A strength of the present review was that the current study provided further details on the specific intervention elements that could be improved to increase the robustness of the findings. The present review has identified possible features that were worth further investigating, like adaptiveness and cognitive targets.

The present review also has limitations that need to be considered when interpreting the data. Having only 20% of the studies subjected to a second reviewer might not have maintained the reliability and validity of the present review's results. Involving a second reviewer throughout the entire review process could have improved the robustness and reliability of the review methods. Additionally, a narrative synthesis was determined to be more suitable due to the large variability observed in the characteristics of the studies. The review included a wide range (direct/indirect) of measures to assess ADL/participation in the RCTs. The 'indirect' measures might not accurately assess ADL/participation compared to 'direct' measures like Timed IADL. Including only 'direct' measures of ADL/participation could have improved the validity of the review.

Some limitations of the included studies were observed. The number of participants in the reviewed studies was relatively low, which seems typical of cognitive intervention studies. The relatively low numbers and large variability in intervention methodology mean that it is difficult to reliably conclude the efficacy of CCT intervention for older adults with MCI.

There is a query about the validity of the ADL assessment used by the reviewed studies. Timed IADL objectively evaluates an individual's ADL performance (Owsley et al., 2002). In contrast, brief self-report questionnaires such as the ones used by Djabelkhir and colleagues may not be as valid or sensitive to ADL changes. The variation in outcomes could therefore bring into question the 'true' efficacy of CCT. Standardised questionnaires and objective measures of ADL would need to be considered, validated, and implemented, similar to how cognitive measures were chosen for intervention studies.

Despite setting the inclusion criteria for the present systematic review to include studies from the year 2000 to the present, only 11 studies met the criteria of an RCT looking at ADL/participation in CCT for older adults with MCI. This could suggest that MCI research on CCT has been less focused on ADL as an outcome. The low numbers of RCTs available highlighted the need for more studies focusing on this particular area.

**Additional Future Research**

Within the reviewed studies, there were various methods by which researchers classified MCI. A future study could investigate the possible differences in ADLs between psychometrically defined MCI and MCI definition based on previous research by Petersen et al. (1997) and Albert et al. (2011). It was difficult to reliably conclude if the features adopted in the interventions helped with improving the intervention's efficacy.  Hence, future studies could assess the efficacy of the different features observed within the current review like adaptiveness, social components and number of sessions. One example was looking at the feature 'adaptiveness' and investigating if the different adaptiveness mechanisms provided varying levels of improvement to intervention efficacy. The studies in the review currently employed a range of measures (e.g., self-reports or performance-based ADL). Therefore, the measures used might not be appropriately sensitive to detect changes in ADL among individuals with MCI. Hence, a potential research study could determine the measures most appropriate to detect ADL changes among MCI individuals.

The reviewed studies methodologies were evaluated using Cochrane's Risk-of-Bias tool to be of moderate quality. However, the findings above highlighted the variable characteristics of CCT methodologies, making it difficult to determine the effectiveness of CCT interventions reliably and the features associated with better outcomes. Due to the variability in study characteristics, caution was still needed when interpreting the data despite being of moderate quality. Hence, it would be necessary for future intervention studies to standardise how MCI was classified, the intervention methodologies/features and the outcome measures used. The standardisation of CCT tasks and outcome measures used to assess ADL could limit possible confounds and contribute to the sensitive evaluation of CCT's efficacy against other forms of intervention.

## Conclusions

Overall, the present review provided some narrative evidence for CCT efficacy, provided certain features were implemented to focus on training specific cognitive domains (i.e., speed of processing). Additionally, several other possible elements observed might contribute to CCT efficacy, such as the adaptiveness and the possible role social and motivational components have in CCT efficacy. This suggested that emotional factors could play an integral part in improving ADL in MCI through CCT. Nonetheless, more research was necessary before a firm conclusion on CCT efficacy could be reached. It was hoped that the present review could be seen as a foundation for standardising elements/features that were potentially useful for CCT to prevent deterioration in or improve ADLs effectively.

## Reference

Albert, M. S., DeKosky, S. T., Dickson, D., Dubois, B., Feldman, H. H., Fox, N. C., ... & Phelps, C. H. (2011). The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & dementia*, *7*(3), 270-279.

Alvarez, J., & Djaouti, D. (2012). Serious games: an introduction. *Limoges, France: Questions Théoriques*.

Anderson-Hanley, C., Snyder, A. L., Nimon, J. P., & Arciero, P. J. (2011). Social facilitation in virtual reality-enhanced exercise: competitiveness moderates exercise effort of older adults. *Clinical interventions in aging*, *6*, 275.

Ball, K., Edwards, J. D., & Ross, L. A. (2007). The impact of speed of processing training on cognitive and everyday functions. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *62*(Special_Issue_1), 19-31.

Birren, J. E. (1974). Translations in gerontology: From lab to life: Psychophysiology and speed of response. *American Psychologist*, *29*(11), 808.

Brown, D. S., Thompson, W. W., Zack, M. M., Arnold, S. E., & Barile, J. P. (2015). Associations between health-related quality of life and mortality in older adults. *Prevention Science*, *16*(1), 21-30.

Burge, W. K., Ross, L. A., Amthor, F. R., Mitchell, W. G., Zotov, A., & Visscher, K. M. (2013). Processing speed training increases the efficiency of attentional resource allocation in young adults. *Frontiers in Human Neuroscience*, *7*, 684.

Chang, C. F., Yang, R. J., Chang, S. F., Chou, Y. H., & Huang, E. W. (2017). The effects of quality of life and ability to perform activities of daily living on mild cognitive impairment in older people living in publicly managed congregate housing. *journal of nursing research*, *25*(3), 187-197.

Chen, C., Hu, Z., Jiang, Z., & Zhou, F. (2018). Prevalence of anxiety in patients with mild cognitive impairment: a systematic review and meta-analysis. *Journal of affective disorders*, *236*, 211-221.

Cintra, F. C. M. D. C., Cintra, M. T. G., Nicolato, R., Bertola, L., Ávila, R. T., Malloy-Diniz, L. F., ... & Bicalho, M. A. C. (2017). Functional decline in the elderly with MCI: Cultural adaptation of the ADCS-ADL scale. *Revista da Associação Médica Brasileira, 63*(7), 590-599.

Colom, R., Román, F. J., Abad, F. J., Shih, P. C., Privado, J., Froufe, M., ... & Jaeggi, S. M. (2013). Adaptive n-back training does not improve fluid intelligence at the construct level: Gains on individual tests suggest that training may enhance visuospatial processing. *Intelligence*, *41*(5), 712-727.

Ćwirlej-Sozańska, A., Wiśniowska-Szurlej, A., Wilmowska-Pietruszyńska, A., & Sozański, B. (2019). Determinants of ADL and IADL disability in older adults in southeastern Poland. *BMC geriatrics*, *19*(1), 1-13.

Dementia Statistics Hub (2018). *Prevalence by age in the UK.* Retrieved 23rd May 2021 from https://www.dementiastatistics.org/statistics/prevalence-by-age-in-the-uk/.

Dementia Statistics Hub (2021) *Global Prevalence*. Retrieved 23rd May 2021 from https://www.dementiastatistics.org/statistics/global-prevalence/

Di Iulio, F., Palmer, K., Blundo, C., Casini, A. R., Gianni, W., Caltagirone, C., & Spalletta, G. (2010). Occurrence of neuropsychiatric symptoms and psychiatric disorders in mild Alzheimer's disease and mild cognitive impairment subtypes. *International Psychogeriatrics*, *22*(4), 629-640.

Djabelkhir, L., Wu, Y. H., Vidal, J. S., Cristancho-Lacroix, V., Marlats, F., Lenoir, H., ... & Rigaud, A. S. (2017). Computerised cognitive stimulation and engagement programs in older adults with mild cognitive impairment: comparing feasibility, acceptability, and cognitive and psychosocial effects. *Clinical interventions in aging*, *12*, 1967.

Dunlosky, J., Kubat-Silman, A. K., & Hertzog, C. (2003). Training monitoring skills improves older adults' self-paced associative learning. *Psychology and aging*, *18*(2), 340.

Edemekong, P. F., Bomgaars, D. L., & Levy, S. B. (2017). Activities of daily living (ADLs).

Edemekong, P. F., Bomgaars, D., Sukumaran, S., & Levy, S. B. (2019). Activities of daily living.

Fragkiadaki, S., Kontaxopoulou, D., Beratis, I. N., Andronas, N., Economou, A., Yannis, G., ... & Papageorgiou, S. G. (2016). Self-awareness of cognitive efficiency: differences between healthy elderly and patients with mild cognitive impairment (MCI). *Journal of clinical and experimental neuropsychology*, *38*(10), 1144-1157.

Fukuda, K., Vogel, E., Mayr, U., & Awh, E. (2010). Quantity, not quality: The relationship between fluid intelligence and working memory capacity. *Psychonomic bulletin & review*, *17*(5), 673-679.

Gagnon, L. G., & Belleville, S. (2012). Training of attentional control in mild cognitive impairment with executive deficits: results from a double-blind randomised controlled study. *Neuropsychological rehabilitation*, *22*(6), 809-835.

García-Casal, J. A., Loizeau, A., Csipke, E., Franco-Martín, M., Perea-Bartolomé, M. V., & Orrell, M. (2017). Computer-based cognitive interventions for people living with dementia: a systematic literature review and meta-analysis. *Aging & mental health*, *21*(5), 454-467.

Garcıa-Pérez, M. A. (1998). Forced-choice staircases with fixed step sizes: asymptotic and small-sample properties. *Vision research*, *38*(12), 1861-1881.

Gates, N. J., Rutjes, A. W., Di Nisio, M., Karim, S., Chong, L. Y., March, E., ... & Vernooij, R. W. (2019). Computerised cognitive training for maintaining cognitive function in cognitively healthy people in late life. *Cochrane database of systematic reviews*, (3).

Gates, N. J., Vernooij, R. W., Di Nisio, M., Karim, S., March, E., Martinez, G., & Rutjes, A. W. (2019). Computerised cognitive training for preventing dementia in people with mild cognitive impairment. *Cochrane database of systematic reviews*, (3).

Gates, N., & Valenzuela, M. (2010). Cognitive exercise and its role in cognitive function in older adults. *Current psychiatry reports*, *12*(1), 20-27.

Haghgoo, H. A., Pazuki, E. S., Hosseini, A. S., & Rassafiani, M. (2013). Depression, activities of daily living and quality of life in patients with stroke. *Journal of the neurological sciences*, *328*(1-2), 87-91.

Hagovska, M., & Nagyova, I. (2017). The transfer of skills from cognitive and physical training to activities of daily living: a randomised controlled study. *European journal of ageing*, *14*(2), 133-142.

Higgins, J. P., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., ... & Sterne, J. A. (2011). The Cochrane Collaboration’s tool for assessing risk of bias in randomised trials. *Bmj*, *343*.

Hooshyar, D., Yousefi, M., & Lim, H. (2019). A systematic review of data-driven approaches in player modeling of educational games. *Artificial Intelligence Review*, *52*(3), 1997-2017.

Hughes, T. F., Flatt, J. D., Fu, B., Butters, M. A., Chang, C. C. H., & Ganguli, M. (2014). Interactive video gaming compared with health education in older adults with mild cognitive impairment: a feasibility study. *International journal of geriatric psychiatry*, *29*(9), 890-898.

Ismail, Z., Elbayoumi, H., Fischer, C. E., Hogan, D. B., Millikin, C. P., Schweizer, T., ... & Fiest, K. M. (2017). Prevalence of depression in patients with mild cognitive impairment: a systematic review and meta-analysis. *JAMA psychiatry*, *74*(1), 58-67.

Jefferson, A. L., Byerly, L. K., Vanderhill, S., Lambe, S., Wong, S., Ozonoff, A., & Karlawish, J. H. (2008). Characterization of activities of daily living in individuals with mild cognitive impairment. *The American journal of geriatric psychiatry*, *16*(5), 375-383.

Knapen, J., Vancampfort, D., Schoubs, B., Probst, M., Sienaert, P., Haake, P., ... & Pieters, G. (2009). Exercise for the treatment of depression. *The Open Complementary Medicine Journal*, *1*(1).

Koepsell, T. D., & Monsell, S. E. (2012). Reversion from mild cognitive impairment to normal or near-normal cognition: risk factors and prognosis. *Neurology*, *79*(15), 1591-1598.

Kueider, A. M., Parisi, J. M., Gross, A. L., & Rebok, G. W. (2012). Computerized cognitive training with older adults: a systematic review. *PloS one*, *7*(7), e40588.

Kumar, M. P., Packer, B., & Koller, D. (2010). Self-Paced Learning for Latent Variable Models. In *NIPS* (Vol. 1, p. 2).

Lampit, A., Hallock, H., & Valenzuela, M. (2014). Computerized cognitive training in cognitively healthy older adults: a systematic review and meta-analysis of effect modifiers. *PLoS medicine*, *11*(11), e1001756.

Law, L. L., Mok, V. C., & Yau, M. M. (2019). Effects of functional tasks exercise on cognitive functions of older adults with mild cognitive impairment: a randomized controlled pilot trial. *Alzheimer's research & therapy*, *11*(1), 1-10.

Law, M., Polatajko, H., Baptiste, S., & Townsend, E. (1997). Core concepts of occupational therapy. *Enabling occupation: An occupational therapy perspective*, 29-56.

Lee, J. Y., & Kim, H. S. (2014). Influences of social support, self-esteem and motivation for rehabilitation on the activities of daily living in stroke patients. *Journal of East-West Nursing Research*, *20*(2), 145-153.

Leifer, B. P. (2003). Early diagnosis of Alzheimer's disease: clinical and economic benefits. *Journal of the American Geriatrics Society*, *51*(5s2), S281-S288.

Leng, M., Yin, H., Zhang, P., Jia, Y., Hu, M., Li, G., ... & Chen, L. (2020). Sleep quality and health-related quality of life in older people with subjective cognitive decline, mild cognitive impairment, and Alzheimer disease. *The Journal of nervous and mental disease, 208*(5), 387-396.

Lin, F., Heffner, K. L., Ren, P., Tivarus, M. E., Brasch, J., Chen, D. G., ... & Tadin, D. (2016). Cognitive and neural effects of vision-based speed-of-processing training in older adults with amnestic mild cognitive impairment: A pilot study. *Journal of the American Geriatrics Society*, *64*(6), 1293-1298.

Lin, J. H., Huang, M. W., Wang, D. W., Chen, Y. M., Lin, C. S., Tang, Y. J., ... & Lane, H. Y. (2014). Late-life depression and quality of life in a geriatric evaluation and management unit: an exploratory study. *BMC geriatrics*, *14*(1), 1-7.

Manenti, R., Gobbi, E., Baglio, F., Macis, A., Ferrari, C., Pagnoni, I., ... & Cotelli, M. (2020). Effectiveness of an Innovative Cognitive Treatment and Telerehabilitation on Subjects With Mild Cognitive Impairment: A Multicenter, Randomized, Active-Controlled Study. *Frontiers in Aging Neuroscience*, *12*, 400.

Michael, D. R., & Chen, S. L. (2005). *Serious games: Games that educate, train, and inform*. Muska & Lipman/Premier-Trade.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., Antes, G., Atkins, D., Barbour, V., Barrowman, N., Berlin, J. A., Clark, J., Clarke, M., Cook, D., D'Amico, R., Deeks, J. J., Devereaux, P. J., Dickersin, K., Egger, M., Ernst, E., Gøtzsche, P. C., ... Tugwell, P. (2014). Ítems de referencia para publicar Revisiones Sistemáticas y Metaanálisis: La Declaración PRISMA. *Revista Espanola de Nutricion Humana y Dietetica*, *18*(3), 172-181.

Oh, S. J., Seo, S., Lee, J. H., Song, M. J., & Shin, M. S. (2018). Effects of smartphone-based memory training for older adults with subjective memory complaints: a randomized controlled trial. *Aging & mental health*, *22*(4), 526-534.

Page, M. J., McKenzie, J., Bossuyt, P., Boutron, I., Hoffmann, T., & Mulrow, C. D. (2020). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. MetaArXiv. 2020.

Park, J. H., & Park, J. H. (2018). Does cognition-specific computer training have better clinical outcomes than non-specific computer training? A single-blind, randomized controlled trial. *Clinical rehabilitation*, *32*(2), 213-222.

Pedullà, L., Brichetto, G., Tacchino, A., Vassallo, C., Zaratin, P., Battaglia, M. A., ... & Bove, M. (2016). Adaptive vs. non-adaptive cognitive training by means of a personalized App: a randomized trial in people with multiple sclerosis. *Journal of neuroengineering and rehabilitation*, *13*(1), 1-10.

Peers, P. V., Astle, D. E., Duncan, J., Murphy, F., Hampshire, A., Das, T., & Manly, T. (2018). A randomised exploratory investigation of the effects of Attention vs Working Memory Training on cognitive performance and everyday functioning following stroke. *BioRxiv*, 296723.

Pereira, F. S., Yassuda, M. S., Oliveira, A. M., Diniz, B. S., Radanovic, M., Talib, L. L., ... & Forlenza, O. V. (2010). Profiles of functional deficits in mild cognitive impairment and dementia: benefits from objective measurement. *Journal of the International Neuropsychological Society*, *16*(2), 297-305.

Petersen, R. C. (2004). Mild cognitive impairment as a diagnostic entity. *Journal of internal medicine*, *256*(3), 183-194.

Petersen, R. C., Smith, G. E., Waring, S. C., Ivnik, R. J., Kokmen, E., & Tangelos, E. G. (1997). Aging, memory, and mild cognitive impairment. *International psychogeriatrics*, *9*(S1), 65-69.

Puente, A. N., Terry, D. P., Faraco, C. C., Brown, C. L., & Miller, L. S. (2014). Functional impairment in mild cognitive impairment evidenced using performance-based measurement. *Journal of geriatric Psychiatry and Neurology*, *27*(4), 253-258.

Reijnders, J., van Heugten, C., & van Boxtel, M. (2013). Cognitive interventions in healthy older adults and people with mild cognitive impairment: a systematic review. *Ageing research reviews*, *12*(1), 263-275.

Richardson, C., Stephan, B. C., Robinson, L., Brayne, C., & Matthews, F. E. (2019). Two-decade change in prevalence of cognitive impairment in the UK. *European journal of epidemiology*, *34*(11), 1085-1092.

Rubio, E., Lázaro, A., & Sánchez-Sánchez, A. (2009). Social participation and independence in activities of daily living: a cross sectional study. *BMC geriatrics*, *9*(1), 1-11.

Russ, T. C., & Morling, J. R. (2012). Cholinesterase inhibitors for mild cognitive impairment. *Cochrane Database of Systematic Reviews*, (9).

Shute, V., Ke, F., & Wang, L. (2017). Assessment and adaptation in games. In *Instructional techniques to facilitate learning and motivation of serious games* (pp. 59-78). Springer, Cham.

Smith, G. E., Housen, P., Yaffe, K., Ruff, R., Kennison, R. F., Mahncke, H. W., & Zelinski, E. M. (2009). A cognitive training program based on principles of brain plasticity: results from the Improvement in Memory with Plasticity-based Adaptive Cognitive Training (IMPACT) Study. *Journal of the American Geriatrics Society*, *57*(4), 594-603.

Sood, P., Kletzel, S. L., Krishnan, S., Devos, H., Negm, A., Hoffecker, L., ... & Heyn, P. C. (2019). Nonimmersive brain gaming for older adults with cognitive impairment: A scoping review. *The Gerontologist*, *59*(6), e764-e781.

Steward, K. A., Bull, T. P., & Wadley, V. G. (2019). Differences in self-awareness of functional deficits between amnestic single- and multidomain mild cognitive impairment. *Journal of clinical and experimental neuropsychology*, *41*(5), 544-553.

Stites, S. D., Harkins, K., Rubright, J. D., & Karlawish, J. (2018). Relationships between Cognitive Complaints and Quality of Life in Older Adults with Mild Cognitive Impairment, Mild

Alzheimer’s Disease Dementia, and Normal Cognition. *Alzheimer disease and associated disorders*, *32*(4), 276.

Tabert, MH, Albert, SM, Borukhova-Milov, L. Functional deficits in patients with mild cognitive impairment: prediction of AD. Neurology. 2002;58(5):758–764.

Tschanz, J. T., Welsh-Bohmer, K. A., Lyketsos, C. G., Corcoran, C., Green, R. C., Hayden, K., ... & Cache County Investigators. (2006). Conversion to dementia from mild cognitive disorder: the Cache County Study. *Neurology*, *67*(2), 229-234.

Tünnermann, J., Petersen, A., & Scharlau, I. (2015). Does attention speed up processing? Decreases and increases of processing rates in visual prior entry. *Journal of vision*, *15*(3), 1-1.

Valdés, E. G., Andel, R., Lister, J. J., Gamaldo, A., & Edwards, J. D. (2019). Can Cognitive Speed of Processing Training Improve Everyday Functioning Among Older Adults With Psychometrically Defined Mild Cognitive Impairment?. *Journal of aging and health*, *31*(4), 595-610.

Watson, R., Bryant, J., Sanson-Fisher, R., Mansfield, E., & Evans, T. J. (2018). What is a ‘timely’diagnosis? Exploring the preferences of Australian health service consumers regarding when a diagnosis of dementia should be disclosed. *BMC health services research*, *18*(1), 1-9.

Weng, W., Liang, J., Xue, J., Zhu, T., Jiang, Y., Wang, J., & Chen, S. (2019). The transfer effects of cognitive training on working memory among Chinese older adults with mild cognitive impairment: a randomized controlled trial. *Frontiers in aging neuroscience*, *11*, 212.

Williams, O. E., Elghenzai, S., Subbe, C., Wyatt, J. C., & Williams, J. (2017). The use of telemedicine to enhance secondary care: some lessons from the front line. *Future healthcare journal*, *4*(2), 109.

Wilson, R. C., Shenhav, A., Straccia, M., & Cohen, J. D. (2019). The eighty five percent rule for optimal learning. *Nature communications*, *10*(1), 1-9.

Winblad, B, Palmer, K, Kivipelto. Mild cognitive impairment--beyond controversies, towards a consensus: report of the international working group on mild cognitive impairment. J Intern Med. 2004;256(3):240–246.

World Health Organization. (1978). *International classification of procedures in medicine* (Vol. 1). World Health Organization.

World Health Organization. (2008). "Social participation.” Retrieved May 23 2021 from https://www.who.int/social_determinants/thecommission/countrywork/within/socialparticipation/en/

Yates, J. A., Clare, L., & Woods, R. T. (2017). “You’ve got a friend in me”: can social networks mediate the relationship between mood and MCI?. *BMC geriatrics, 17*(1), 1-7.

# Chapter 3: Bridging Chapter

This concludes the first section of the thesis. The systematic review findings provided evidence of a small yet positive effect size of CCT improving ADL in MCI individuals. The review accumulated and appraised the different methodologies that were used in the reviewed RCTs. Interestingly, the review identified several common cognitive domains that were intervention targets in high efficacy RCTs. The empirical paper in the next section of the thesis aimed to use stroke survivors to explore the cognitive domains that best predict the quality of life.

Previous research had associated stroke with an increased risk of dementia (Tatemichi et al., 1993; Pohjasvaara et al., 1998; Sachdev et al., 2006). The association could be linked by the commonality that both stroke and specific subtypes of dementia are known to be caused by vascular-related deficits (Savva et al., 2009; Vijayan & Reddy, 2016). By extension, vascular risk factors were also associated with increased risk of MCI among older adults (Wang et al., 2015). Additionally, previous research associated MCI with post-stroke individuals (Sachdev et al., 2009; Pasi et al., 2012), and the potential for reversibility was similarly observed in a percentage of stroke individuals with MCI (Rasquin, Lodder & Verhey, 2005). Hence, the MCI status was not exclusive to dementia.

It was not clear if the MCI were of vascular origins in the reviewed studies in the current review. However, given the possible overlap in causal factors between MCI and stroke (i.e., vascular factors), it would be interesting to compare the systematic review findings with the empirical paper on the cognitive domains that best predict the quality of life. It was hoped that the findings yielded from the empirical paper on stroke survivors could be generalised to a certain degree to the MCI/dementia population.

# Chapter 4: Empirical Paper

## Secondary Data Analysis of Specific Cognitive Domains that Best Predict Quality of Life

Prepared for submission to Journal of the International Neuropsychological Society

**Empirical Paper**

# Secondary Data Analysis of Specific Cognitive Domains that Best Predict Quality of Life

Chai, C. H. [1], Peers, P. [2], Murphy, F. [2], Manly, T. [2], Sami, S. [1], and Gracey, F. [1]

[1]Norwich Medical School, University of East Anglia

[2]MRC Cognition and Brain Sciences Unit, University of Cambridge

Abstract Word Count: 248

Manuscript Word Count: 6870

**Author Note**

There is no conflict of interest needed to be disclosed for the current review paper. The review was written as part of the thesis portfolio for the Clinical Psychology Doctorate programme.

Correspondence concerning the review article should be addressed to Chai Chung Han, Norwich Medical School, University of East Anglia, Norwich NR4 7TJ. Email: ccb18zpu@uea.ac.uk

**Abstract**

**Objective:** Stroke is the second leading cause of death and accounts for 10% of deaths globally. Quality of Life (QoL) is a parameter for measuring the outcome of modern medicine and highly critical in assessing the multifaceted impact of diseases like a stroke on an individual's life. The study aimed to improve understanding of cognitive processes associated with QoL among stroke individuals.

**Methods:** Participants (N=80) were stroke survivors recruited to a separately reported trial of cognitive rehabilitation. QoL was operationalised using the two measures, the EuroQol 5-Dimension 5-Level Visual Analogue Scale (EQ5D-VAS) and European Brain Injury Questionnaire Core subscale (EBIQ-Core). Cognition was assessed using various tasks, including the Attention Network Test or Theory of Visual Attention (TVA) Task. The data were analysed using two hierarchical regression analyses.

**Results:** $R^2$ (variance) contributed by cognitive domains were non-significant for EBIQ-Core and EQ5D-VAS model. EBIQ motivation ($\beta = .36$, $p<.05$) and motivation ($\beta = .61$, $p<.05$) subscale were significant independent predictors of EBIQ-Core. TVA spatial ($\beta = -.41$) and non-spatial ($\beta = .45$) attention measures became significant

predictors after removing the EBIQ motivation and depression subscale. Additionally, the addition of non-spatial attention predictors ($R^2$=.17) contributed significantly to the model, F (2, 35) = 4.53, p<.05. No variables contributed significantly to the EQ5D-VAS model.

**Conclusion:** The results showed tentative support for non-spatial attention contributed significantly to the EBIQ-Core model when depression and motivation subscales were removed. Spatial and non-spatial attention measures from the TVA task were significant independent predictors of EBIQ-Core. Results and implications were discussed.

Keyword: *quality of life, stroke, cognitive training, cognitive rehabilitation, non-spatial attention, hierarchical regression*

## Secondary Data Analysis of Specific Cognitive Domains that Best Predict Quality of Life

Stroke is a common medical health condition that is the second leading cause of death globally (Truelsen, Begg, & Mathers 2006), accounting for 10% of deaths globally (Naghavi et al., 2017). Individuals post-stroke are at higher risk of dementia (Leys et al., 2005), depression and anxiety (Schottke & Giabbiconi, 2015).

Quality of Life (QoL) is an essential parameter for measuring the outcome of modern medicine and highly critical in assessing the multifaceted impact of diseases on an individual's life (Salter, Moses, Foley & Teasell, 2008). Individuals with stroke were often affected, with half of the stroke survivors having some form of physical, psychological, and social functioning impairment (De Wit et al., 2017). Some self-reported questionnaires, such as Stroke-Specific QoL Scale (Williams, Weinberger, Harris, Clark & Biller, 1999) or the 5-Level EQ-5D (Herdman et al., 2011), allowed more sensitive and specific assessment.

QoL was significantly correlated with activities of daily living (ADL) post-stroke (Van Mierlo et al., 2016). The relationship between the two aspects was especially notable for instrumental ADL

(IADL), which are more physically and cognitively demanding (van de Port, Kwakkel, Schepers, Heinemans & Lindeman, 2007). Reduced cognitive function, typically observed in stroke individuals, had been associated with reduced capacity to perform ADL (Marshall et al., 2011). While some stroke survivors might be able in 'basic ADL' like dressing and eating, they might experience difficulties when it comes to IADL, like paying the bills or taking public transport due to deficits in executive functioning (EF) (Lipskaya-Velikovsky, Zeilig, Weingarden, Rozental-Iluz & Rand, 2018).

**Executive and Attention Dysfunction**

An impairment of EF is a critical neuropsychological consequence of stroke (Shea-Shumsky, Schoeneberger & Grigsby, 2019) that typically occurs following damage to frontal areas or systems. EF comprises an individual's ability to plan, organise, and successfully execute goal-directed actions (Williams, Tinajero & Suchy, 2017). EF serves as an essential future determinant of functional outcome or ADL (Shea-Shumsky et al., 2019). Previous research indicated that EF significantly contributes to IADL functioning (Nguyen, Copeland, Loew, Heyanka, & Linck, 2020). With deficits in EF, stroke survivors were more prone to depressive symptoms, resulting in poor prognostic outcomes (Bour et al., 2010) and reduction in QoL (Kim, Liu, Nakaoka, Jang, & Browne, 2018).

Alongside EF, attentional impairment is a common feature in stroke survivors. Attention is a cognitive component that mediates other cognitive processes, and impairment in this domain is likely to affect higher cognitive functions (Lezak, Howieson, Loring & Fischer, 2004). Attentional impairment is a common feature in stroke survivors associated with right hemispherical lesions (Karnath, Rorden & Ticini, 2009). The impairment often manifests as spatial inattention or visual neglect in which individuals with stroke would neglect the left side of space (Halligan & Marshall, 1998).

**Stroke Interventions and Targets for Intervention**

Stroke survivors with spatial neglect report worse QoL than non-neglect stroke survivors (Nys et al., 2006; Franceschini, La Porta, Agosti & Massucci, 2010). Therefore it is often the focus of rehabilitation where this deficit is present (Azouvi, Jacquin-Courtois & Luaute, 2017). Rehabilitation for stroke survivors has been focusing mainly on spatial inattention. There have been numerous intervention studies evaluating spatial attention as a cognitive target (Peers et al., 2018; Huygelier et al., 2020). However, Bowen and colleagues (2013) posited a lack of evidence for generalisable and persistent gain from cognitive rehabilitation for neglect, such as visual scanning, cueing, prism adaptation, or patching. Therefore, current interventions targeting spatial aspects of attention might not be as effective as previously thought to reduce the deficit or improve QoL. Bickerton and colleagues (2015) observed that an individual's sustained attention helped predict better functional outcomes deficits related to spatial attention. The authors suggested that functional spatial attention deficits might be impacted directly by spatial attention in addition to non-spatial attentional deficits that also accompany right hemisphere lesions.

Deficits in sustained attention were frequently identified and subjectively reported as an impairment after stroke (Barker-Collo, Feigin, Lawes, Parag & Senior, 2010; Chen, Koh, Hsieh & Hsueh, 2009). Sustained attention has been known as a prerequisite for motor recovery in stroke rehabilitation, and its deficits are often associated with a reduction in QoL (Robertson, Ridgeway, Greenfield & Parr, 1997). Past research has suggested that non-spatial attention (e.g., sustained attention) in addition to spatial attention might need to be targeted for successful rehabilitation (Husain & Rorden, 2003).

However, it has been less focused as a target compared to spatial attention.

Current evidence from a review suggested possible immediate effects on alertness, selective attention and sustained attention following cognitive stroke rehabilitation (Loetscher, Potter, Wong, & das Nair, 2019). However, the authors argued that more research was needed to generalise the effects on everyday functioning and QoL. The present lack of evidence could be due to the shortage of studies that focused on non-spatial attention as a target for cognitive rehabilitation. Given the recent revival of interest and evidence on non-spatial attention as a factor impacting stroke rehabilitation, it would be necessary for more research to be done before another review is carried on the evidence.

The present empirical study aimed to improve the understanding of cognitive processes relevant to QoL among stroke individuals to understand better which domains should be targeted in cognitive rehabilitation to maximise the likelihood of improving QoL. Specifically, it was posited that non-spatial attention might play a role in QoL post-stroke more than other cognitive domains, including working memory and spatial inattention. The study hypothesised that non-spatial attention, in which poorer performance of the TVA variability task and Choice-Reaction Task variability, could be correlated with lower QoL than other cognitive domains. Secondly, non-spatial attention could account for a significant amount of variance in an individual's QoL.

## Methods

### Design

The study employed a correlational cross-sectional design. The study conducted a hierarchical regression analysis on data collected from an existing study. The data used was from the baseline phase of a trial that looked at the effects of brain training on improving people's attention and working memory (Peers et al., 2021). The primary outcome for the analysis is QoL, operationalised as the EuroQol 5-Dimension 5-Level Visual Analogue Scale (EQ5D-VAS)(Herdman et al., 2011) and European Brain Injury Questionnaire-Core Scale (EBIQ-Core) (Teasdale et al., 1997).

### Participants

The data for the analysis was obtained from a total of 80 older adults. The participants included in the analysis range between 20 – 65 years old. The participants mean age is 59.9. The inclusion criteria followed those of the preliminary study (Peers et al., 2021). The study included participants: 1) who had a previous stroke diagnosis, 2) able to give informed consent, and 3) having sufficient language, motor function and general health to undertake training. In some cases, assessments were conducted in participants' own homes. The original study did not state if participants with poor QoL (e.g., impaired ADLs) were included/excluded from the study.

## Measures

### *Dependent variable*

**European Brain Injury Questionnaire (EBIQ).** The EBIQ consists of 63 items related to a wide range of everyday problems affecting someone with brain injury (Sopena, Dewar, Nannery, Teasdale & Wilson, 2007). These items were split into different domains (i.e., cognitive, somatic, motivation, impulsivity, depression, isolation, physical consequences, and communication). The individual with brain injury and an informant who knows the individual well completed the questionnaire. The items are recorded with either 'not at all' (coded as '1'), 'a little' (coded as '2') or 'a lot' (coded as '3'). Each item corresponds to a specific domain with a ninth overall 'core' scale derived from each subscale's selected items.

The ninth scale, EBIQ-Core, is one of the dependent variables used for the analysis. The EBIQ showed significant and satisfactory test-retest reliability (r = 0.55–0.90) in the brain injury group, family members of the brain injury group and healthy controls (Sopena et al., 2007).

QoL was conceptualised as self-reported overall contentment across different life domains like physical well-being, social and personal fulfilment (Burckhardt & Anderson, 2003). EBIQ was designed and typically used to assess the subjective experience of cognitive, emotional and social difficulties of individuals with brain injury (Sopena et al., 2007). Therefore, EBIQ could be considered an appropriate measure of QoL and had been considered a useful assessment of health-related QoL for brain injury (Nichol et al., 2011). Hence, EBIQ scores of stroke survivors were used instead of the informants' score. The statements in the EBIQ were written, which asked individuals the difficulties they experienced with daily functioning across different domains (e.g., Having to do things correctly or needing to be reminded about personal hygiene). Lower scores denoted better everyday functioning.

**5-Level EQ-5D version (EQ5D-5L).** The EQ5D-5L is a questionnaire designed to measure QoL consisting of five dimensions (i.e., mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). Individuals are instructed to indicate the degree of problems in those dimensions. A single visual analogue scale (0 – 100), the dependent variable used for the present analysis, indicated the participant's subjective perception of health state and was used in the present analysis as a dependent variable of QoL. The EQ5D-VAS showed moderate to strong ($0.35<r<0.75$) convergent validity to the EQ5D-5L dimensions and other measures of stroke such as the Modified Rankin Scale for Neurologic Disability and Barthel Index (Golicki et al., 2015a). The EQ5D-5L is an assessment tool that was designed to assess QoL. However, as the outcome of the EQ5D-5L is a profile score, it is difficult to implement the outcome into a hierarchical regression. Hence, the EQ5D-VAS was implemented as a measure of QoL.

***Control Variables***

**Demographic Data.** Variables collected like age, sex and lesion side were included as controlled variables. Additionally, the

EBIQ depression and motivation subscale was included as part of the controlled variable.

**National Adult Reading Test (NART).** The NART is a 50-item single oral test that requires individuals to pronounce a given word (Nelson & Willison, 1991). The presented words are irregular, which meant that intelligent guess would not provide correct pronunciation. This allows assessors to measure an individual's word knowledge. The test only requires reading single words and would therefore require minimal current cognitive capacity. The test is most widely used to estimate premorbid ability (Johnstone, Owens & Lawrie, 2010).

**Cattell Culture-Fair Test.** The Cattell Culture-Fair test is a non-verbal test designed to measure intelligence presented with minimum use of language (Smith, 1970). The test aims to measure an individual's fluid intelligence. The test has a strong construct validity based on factor analysis (Cattell, 1978).

***Independent Variables***

**Automated Working Memory Assessment (AWMA).** The AWMA is an assessment that measures short-term verbal memory through non-word recall (Alloway, 2007). The assessments used for the analysis are the dot-matrix task (visual-spatial short-term memory) and spatial recall (visual-spatial working memory) task. Two composite scores were created with the OCS-BRIDGE digit span forward and backward tasks. The composite scores: working memory (i.e., spatial recall and digit span backwards) and working memory capacity (i.e., dot matrix and digit spans forward) are used for the regression analysis.

**Attention Networks Test (ANT).** The ANT is a cognitive measure that independently assesses the efficiency of the three attention networks (i.e.. alerting, orienting, and executive attention) using a quick and simple computerised task (Fan et al., 2002). Participants would indicate if the central arrow that is flanked by four arrows (two arrows on each side) is congruent (i.e., pointing in the same direction as the four arrows, incongruent (i.e., point in the opposite direction) or neutral (i.e. only the central arrow is present or flanked by four horizontal lines). Either one of three types of cues (centre cue, double cue, spatially informative cue) or no cues would be given before the appearance of the arrows. The centre and double cues indicate that the stimulus would occur soon. The spatially informative cue (i.e., appearing either above or below the centre of the screen) shows where the stimulus would appear. The task measures participants’ response time (i.e., time taken between the appearance of stimuli and participant pressing the key) and accuracy (i.e., the number of correct responses) in congruent, incongruent, or neutral task.

The current study is interested in the ability of an individual to ignore distracting stimulus. Specifically, the proportion of correct response in the 3T condition and the 6T condition with the 3T3NT condition using the formula: $\alpha' = (pcorr3T + pcorr6T)/(2 \times pcorr3T3NT)$. A higher α’ value shows poorer attentional control.

**Theory of Visual Attention (TVA) Task.** The TVA task assesses an individual’s visual attention and ability to select and encode visual stimuli into short-term memory. One or more letters were flashed on the computer screen for a specific time. The stimuli disappear, and pattern masks appear, aiming to erase the visual afterimage and precisely control when the stimuli are available for processing. Participants were instructed to identify and report the presented letters but were cautioned against guessing the letters (Habekost, 2015). The TVA task looked at participants’ accuracy at identifying the target stimuli on either the left or right side of the screen. It is operationalised as increased scores on one side meant increased spatial bias. The data extracted is the relative reduction in performance between the 3T and 6T conditions for items presented on the left versus right sides of space, using the following formula:

Absolute spatial bias=ABS 0.5- ( ($pcorr\ 6Tleft/pcorr3Tleft$)

($pcorr6Tleft/pcorr3Tleft$) + ($pcorr\ 6Tright/pcorr3Tright$) )

Additionally, an additional measure of variability in performance was derived. The variability in performance was suggested to indicate poor sustained attention, which was also linked to poor spatial awareness (Stuss et al., 1989). This is defined as the coefficient of variation (standard deviation divided by the mean) of correct letter reports from the 6T condition. The larger the variability, the more indicative of poor sustained attention.

**Oxford Cognitive Screen (OCS)-BRIDGE.** The OCS-BRIDGE assessed five domains (i.e., attention and executive function, language, memory, number processing, and praxis). The OCS is designed to test deficits in the stroke population (Demeyere, Riddoch, Slavkova, Bickerton & Humphreys, 2015). The tasks were designed to allow participants to complete them using one hand to reduce any overall impact of commonly found upper limb weakness. The screen can be administered within 15 minutes. The OCS consists of ten tasks that were administered following a pre-determined order. For the current analysis, only the data on the broken-heart task and digit spans forward/backwards were used as part of the analysis. The task requires participants to cancel out ‘complete hearts’ only while avoiding crossing any ‘Broken’ hearts in three minutes. Space asymmetry scores are computed by subtracting the number of hearts cancelled in the four left-most blocks from the number of hearts cancelled in the right-most four blocks. A positive score could indicate the participant has cancelled more right-side hearts than the left side and shows left egocentric neglect (neglect of the left side of space) and vice versa.

**Choice Reaction Time Task (CRT).** The CRT is a two-choice reaction time task that assesses alertness and motor speed. The task provides two possible stimuli and two possible responses. An arrow is displayed on either the left or right side of the screen. Participants are instructed to press the left or right button, depending on where the stimulus is displayed. The task looks at the accuracy (i.e., the percentage of correct over total) and participants' reaction time to the stimuli. The current analysis looked at the coefficient of variation (standard deviation divided by the mean) of correct stimuli response. The larger the variability, the more indicative of poor sustained attention.

## Statistical Analyses

### *Data Cleaning Prior to Inferential Data Analysis*

The variables were tested for homoscedasticity, normality, skewness, kurtosis, and collinearity. Data were checked for outliers and whether the data was normally distributed to ensure a reliable and valid analysis. Outliers could potentially inflate results. However, it has been argued that the external validity of the results might be reduced by removing outliers. Southworth (2012) suggested that the data point be included if outliers do not affect study results. Additional analysis compared non-transformed data versus transformed data (refer to Extended Results Chapter). Data that does not fit into a typical distribution pattern and skewed were transformed. Normality and skewness were assessed after the variables were transformed. Collinearity was assessed for each variable before outliers were removed. The comparative analysis showed no observable difference between ‘cleaned’ (i.e., transformed data with outliers removed) and raw data. Hence, the present study chose to analyse the raw data without removing outliers or transforming the data.

### ***Hierarchical Regression Analysis***

Stepwise hierarchical regression was carried out for each dependent variable (EBIQ-Core and EQ5D-VAS). Socio-demographic (i.e., age and gender) and clinical control variables (i.e., mood and general intellectual functioning) were entered into the first stage of the hierarchical regression analyses. The independent variables were entered into stage two, three and four. Cognitive domains relating to top-down control and working memory were entered in the second stage. The third step of the regression model included measures of spatial attention, and stage four included non-spatial attention measures. The level of statistical significance was set at 0.05.

## Results

### Descriptive Statistics

The descriptive statistics of the data could be seen in Table 1. Based on the data, 50 of the participants were male, and the lesion side was approximately equal between the left and right groups: left side (35), right side (28) and bilateral (15). The NART score (mean = 33.02, standard deviation = 8.57) and Cattell score (mean = 26.29, standard deviation = 6.55) suggested that participants had an average premorbid cognitive ability. It was observed that the control variables (i.e., NART, Cattell, EBIQ Motivation and Depression) had values across the spectrum.

The EBIQ-Core and EQ5D-5L-VAS were used as dependent variables for QoL. The EQ5D-VAS mean is 71.49, suggesting that participants perceived their health as positive on average. Similarly, the EBIQ-Core has a mean of 1.66 (1 = not at all, 3 = a lot), indicating that participants rated their functioning between 'unimpaired' and 'slightly impaired'. The range of the EQ5D-VAS was 9 – 100 (100 = perfect health), and the EBIQ value ranged between 1 to 2.6 (1 = not at all, 3 = a lot) suggested participants ratings and perceptions of their health ranged across the spectrum.

**Table 1**

*Descriptive Statistics for the Sample Characteristics including Performance in Various Cognitive Performance*

| Variables | N | % | Mean | Standard Deviation | Range | No. Missing Data (%) |
|---|---|---|---|---|---|---|
| Sex | | | | | | - |
| Male | 50 | 62.5 | | | | |
| Female | 30 | 37.5 | | | | |
| Lesionside | | | | | | 2 (2.5) |
| Left | 35 | 43.75 | | | | |
| Right | 28 | 35 | | | | |
| Bilateral | 15 | 18.75 | | | | |
| Age | | | 59.9 | 14.5 | 20 - 85 | - |
| NART | | | 33.02 | 8.57 | 7 - 50 | 14 (17.5) |
| Cattell | | | 26.29 | 6.55 | 11 - 41 | 5 (6.25) |
| EBIQ Motivation | | | 1.66 | 0.45 | 1 - 2.6 | - |
| EBIQ Depression | | | 1.58 | 0.45 | 1 - 3 | - |
| TopDownControl | | | 1.2 | 0.25 | 0.81 - 2.64 | - |
| Digit Span Forward | | | 6.05 | 1.19 | 3 - 8 | 16 (20) |
| Digit Span Backward | | | 4.33 | 1.31 | 2 -8 | 16 (20) |
| Dot Matrix | | | 21.58 | 5.55 | 7 - 35 | 1 (1.25) |
| Spatial Recall | | | 15.53 | 5.25 | 3 - 29 | 2 (2.5) |
| Working Memroy | | | 8.14 | 3.05 | 0.763 - 17 | - |
| Working Memory Capacity | | | 1.42 | 1.99 | -3.12 - 6.67 | - |

| | | | | |
|---|---|---|---|---|
| TVA Absolute Bias | 0.09 | 0.09 | 0.002 - 0.36 | 2 (2.5) |
| Oxbridge Cancellation Task | 0.06 | 0.13 | 0 - 1 | 1 (1.25) |
| TVA variability | 0.35 | 0.15 | 0.11 - 0.94 | - |
| CRT Variability | 0.36 | 0.22 | 0.15 - 1.62 | 2 (2.5) |
| EQ5D-5L-VAS | 71.49 | 20.73 | 9 - 100 | - |
| EBIQ-Core | 1.66 | 0.34 | 1 - 2.6 | - |

**Correlation Matrix**

Given the varying types of data used, three different types of correlation tests were used. Pearson correlation coefficient was used between two continuous variables. A Pearson's point-biserial correlation was conducted in SPSS to assess the association between the two categorical variables (i.e., sex and lesion side) with continuous variables (e.g., Age, NART, TVA tasks). Cramer’s V, a statistical correlation that measured the association between two categorical variables when more than two levels were within one variable, was conducted for sex and lesion side variables. Finally, a Pearson chi-square was used to assess the significance between the two variables (i.e., sex and lesion side). Table 2 showed the correlation matrix for dependent and independent variables.

As expected, the two working memory composite scores and the variables from which the variables were derived were significantly correlated. The TVA tasks (i.e., TVA Variability and Absolute Bias) were significantly correlated with the EBIQ-Core. Similarly, the EBIQ-Core was significantly correlated with the depression and motivation subscale, from which the variable was partly derived. Additionally, the EBIQ-Core was observed to be significantly correlated with the EQ5D-5L-VAS. Analysis of collinearity (i.e., tolerance and VIF values) suggested no collinearity issues (Refer to Extended Results Chapter).

**Table 2**

Correlation Matrix for Both Independent and Dependent Variables

| | Sex | Lesion LeftVSOthers | Lesion RightVSOthers | Lesion BilateralVS Others | Age | NART | Cattell | EBIQ Motivation | EBIQ Depression | Top-Down Control | Dot Matrix | Spatial Recall | Digit Span Forward | Digit Span Backward | Working Memory (Composite) | Working Memory Capacity (Composite) | TVA Absolute Bias | Oxbridge Cancellation Task | TVA Variability | CRT Variability | EQ5D-5D-VAS | EBIQ-Core |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sex | - | | | | | | | | | | | | | | | | | | | | | |
| Lesion Side (all) | **0.109** | | | | | | | | | | | | | | | | | | | | | |
| Lesion LeftVSOthers | 0.107 | - | | | | | | | | | | | | | | | | | | | | |
| Lesion RightVSOthers | -0.088 | -.675** | - | | | | | | | | | | | | | | | | | | | |
| Lesion BilateralVSOthers | -0.028 | -.440** | -.365** | - | | | | | | | | | | | | | | | | | | |
| Age | 0.107 | 0.076 | -0.001 | -0.094 | - | | | | | | | | | | | | | | | | | |
| NART | 0.052 | -0.131 | 0.062 | 0.087 | 0.132 | - | | | | | | | | | | | | | | | | |
| Cattell | -0.160 | 0.016 | -0.198 | 0.229 | -.354** | 0.169 | - | | | | | | | | | | | | | | | |
| EBIQ Motivation | -0.131 | 0.182 | 0.033 | -.269* | -0.070 | -0.056 | -0.138 | - | | | | | | | | | | | | | | |
| EBIQ Depression | -0.136 | 0.079 | -0.031 | -0.062 | -0.105 | -0.103 | -0.020 | .497** | - | | | | | | | | | | | | | |
| Top-Down Control | 0.067 | 0.066 | -0.027 | -0.050 | 0.128 | 0.149 | -0.082 | -0.082 | -0.192 | - | | | | | | | | | | | | |
| Dot Matrix | 0.045 | 0.035 | -0.094 | 0.070 | -.305** | 0.027 | .500** | -0.176 | -0.054 | -.374** | - | | | | | | | | | | | |
| Spatial Recall | 0.140 | 0.169 | -.262* | 0.104 | -.393** | 0.021 | .655** | -0.151 | -0.029 | -.328** | .673** | - | | | | | | | | | | |
| Digit Span Forward | -0.048 | -.281* | 0.167 | 0.158 | -0.140 | -0.069 | -0.173 | 0.003 | -0.078 | -.260* | 0.018 | -0.145 | - | | | | | | | | | |
| Digit Span Backward | -0.060 | -0.094 | -0.004 | 0.127 | -0.057 | -.287* | -0.025 | -0.121 | -0.024 | -0.106 | 0.160 | 0.064 | .429** | - | | | | | | | | |
| Working Memory (Composite) | 0.061 | 0.023 | -0.124 | 0.124 | -.323* | -0.219 | .439** | -0.140 | -0.009 | -0.151 | .531** | .736** | 0.183 | .723** | - | | | | | | | |
| Working Memory Capacity (Composite) | -0.026 | -0.204 | 0.104 | 0.136 | -.385** | -0.158 | 0.214 | -0.100 | -0.076 | -.430** | .705** | .357** | .722** | .429** | .510** | - | | | | | | |
| TVA Absolute Bias | -0.090 | 0.013 | 0.113 | -0.152 | -0.050 | 0.226 | -.273* | 0.100 | -0.113 | -0.029 | -0.102 | -0.177 | -0.052 | 0.042 | -0.115 | -0.138 | - | | | | | |
| Oxbridge Cancellation Task | 0.077 | -0.224 | .305** | -0.092 | 0.037 | -0.157 | -.344** | 0.013 | -0.076 | 0.001 | -.240* | -0.216 | -0.064 | -0.009 | -0.165 | -0.178 | -0.003 | - | | | | |
| TVA Variability | 0.184 | 0.073 | -0.021 | -0.066 | 0.050 | -.281* | -.305** | 0.200 | 0.132 | 0.209 | -.298** | -.392** | -0.043 | 0.040 | -0.242 | -0.202 | 0.220 | 0.134 | - | | | |
| CRT Variability | 0.098 | 0.023 | 0.005 | -0.036 | .287* | -0.064 | -.397** | 0.163 | .296** | -0.009 | -.346** | -.367** | 0.025 | -0.006 | -.294* | -.307* | 0.021 | .277* | .286* | - | | |
| EQ5D-5D-VAS | 0.081 | 0.052 | -0.036 | -0.022 | 0.058 | -0.077 | -0.036 | -.396** | -.282* | 0.051 | 0.093 | 0.168 | -0.219 | 0.099 | 0.208 | -0.076 | 0.035 | 0.012 | -0.190 | -0.196 | - | |
| EBIQ-Core | -0.125 | 0.100 | -0.049 | -0.066 | -0.133 | -0.035 | -0.015 | .679** | .813** | -0.130 | -0.028 | -0.084 | -0.102 | -0.109 | -0.118 | -0.062 | -0.093 | -0.006 | .266* | .253* | -.500** | - |

*Note.* Composite variables are labelled with (composite). The value in **bold** within the 'Lesion Side' row is the Cramer' V correlation coefficient with the variable 'sex'. Categorical variables (Age and Lesion Side), Pearson's Point-Biserial Correlation were automatically used in SPSS to calculate the correlation between a continuous variable and a binary correlation. Correlation denoted with ** or * are significant at the 0.01 or 0.05 level, respectively (2-tailed).

## Main Analysis

### *EBIQ Core*

A four-stage hierarchical multiple regression was conducted with EBIQ Core as the dependent variable. Age, Sex, Lesion Side, NART, Cattell, EBIQ Depression and Motivation were entered at stage one of the regressions to control the variables' impact on cognitive performance. Cognitive domains related to memory and decision-making/planning (i.e., working memory and top-down control) were entered at stage two. Cognitive performance relating to spatial bias/inattention (i.e., Bias) was added in stage three. Finally, non-spatial attention (i.e., sustained attention) was entered into stage four. The variables were entered in order based on previous research on QoL and cognitive domains (Table 1).

The hierarchical multiple regression revealed that at stage one, the variance accounted for by the control variables was = 0.77, which was significantly different from zero, $F(9, 40) = 15.04$, $p < .05$). Two control predictors were statistically significant in the model: EBIQ motivation, $\beta = .29$, $p < .05$ and EBIQ Depression, $\beta = .47$, $p < .05$.

In stage two, the cognitive domains related to memory and decision-making were entered into the regression equation. The total variance accounted ($R^2$) for by the addition of the cognitive domains equalled 0.79. The ‘change in variance accounted’ ($\Delta R^2$) for was equal to .015. The $\Delta R^2$ was not significantly different from zero $F(3,37) = .89$, $p = .45$. None of the added predictors was statistically significant.

Adding spatial cognitive domains to stage three of the regression model accounted for 0.79 of the total variance. The $\Delta R^2$ from the addition of the spatial cognitive domain equalled to .007. The $\Delta R^2$ from the addition of stage three was not significant, $F(2,35) = .6$, $p = .56$. None of the added spatial cognitive predictors was statistically significant.

Finally, the addition of non-spatial cognitive domains to stage four of the regression model accounted for .82 of the total variances. The $\Delta R^2$ from the addition of stage four equalled.022, and the change in variance was not significant $F(2,33) = 1.93$, $p=.16$. When all predictors were included in stage four, the overall model was significant, $F(16,33) = 9.14$, $p<.05$. EBIQ motivation and depression remained the only statistically significant predictor, $\beta = .36$, $p < .05$ and $\beta = .61$, $p < .05$, respectively.

The adjusted $R^2$ value in stage two and three went down, which suggested that the predictors in both stages do not meaningfully contribute to the model. A larger $\Delta R^2$ change was observed for the non-spatial factors (Stage 4) than other cognitive domains, although the $\Delta R^2$ was not significant. The standardized regression coefficients ($\beta$), $R^2$, $R^2$ Adjusted and $\Delta R^2$ for the EBIQ Core's full model are reported in Table 1.

**Table 3**

*Predictors of EBIQ Core with regression coefficients (β), $R^2$, $R^2$ Adjusted, $\Delta R^2$, $\Delta R^2$ Adjusted.*

| Stage | Predictors | B | $R^2$ | $R^2$ Adjusted | $\Delta R^2$ | $\Delta R^2$ Adjusted |
|---|---|---|---|---|---|---|
| 1 | Sex | -.04 | .77 | .72 | .77 | .73 |
| | Age | -.05 | | | | |
| | NART | .14 | | | | |
| | Cattell | .04 | | | | |
| | EBIQ Motivation | .36* | | | | |
| | EBIQ Depression | .61* | | | | |
| | Lesion Side (bilateral) | .01 | | | | |
| | Lesion Side (right) | -.07 | | | | |
| | Lesion Side (missing) | -.06 | | | | |
| 2 | Top-Down Control | -.02 | .79 | .72 | .02 | -.003 |
| | Working Memory | -.09 | | | | |
| | Working Memory Capacity | .08 | | | | |
| 3 | TVA Absolute Bias | -.13 | .79 | .71 | .007 | -.006 |
| | Oxbridge Cancellation Task | .07 | | | | |
| 4 | TVA Variability | .20 | .82 | .73 | .02 | 0.02 |
| | CRT Variability | -.02 | | | | |

* $p<0.05$

**EQ5D-VAS**

The same four-stage procedure was conducted with EQ5D-VAS as the dependent variable, with all other variables entered in the same way as described above. The regression statistics are in the table below Table 2.

The hierarchical multiple regression revealed that at stage one, the variance accounted ($R^2$) for by the controlled predictors equalled to .21, with the variance being non-significant, F (9,40) = 1.18, p=.33. EBIQ motivation subscale was statistically significant in the model, β= -.39, p<.05.

Adding the cognitive domains (i.e., memory and decision-making) accounted for .32 of the total variance. The $\Delta R^2$ equalled .11 and was not significantly different from zero F (3,37) = 2.04, p =.126. The $\Delta R^2$ was equal to 0.077. None of the added predictors was statistically significant.

Spatial attention in stage three of the regression model accounted for 0.32. The $\Delta R^2$ equalled .002 and the change in the variance was not significant, F (2,35) = .06, p = .94. None of the added spatial cognitive predictors was statistically significant.

Finally, the addition of non-spatial cognitive domains to stage four of the regression model accounts for 0.354 of the total variances. The $\Delta R^2$ for non-spatial predictors in EQ5D-VAS equalled .03 and were not significant, $F(2,33) = .77$, $p=.47$. When all predictors were included in stage four of the regression model, the overall model was not significant, $F(16,33) = 1.13$, $p=.37$. EBIQ motivation, the controlled predictor, which was statistically significant in stage one, became non-significant, $\beta= -.35$ $p=.055$.

The adjusted R2 value in stage three and four went down, which suggested that the predictors in both steps do not meaningfully contribute to the model. A larger $R^2$ change was observed for cognitive variables related to memory and planning (stage two) compared to other cognitive domains. The standardized regression coefficients ($\beta$), $R^2$, $R^2$ Adjusted and $\Delta R^2$ for EQ5D-VAS hierarchical model were reported in Table 2.

**Table 4**

*Predictors of EQ5D-VAS with regression coefficients (β), $R^2$, $R^2$ Adjusted, $\Delta R^2$, $\Delta R^2$Adjusted.*

| Stage | Predictors | B | $R^2$ | $R^2$ Adjusted | $\Delta R^2$ | $\Delta R^2$ Adjusted |
|---|---|---|---|---|---|---|
| 1 | Sex | .009 | .21 | .03 | .21 | .03 |
| | Age | -.020 | | | | |
| | NART | -.071 | | | | |
| | Cattell | -.25 | | | | |
| | EBIQ Motivation | -.35 | | | | |
| | EBIQ Depression | -.09 | | | | |
| | Lesion Side (bilateral) | -.14 | | | | |
| | Lesion Side (right) | -.08 | | | | |
| | Lesion Side (missing) | .08 | | | | |
| 2 | Top-Down Control | -.07 | .32 | .10 | .11 | 0.07 |
| | Working Memory | .38 | | | | |
| | Working Memory Capacity | -.36 | | | | |
| 3 | TVA Absolute Bias | .037 | .32 | .05 | .002 | -0.05 |
| | Oxbridge Cancellation Task | -.020 | | | | |
| 4 | TVA Variability | -.13 | .35 | .04 | .03 | -0.01 |
| | CRT Variability | -.16 | | | | |

**Secondary Data Effect Size and Power Calculation**

The present study used secondary data, a post-hoc calculation, looking at the effect size (Cohen's $f^2$) and power achieved from the multiple linear regression model based on $R^2$ increase after each subsequent step was conducted. The effect size calculated for the $R^2$ increase was calculated using the formula: $f^2 = (R^2_{inc})/(1-R^2_{inc})$, where $R^2_{inc}$ was the increase in $R^2$ for the set of predictors over another set of predictors. The cut-off values for the effect size were: 0.02 (small), 0.15 (medium) and 0.35 (large). The calculated effect sizes for non-spatial cognitive variables (stage four) for the EBIQ-Core and EQ5D-VAS model were .02(small) and .03 (small), respectively. Power analysis was completed using the G* Power software package. The parameters used were: effect size = 0.02 (EBIQ-Core)/0.03 (EQ5D-5L-VAS), $\alpha$ level = 0.05, sample size = 80, with two predictors being tested and 14 predictors in total (i.e., including control and independent variables). Conventionally, it was recommended for the power value to be at 0.8. The regression model achieved power = 0.18 (EBIQ-Core) and 0.25 (EQ5D-5L-VAS) with the above parameters.

The same formula was used to calculate the effect size of the model. $R^2_{inc}$ was replaced with $R^2_{model}$, which was the $R^2$ value of the entire model. The effect size for EBIQ-Core and EQ5D-5L-VAS were 4.56 and 0.54, respectively. The parameters used for the power analysis were the same as the ones above. Both models achieved a power value of greater than .8.

**Exclusion of EBIQ Depression and Motivation Domains from Regression Models**

Given the significant contributions of EBIQ Depression and Motivation on the variance EBIQ Core and EQ5D-VAS, hierarchical regression models were repeated with EBIQ depression and motivation scales excluded.

***EBIQ Core***

Stage one did not significantly account for the variance when both EBIQ domains were excluded from the model (Table 3). The negative adjusted $R^2$ values in stage one and two showed that the included variables included in those steps do not contribute meaningful or negligible to the overall variance in QoL. The $\Delta R^2$ in stage four equalled .17 and reached significance, $F(2, 35) = 4.53$, $p<.05$ after removing the two domains. The final hierarchical model was not significantly different, $F(14,35) = 1.3$ $p=.26$. Only the addition of non-spatial attention (stage four) showed a significant increase in variance explained. In the final model, two cognitive variables measuring spatial and non-spatial attention were statistically significant: TVA Absolute Bias, β= -.41, p<.05 and TVA Variability, β= .45, p<.05. This could suggest that the TVA paradigm is sensitive to EBIQ-Core changes.

**Table 5**

*Hierarchical Regression Model for EBIQ-Core after exclusion of depression and motivation domain.*

| Stage | Predictors | B | $R^2$ | $R^2$ Adjusted | $\Delta R^2$ | $\Delta R^2$ Adjusted |
|---|---|---|---|---|---|---|
| 1 | Sex | -0.26 | .06 | -0.09 | 0.06 | -0.09 |
| | Age | -0.32 | | | | |
| | NART | 0.3 | | | | |
| | Cattell | -0.17 | | | | |
| | Lesion Side (bilateral) | -.15 | | | | |
| | Lesion Side (right) | -.07 | | | | |
| | Lesion Side (missing data) | -.16 | | | | |
| 2 | Top-Down Control | -0.32 | 0.12 | -0.10 | 0.6 | -0.01 |
| | Working Memory | 0.06 | | | | |
| | Working Memory Capacity | -0.20 | | | | |
| 3 | TVA Absolute Bias | -0.41* | 0.17 | -0.1 | 0.05 | 0.09 |
| | Oxbridge Cancellation Task | -0.12 | | | | |
| 4 | TVA Variability | 0.45* | 0.34 | 0.08 | 0.17 | 0.18 |
| | CRT Variability | 0.17 | | | | |

* p<0.05

***EQ5D-VAS***

The hierarchical regression model remained non-significant even after the removal of the two domains (Table 4). The final hierarchical model was not significantly different, $F\ (14,35) = .78$ $p=.69$. The negative change adjusted $R^2$ values at stage one and three showed that the included predictors (i.e., controlled and spatial attention) do not contribute meaningfully to the overall variance in QoL. None of the predictors was statistically significant.

**Table 6**

*Hierarchical Regression Model for EQ5D- VAS after exclusion of depression and motivation*

| Stage | Predictors | B | $R^2$ | $R^2$ Adjusted | $\Delta R^2$ | $\Delta R^2$ Adjusted |
|---|---|---|---|---|---|---|
| 1 | Sex | 0.10 | .033 | -0.128 | 0.033 | -0.128 |
| | Age | 0.084 | | | | |
| | NART | -0.140 | | | | |
| | Cattell | -0.164 | | | | |
| | Lesion Side (bilateral) | 0.035 | | | | |
| | Lesion Side (right) | 0.005 | | | | |
| | Lesion Side (missing) | 0.162 | | | | |
| 2 | Top-Down Control | 0.036 | 0.149 | -0.069 | 0.116 | 0.06 |
| | Working Memory | 0.348 | | | | |
| | Working Memory Capacity | -0.272 | | | | |
| 3 | TVA Absolute Bias | 0.119 | .151 | -0.124 | 0.002 | -0.06 |
| | Oxbridge Cancellation Task | 0.033 | | | | |
| 4 | TVA Variability | -0.245 | 0.237 | -0.069 | 0.85 | 0.06 |
| | CRT Variability | -0.213 | | | | |

## Discussions

The main aim of the present study was to identify the main cognitive predictors associated with QoL post-stroke. The EBIQ motivational and depression subscale were significant predictors of the EBIQ Core. None of the cognitive predictors contributed significantly to either of the models shown. While statistically non-significant, non-spatial predictors were observed to contribute the most variance compared to other cognitive domains entered in the EBIQ Core regression model. None of the individual variables (i.e., control and independent) entered in the EQ5D-VAS model were significant. EQ5D-VAS as a dependent variable might not be a robust QoL assessment. It was suggested that the EQ5D-VAS was less responsive in detecting QoL than other measures of QoL used in stroke (Golicki et al., 2015b).

After removing EBIQ depression and motivation subscales, the variance contributed by non-spatial attention to the EBIQ-Core model became significant. Hence, it could also be suggested that non-spatial cognitive domains contributed to predicting QoL through EBIQ-Core but only after the removal of motivation and depression variables. As an independent predictor, TVA Variability (non-spatial attention) was a significant predictor of EBIQ Core. TVA Absolute Bias (i.e., an independent spatial attention predictor) was significant in predicting QoL. The TVA assessment task might be more sensitive to assessing spatial and non-spatial attention than OCS-BRIDGE or CRT. Tentatively, any possible contribution non-spatial attention has to QoL could be attributed to cognitive aspects of mood and motivation. Therefore, further research on the possible link between cognition, mood, motivation and QoL was warranted.

There were several explanations for the findings obtained. The near significant effect of non-spatial attention when depression and motivation were removed as control variables might be a false positive result because of a possible relationship between a measure of cognitive deficits (i.e., cognitive tasks) and a measure sensitive to the impact of brain injury (i.e., EBIQ). The alternative explanation was that there might be a real effect of non-spatial attention on QoL. However, due to the inadequately powered analysis and the small effect size, the effect might be difficult to detect.

The third explanation for the non-significance could be attributed to false-negative due to issues with the measurements used (i.e., EBIQ), which added further caution to the interpretation of the results. The EBIQ has been validated and widely used in research and clinical practice to assess QoL among individuals with acquired brain injuries (Sopena et al., 2007). The contents of the EBIQ overlapped with measures like the Quality of Life in Brain Injury (QOLIBRI) questionnaire, which was explicitly designed to assess QoL across different domains of QoL for individuals with brain injury (von Steinbuechel & et al., 2005). For example, both measures assessed physical functioning, social relationships, emotions and cognition. However, the differences between the two measures could lie in how the statements were presented, leading to the assessments of different constructs.

The EBIQ worded the statements based on an individual's perception if they have experienced any of the difficulties listed over the past month (i.e., how much have you experienced these difficulties over the past month). Therefore, when completing the EBIQ, participants could assume that the EBIQ was asking them about the impact of their brain injury. While the EBIQ statements provided researchers with an insight into an individuals' perception of their current capability across different domains, they might not assess an individual's emotional perception of their functioning. The

QOLIBRI questionnaire presented the statements as ‘how satisfied/bothered individuals were with the different domains assessed’. This was an essential aspect as QoL has been defined as a subjective concept that included mental, social and physical aspects of life (Whoqol Group, 1995, Zbolralski et al., 2007).

Previous research has shown the association between stroke-related functional deficits with spatial attention (Nys et al., 2006). Bickerton and colleagues (2015) posited that functional outcome deficits related to spatial attention were better predicted when sustained attention, response inhibition and executive function were considered together with spatial attention. Considering recent evidence (Bickerton et al., 2015; Peers et al., 2018) with the present findings, non-spatial attention might be an underpinning cognition mediating with other cognitive domains impacted in stroke individuals. However, the scope of the present study does not provide strong evidence to support this claim, especially when the significance was only attained when EBIQ motivation and depression was removed from the model. More research is needed to explore the role of non-spatial attention and determine how it relates to spatial attention and with QoL/functional outcomes.

The current study results showed that the removal of depression and motivation as control variables caused variance contributed by the models' social and clinical control variables to become non-significant. This could suggest that above all other known variables such as age, gender, lesion side and premorbid intelligence, an individual’s motivation, and depressive symptoms are the core predictors of their QoL. This contradicts previous research on the role of gender (Mahesh, Gunathunga, Jayasinghe, Arnold & Liyanage, 2018) and lesion side (Salehi, Tahan, Bagheban, & Monfared, 2019) on QoL. Therefore, despite the established link between these variables with QoL and ADL, these variables might not be relevant for predicting QoL among stroke individuals. However, more studies are needed before a conclusion can be reached.

The findings of the regression model suggested that depression and motivation factors are essential variables to predict QoL more than cognitive domains. Previous research has shown evidence of an individual’s motivation and depression impacting cognition and QoL (Gbiri, Akinpelu, & Odole, 2010; Haghgoo, Pazuki, Hosseini & Rassafiani, 2013). However, EBIQ-Core was a composite score derived from all the EBIQ symptom subscales, including depression and motivation. It was suggested that the EBIQ subscales used in the present study to assess motivation and depression might also assess additional constructs such as perceived cognitive capability. This could explain the large variance of EBIQ depression and motivation to the EBIQ-Core and not to the EQ5D-VAS model. Future research could consider assessing motivation and depression using questionnaires or scales using separate measures that are minimally related to the measures used to assess QoL.

Visuospatial neglect was commonly associated with right hemispherical lesions (Karnath et al., 2009). A large portion of the attentional network resides in the right hemisphere (Sturm & Willmes, 2001; Shulman et al., 2010). Therefore, stroke individuals with right-side lesions should present with increased attentional difficulties and result in poorer QoL. Future research could explore the impact the lesion side has on the relationship between cognition and QoL assessment.

Premorbid intelligence could be thought of as a cognitive reserve (Whalley, Deary, Appleton, & Starr, 2004) and was suggested to reduce the burden of disability post-stroke (Rosenich, Hordacre, Paquet, Koblar & Hillier, 2020), which could impact an individual's QoL. Cognitive reserve in an individual was associated with higher QoL in older adults (Lara et al., 2017). The same association was observed in the Alzheimer's population, where higher cognitive reserve (i.e., higher premorbid intelligence) showed better functional capability and QoL (Sánchez-Rodríguez, Torrellas-Morales, Fernández-Gómez, & Martín-Vallejo, 2013). However, current evidence for the role of the cognitive reserve as a predictor of QoL in brain injury/stroke is still insufficient (Nunnari, Bramanti & Marino, 2015).

**Strengths and Limitations of Study**

The present research questions were formed around the given data, which reduces the likelihood of unsuitable data to answer the questions. The experimental tasks used in the original study were specific and in-depth measures of cognitive domains. Previous studies looking at stroke and rehabilitation had assessed the cognitive domain using broad measures, which might not examine precisely the roles specific cognitive domains have on QoL. Additionally, the current analysis is blind to the hypothesis of the original study. This reduces the risk-of-bias related to data collection to a minimum. Any data removal would be unbiased and led by statistical objectivity.

There are several limitations to the present empirical study. The first limitation observed was the low sample size and power achieved from the analysis. If there was an effect to be found, replicating the study with a larger sample size could increase the statistical power to observe it. Additionally, the regression model also assumes a linear relationship between the predictors and dependent variable. Real-world data are often non-linear (Micceri, 1989). In statistics, the consensus was to transform data linearly and as well as to remove outliers. However, in doing so, we risk losing the typical data variability observed because of brain injury. Therefore, there need to be considerations if the analyses should be done parametrically or should a non-linear analysis model be adopted.

The multiple analyses carried out increases the risk of false-positive results. Although collinearity was observed to be a non-issue based on Tolerance and VIF values, there is the issue that other variables that may influence the QoL were not considered as a possible limitation. An example of this was sleep quality on cognitive tasks, a particularly crucial impact on the stroke population. Additionally, there is also the issue of confound when EBIQ motivation and depression domain were excluded. Future research needs to assess these confounds.

Another potential limitation regarding measurement is the construct validity of the EBIQ. Bateman, Teasdale and Willmes (2009) showed that the subscales used in the original 63-item EBIQ were not uni-dimensional using Rasch Analysis. The authors posited that the EBIQ motivation and depression subscale might also assess additional constructs such as the perceived cognitive capability. Therefore, participants might have thought they were providing answers to their perceived everyday ability rather than indicating their motivation or depressive level when completing the EBIQ. This could potentially impact the reliability and validity of the EBIQ motivation and depression subscale.

Previous research has used various outcome measures to detect changes in QoL (de Haan et al., 1993; Sturm et al., 2004). Like the Quality of Life After Brain (QOLIBRI), these measures were often more detailed, looked at various components that made up QoL (e.g., physical functioning, emotional well-being or ADL), and were often assessed as a whole to provide an overall indication of QoL. The EQ5D-5L-VAS subset, which required participants to provide a single numerical value to denote participants' perception of health, was suggested to provide a summary of an individual's overall health close to the patient's perspective (Feng, Parkin & Devlin, 2014). However, a single numerical value could be another limitation of the model and study as the variable might not encapsulate the entirety of stroke's impact on QoL. If the study was replicated, it might be more appropriate for an alternative QoL measure to be used instead of the EQ5D-5L-VAS.

The EBIQ was initially designed to assess the impact brain injury has on an individual. For the current study, the EBIQ was used as an indirect measure of QoL. This meant that the reliability and validity of the findings observed from the present analysis were impacted potentially. The solution to this could be the use of assessment tools that were designed to measure QoL like the World Health Organisation Quality of Life -BREF (WHOQOL-BREF) (Whoqol Group, 1998), which had been used in the stroke population (Jeong et al., 2012). Alternatively, the Quality of Life After Brain Injury – Overall Scale (QOLIBRI-OS) was designed specifically for individuals with brain injury (von Steinbuechel et al., 2012) and was validated for use in the stroke population (Heiberg et al., 2018). Hence, based on what was discussed in the last two paragraphs, the measures used to assess QoL could be another limitation of the current empirical study.

**Possible Changes to the Empirical Study if Replicated**

The mentioned limitations above provided several factors that would need to be addressed in the future. If the study were replicated, a few changes could help improve the validity and reliability of the results obtained.

As mentioned above, the first aspect being considered would be the outcome measures used. Alternative measures of ADL like the WHOQOL-BREF and QOLIBRI-OS, which were designed and validated to assess QoL among individuals with stroke. On the other hand, previous research had linked poorer QoL with poorer everyday functioning. Older adults with stroke or other neurological deficits were observed to have a certain degree of difficulties with everyday functioning. Impairment of everyday functioning was associated with impaired executive functioning, which has impacted an individual’s awareness of their deficits (Hurst et al., 2017). Therefore, self-report measures might not assess an individual's ADLs or QoL accurately. Therefore, a performance-based measure of everyday functioning like the Timed Instrumental Activities of Daily Living (Owsley et al., 2002) or the Behavioural Assessment of Dysexecutive Syndrome (BADS) (Espinosa et al., 2009) might be a more appropriate measure of ADL.

The current study results suggested the contribution of emotional factors like motivation and depression have on QoL. It would be essential to assess these factors with psychometrically valid measures unrelated to the dependent variables to reduce the variance observed in the current analysis. The current cognitive assessments used will remain the same as the variables derived from the assessments represent specific and in-depth cognitive domains.

An alternative important next step could be using other statistical techniques like structural equation modelling to investigate the relationship between the different variables. This could help researchers develop a deeper understanding of the relationship between cognition, mood and expected outcomes. For example, it might be helpful to ascertain whether depression and motivation were possible moderators that could influence cognitive tasks and QOL.

Additionally, longitudinal data could illuminate further if specific early cognitive impairments (e.g., non-spatial attention) or early emotional impairments (i.e., motivation and depression) could lead to lower QOL first. This could potentially lead to future innovations in clinical interventions.

Finally, future replications might reduce the number of predictors being included in the regression model. The current regression model included various control variables, which did not contribute to the overall model. For example, it was shown that the lesion side, gender and age, had not contributed to the regression model. Alternatively, other confounds such as sleep quality which has been shown to impact cognitive performance and quality of life (Fulk, Duncan & Klingman, 2020), might be worth exploring.

**Conclusions**

In summary, the present study did not find evidence of non-spatial attention being a stronger predictor of QoL than other cognitive predictors. Weak evidence of some role of non-spatial attention was observed after removing depression and motivation domains as control variables. Therefore, care is needed when interpreting the results of the present analysis. QoL/everyday functioning changes are not likely due to a single domain of cognition based on the evidence from previous research and current results. As predictors, emotional issues might also play a role in predicting the QoL of stroke individuals. The TVA paradigm could be a potential cognitive assessment sensitive to changes in QoL. As reported, the evidence to back up the assertion is tentative at best. More research is needed to explore the findings further.

**Reference**

Alloway, T. P. (2007). *Automated Working: Memory Assessment: Manual*. Pearson.

Azouvi, P., Jacquin-Courtois, S., & Luauté, J. (2017). Rehabilitation of unilateral neglect: Evidence-based medicine. *Annals of physical and rehabilitation medicine*, *60*(3), 191-197.

Barker-Collo, S. L., Feigin, V. L., Lawes, C. M. M., Parag, V., & Senior, H. (2010). Attention deficits after incident stroke in the acute period: Frequency across types of attention and relationships to patient characteristics and functional outcomes. Topics in Stroke Rehabilitation, 17(6), 463–476. doi:10.1310/tsr1706-463

Bateman, A., Teasdale, T. W., & Willmes, K. (2009). Assessing construct validity of the self-rating version of the European Brain Injury Questionnaire (EBIQ) using Rasch analysis. *Neuropsychological rehabilitation*, *19*(6), 941-954.

Bickerton, W. L., Demeyere, N., Francis, D., Kumar, V., Remoundou, M., Balani, A., ... & Humphreys, G. W. (2015). The BCoS cognitive profile screen: Utility and predictive value for stroke. *Neuropsychology*, *29*(4), 638.

Bour, A., Rasquin, S., Aben, I., Boreas, A., Limburg, M., & Verhey, F. (2010). A one-year follow-up study into the course of depression after stroke. *The journal of nutrition, health & aging*, *14*(6), 488-493.

Bowen, A., Hazelton, C., Pollock, A., & Lincoln, N. B. (2013). Cognitive rehabilitation for spatial neglect following stroke. *Cochrane Database of Systematic Reviews*, (7).

Burckhardt, C. S., & Anderson, K. L. (2003). The Quality of Life Scale (QOLS): reliability, validity, and utilization. *Health and quality of life outcomes*, *1*(1), 1-7.

Cattell, R. B. (1978). *Use of factor analysis in the behavioral and life sciences*. New York: Plenum

Chen, H.-C., Koh, C.-L., Hsieh, C.-L., & Hsueh, I. P. (2009). Test–re-test reliability of two sustained attention tests in persons with chronic stroke. Brain Injury, 23(9), 715–722. doi:10.1080/02699050903013602

de Haan, R. D., Aaronson, N., Limburg, M., Hewer, R. L., & Van Crevel, H. (1993). Measuring quality of life in stroke. *stroke*, *24*(2), 320-327.

de Haan, R. D., Aaronson, N., Limburg, M., Hewer, R. L., & Van Crevel, H. (1993). Measuring QoL in stroke. *stroke*, *24*(2), 320-327.

De Wit, L., Theuns, P., Dejaeger, E., Devos, S., Gantenbein, A. R., Kerckhofs, E., ... & Putman, K. (2017). Long-term impact of stroke on patients' health-related quality of life. *Disability and rehabilitation*, *39*(14), 1435-1440.

Demeyere, N., Riddoch, M. J., Slavkova, E. D., Bickerton, W. L., & Humphreys, G. W. (2015). The Oxford Cognitive Screen (OCS): validation of a stroke-specific short cognitive screening tool. *Psychological assessment*, *27*(3), 883.

Espinosa, A. N. A., Alegret, M., Boada, M., Vinyes, G., Valero, S., Martínez-Lage, P., ... & Tárraga, L. (2009). Ecological assessment of executive functions in mild cognitive impairment and mild Alzheimer's disease. *Journal of the International Neuropsychological Society*, *15*(5), 751-757.

Falck, R. S., Best, J. R., Davis, J. C., Eng, J. J., Middleton, L. E., Hall, P. A., & Liu-Ambrose, T. (2019). Sleep and cognitive function in chronic stroke: a comparative cross-sectional study. *Sleep*, *42*(5), zsz040.

Feng, Y., Parkin, D., & Devlin, N. J. (2014). Assessing the performance of the EQ-VAS in the NHS PROMs programme. *Quality of Life Research*, *23*(3), 977-989.

Franceschini, M., La Porta, F., Agosti, M., & Massucci, M. (2010). Is health-related-quality of life of stroke patients influenced by neurological impairments at one year after stroke?. *European journal of physical and rehabilitation medicine, 46*(3), 389-399.

Fulk, G., Duncan, P., & Klingman, K. J. (2020). Sleep problems worsen health-related quality of life and participation during the first 12 months of stroke rehabilitation. *Clinical Rehabilitation, 34*(11), 1400-1408.

Gbiri, C. A., Akinpelu, A. O., & Odole, A. C. (2010). Prevalence, pattern and impact of depression on quality of life of stroke survivors. *International Journal of Psychiatry in Clinical Practice*, *14*(3), 198-203.

Golicki, D., Niewada, M., Buczek, J., Karlińska, A., Kobayashi, A., Janssen, M. F., & Pickard, A. S. (2015). Validity of EQ-5D-5L in stroke. *Quality of Life Research, 24*(4), 845-850.

Golicki, D., Niewada, M., Karlińska, A., Buczek, J., Kobayashi, A., Janssen, M. F., & Pickard, A. S. (2015). Comparing responsiveness of the EQ-5D-5L, EQ-5D-3L and EQ VAS in stroke patients. *Quality of Life Research, 24*(6), 1555-1563.

Habekost, T. (2015). Clinical TVA-based studies: a general review. *Frontiers in psychology, 6*, 290.

Haghgoo, H. A., Pazuki, E. S., Hosseini, A. S., & Rassafiani, M. (2013). Depression, activities of daily living and quality of life in patients with stroke. *Journal of the neurological sciences, 328*(1-2), 87-91.

Halligan, P. W., & Marshall, J. C. (1998). Neglect of awareness. *Consciousness and cognition, 7*(3), 356-380.

Heiberg, G., Pedersen, S. G., Friborg, O., Nielsen, J. F., Holm, H. S., Arntzen, C., & Anke, A. (2018). Can the health related quality of life measure QOLIBRI-overall scale (OS) be of use after stroke? A validation study. *BMC neurology, 18*(1), 1-10.

Herdman, M., Gudex, C., Lloyd, A., Janssen, M. F., Kind, P., Parkin, D., ... & Badia, X. (2011). Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of life research, 20*(10), 1727-1736.

Hurst, F. G., Ownsworth, T., Beadle, E., Shum, D. H., & Fleming, J. (2020). Domain-specific deficits in self-awareness and relationship to psychosocial outcomes after severe traumatic brain injury. *Disability and rehabilitation*, *42*(5), 651-659.

Husain, M., & Rorden, C. (2003). Non-spatially lateralized mechanisms in hemispatial neglect. *Nature Reviews Neuroscience*, *4*(1), 26-36.

Huygelier, H., Schraepen, B., Lafosse, C., Vaes, N., Schillebeeckx, F., Michiels, K., ... & Gillebert, C. R. (2020). An immersive virtual reality game to train spatial attention orientation after stroke: A feasibility study. *Applied Neuropsychology: Adult*, 1-21.

Jeong, B. O., Kang, H. J., Bae, K. Y., Kim, S. W., Kim, J. M., Shin, I. S., ... & Yoon, J. S. (2012). Determinants of quality of life in the acute stage following stroke. *Psychiatry Investigation*, *9*(2), 127.

Johnstone, E. C., Owens, D. C., & Lawrie, S. M. (2010). *Companion to psychiatric studies e-book*. Elsevier Health Sciences.

Karnath, H. O., Rorden, C., & Ticini, L. F. (2009). Damage to white matter fiber tracts in acute spatial neglect. *Cerebral Cortex*, *19*(10), 2331-2337.

Kim, B. J., Liu, L., Nakaoka, S., Jang, S., & Browne, C. (2018). Depression among older Japanese Americans: The impact of functional (ADL & IADL) and cognitive status. *Social work in health care*, *57*(2), 109-125.

Lara, E., Koyanagi, A., Caballero, F., Domènech-Abella, J., Miret, M., Olaya, B., ... & Haro, J. M. (2017). Cognitive reserve is associated with QoL: A population-based study. *Experimental gerontology*, *87*, 67-73.

Leys, D., Hénon, H., Mackowiak-Cordoliani, M. A., & Pasquier, F. (2005). Poststroke dementia. *The Lancet Neurology*, *4*(11), 752-759.

Lezak, M. D., Howieson, D. B., Loring, D. W., & Fischer, J. S. (2004). *Neuropsychological assessment*. Oxford University Press, USA.

Lipskaya-Velikovsky, L., Zeilig, G., Weingarden, H., Rozental-Iluz, C., & Rand, D. (2018). Executive functioning and daily living of individuals with chronic stroke: measurement and implications. *International journal of rehabilitation research*, *41*(2), 122-127.

Loetscher, T., Potter, K. J., Wong, D., & das Nair, R. (2019). Cognitive rehabilitation for attention deficits following stroke. *Cochrane Database of Systematic Reviews*, (11).

Mahesh, P. K. B., Gunathunga, M. W., Jayasinghe, S., Arnold, S. M., & Liyanage, S. N. (2018). Factors influencing pre-stroke and post-stroke QoL among stroke survivors in a lower middle-income country. *Neurological Sciences*, *39*(2), 287-295.

Marshall, G. A., Rentz, D. M., Frey, M. T., Locascio, J. J., Johnson, K. A., Sperling, R. A., & Alzheimer's Disease Neuroimaging Initiative. (2011). Executive function and instrumental activities of daily living in mild cognitive impairment and Alzheimer's disease. *Alzheimer's & Dementia*, *7*(3), 300-308.

Micceri, T. (1989). The unicorn, the normal curve, and other improbable creatures. *Psychological bulletin*, *105*(1), 156.

Naghavi, M., Abajobir, A. A., Abbafati, C., Abbas, K. M., Abd-Allah, F., Abera, S. F., ... & Fischer, F. (2017). Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the

Global Burden of Disease Study 2016. *The Lancet*, *390*(10100), 1151-1210.

Nelson, H. E., & O'Connell, A. (1978). Dementia: the estimation of premorbid intelligence levels using the New Adult Reading Test. *Cortex*, *14*(2), 234-244.

Nguyen, C. M., Copeland, C. T., Lowe, D. A., Heyanka, D. J., & Linck, J. F. (2020). Contribution of executive functioning to instrumental activities of daily living in older adults. *Applied Neuropsychology: Adult*, *27*(4), 326-333.

Nichol, A. D., Higgins, A. M., Gabbe, B. J., Murray, L. J., Cooper, D. J., & Cameron, P. A. (2011). Measuring functional and quality of life outcomes following major head injury: common scales and checklists. *Injury*, *42*(3), 281-287.

Nunnari, D., Bramanti, P., & Marino, S. (2014). Cognitive reserve in stroke and traumatic brain injury patients. *Neurological Sciences*, *35*(10), 1513-1518.

Nys, G. M. S., Van Zandvoort, M. J. E., Van Der Worp, H. B., De Haan, E. H. F., De Kort, P. L. M., Jansen, B. P. W., & Kappelle, L. J. (2006). Early cognitive impairment predicts long-term depressive symptoms and QoL after stroke. *Journal of the neurological sciences*, *247*(2), 149-156.

Owsley, C., Sloane, M., McGwin Jr, G., & Ball, K. (2002). Timed instrumental activities of daily living tasks: relationship to cognitive function and everyday performance assessments in older adults. *Gerontology*, *48*(4), 254-265.

Peers, P. V., Astle, D. E., Duncan, J., Murphy, F., Hampshire, A., Das, T., & Manly, T. (2018). A randomised exploratory investigation of the effects of Attention vs Working Memory Training on cognitive performance and everyday functioning following stroke. *BioRxiv*, 296723.

Peers, P. V., Punton, S. F., Murphy, F. C., Watson, P., Bateman, A., Duncan, J., ... & Manly, T. (2021). A randomised control trial of the effects of home-based online attention training and working memory training on cognition and everyday function in a community stroke sample. *medRxiv*.

Robertson, I. H., Ridgeway, V., Greenfield, E., & Parr, A. (1997). Motor recovery after stroke depends on intact sustained attention: a 2-year follow-up study. *Neuropsychology*, *11*(2), 290.

Rosenich, E., Hordacre, B., Paquet, C., Koblar, S. A., & Hillier, S. L. (2020). Cognitive reserve as an emerging concept in stroke recovery. *Neurorehabilitation and neural repair*, *34*(3), 187-199.

Salehi, S., Tahan, N., Bagheban, A. A., & Monfared, M. E. (2019). Quality of Life Within Three Months After Stroke: A Study in the City of Arak, Iran. *Journal of the National Medical Association*, *111*(5), 475-480.

Sánchez-Rodríguez, J. L., Torrellas-Morales, C., Fernández-Gómez, M. J., & Martín-Vallejo, J. (2013). Influencia de la reserva cognitiva en la calidad de vida en sujetos con enfermedad de Alzheimer. *Anales de Psicología/Annals of Psychology*, *29*(3), 762-771.

Schöttke, H., & Giabbiconi, C. M. (2015). Post-stroke depression and post-stroke anxiety: prevalence and predictors. *International Psychogeriatrics*, *27*(11), 1805-1812.

Shea-Shumsky, N. B., Schoeneberger, S., & Grigsby, J. (2019). Executive functioning as a predictor of stroke rehabilitation outcomes. *The Clinical Neuropsychologist*, *33*(5), 854-872.

Shulman, G. L., Pope, D. L., Astafiev, S. V., McAvoy, M. P., Snyder, A. Z., & Corbetta, M. (2010). Right hemisphere dominance during spatial selective attention and target detection occurs outside the dorsal frontoparietal network. *Journal of Neuroscience*, *30*(10), 3640-3651.

Sopena, S., Dewar, B. K., Nannery, R., Teasdale, T. W., & Wilson, B. A. (2007). The European Brain Injury Questionnaire (EBIQ) as a reliable outcome measure for use with people with brain injury. *Brain Injury*, *21*(10), 1063-1068.

Southworth, C. (2012). Making Sense of Biostatistics: Outliers in Clinical Data. *Clinical research Journal*, *6*(1), 2-3.

Sturm, J. W., Donnan, G. A., Dewey, H. M., Macdonell, R. A., Gilligan, A. K., Srikanth, V., & Thrift, A. G. (2004). Quality of life after stroke: the North East Melbourne stroke incidence study (NEMESIS). *Stroke*, *35*(10), 2340-2345.

Sturm, W., & Willmes, K. (2001). On the functional neuroanatomy of intrinsic and phasic alertness. *Neuroimage*, *14*(1), S76-S84.

Stuss, D. T., Stethem, L. L., Hugenholtz, H., Picton, T., Pivik, J., & Richard, M. T. (1989). Reaction time after head injury: fatigue, divided and focused attention, and consistency of performance. *Journal of Neurology, Neurosurgery & Psychiatry*, *52*(6), 742-748.

Teasdale, T. W., Christensen, A. L., Willmes, K., Deloche, G., Braga, L., Stachowiak, F., ... & Leclercq, M. (1997). Subjective experience in brain injured patients and their close relatives: A European Brain Injury Questionnaire study. *Brain Injury*, *11*(8), 543-564.

Truelsen, T., Begg, S., & Mathers, C. (2006). The global burden of cerebrovascular. In *Who Int*.

van de Port, I. G., Kwakkel, G., Schepers, V. P., Heinemans, C. T., & Lindeman, E. (2007). Is fatigue an independent factor associated with activities of daily living, instrumental activities of daily living and health-related quality of life in chronic stroke?. *Cerebrovascular Diseases*, *23*(1), 40-45.

Van Mierlo, M. L., Van Heugten, C. M., Post, M. W., Hajos, T. R., Kappelle, L. J., & Visser-Meily, J. M. (2016). Quality of life during the first two years post stroke: the Restore4Stroke cohort study. *Cerebrovascular Diseases*, *41*(1-2), 19-26.

von Steinbuechel, N., Petersen, C., Bullinger, M., & QoLIBRI Group. (2005). Assessment of health-related quality of life in persons after traumatic brain injury—development of the Qolibri, a specific measure. *Re-Engineering of the Damaged Brain and Spinal Cord*, 43-49.

Von Steinbuechel, N., Wilson, L., Gibbons, H., Muehlan, H., Schmidt, H., Schmidt, S., ... & Truelle, J. L. (2012). QOLIBRI overall scale: a brief index of health-related quality of life after traumatic brain injury. *Journal of Neurology, Neurosurgery & Psychiatry*, *83*(11), 1041-1047.

Whalley, L. J., Deary, I. J., Appleton, C. L., & Starr, J. M. (2004). Cognitive reserve and the neurobiology of cognitive aging. *Ageing research reviews*, *3*(4), 369-382.

Whoqol Group. (1995). The World Health Organization quality of life assessment (WHOQOL): position paper from the World Health Organization. *Social science & medicine*, *41*(10), 1403-1409.

Whoqol Group. (1998). Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychological medicine*, *28*(3), 551-558.

Williams, L. S., Weinberger, M., Harris, L. E., Clark, D. O., & Biller, J. (1999). Development of a stroke-specific QoL scale. *Stroke*, *30*(7), 1362-1369.

Williams, P. G., Tinajero, R., & Suchy, Y. (2017). Executive functioning and health. *Oxford Handbooks Online*.

Zboralski1ABCD, K., Florkowski1G, A., Talarowska-Bogusz1BCDE, M., Macander2B, M., & Gałecki1F, P. (2008). Quality of life and emotional functioning in selected psychosomatic diseases Jakość życia i funkcjonowanie emocjonalne w wybranych schorzeniach psychosomatycznych. *Postepy Hig Med Dosw.(online)*, *62*, 36-41.

# Chapter 5: Extended Results

This chapter provides additional details concerning the analyses conducted.

## Assumptions for Hierarchical Regression

Five assumptions needed to be met before a hierarchical regression could be done. Each assumption was tested using statistical tools if appropriate.

### *Linearity*

This assumed that the relationships between the predictors and the outcome variable should be linear. This assumption was met based on the previous evidence on the relationship between the dependent variables (i.e., QoL outcomes) and predictors (i.e., cognitive domains).

### *Independence of Residual Values*

The Durbin-Watson statistic showed that the assumption had been met, as the obtained value was close to 2 (Durbin-Watson = 1.93).

### *Homogeneity of Variance (Homoscedasticity)*

One assumption was the requirement for the error variance of the dependent variable to be constant. A scatterplot of standardised residuals versus the standardised predicted values was plotted. If there is no clear pattern in the distribution, homoscedasticity was retained. The following scatterplots were used for the two dependent variables, EQ5D-5L and EBIQ, respectively.

**Figure 1**

*Scatterplot of Standardised Residual and Predicted Value for EBIQ-Core.*

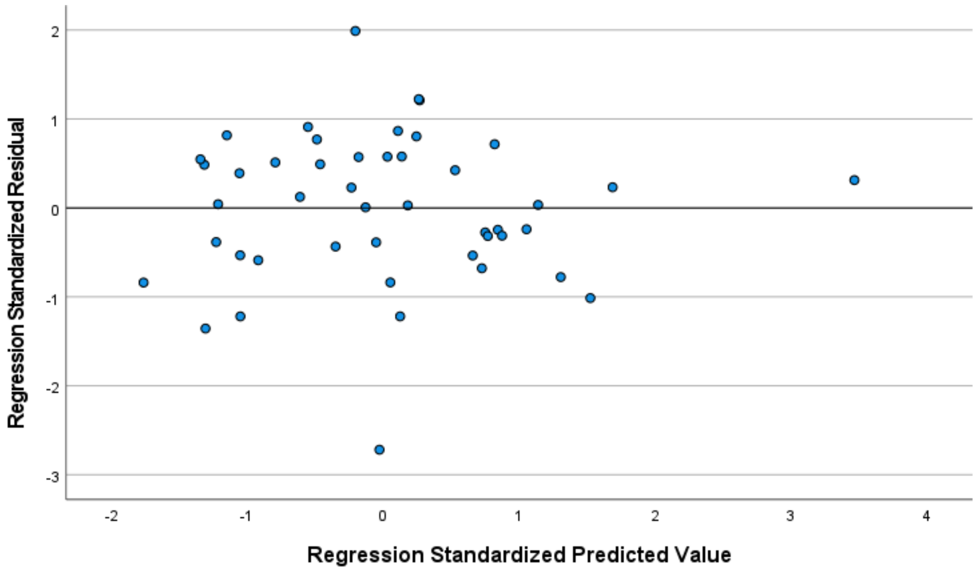
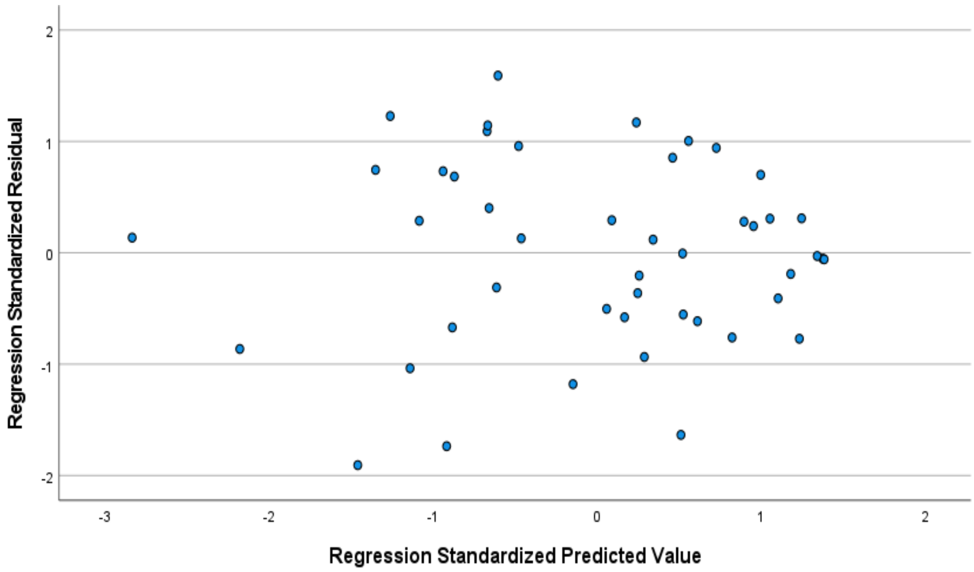


**Figure 2**

*Scatterplot of Standardised Residual and Predicted Value for EQ5D-VAS.*




In both scatterplots, the standardised values seemed to be tapered at the end. However, there was no funnel pattern observed, which suggested homoscedasticity was maintained in both models.

***Normality***

Normality is a common assumption requirement for many parametric tests. The values of the residuals were assumed to be normally distributed. The assumption was tested by looking at the P-P plot of the model (Figure 3 and 4). This violation of normality was understandable as data yielded from health, education, and social sciences often deviated from a normal distribution (Blanca et al., 2013).

**Figure 3**

*P-P Plot to assess normality for EBIQ Core.*

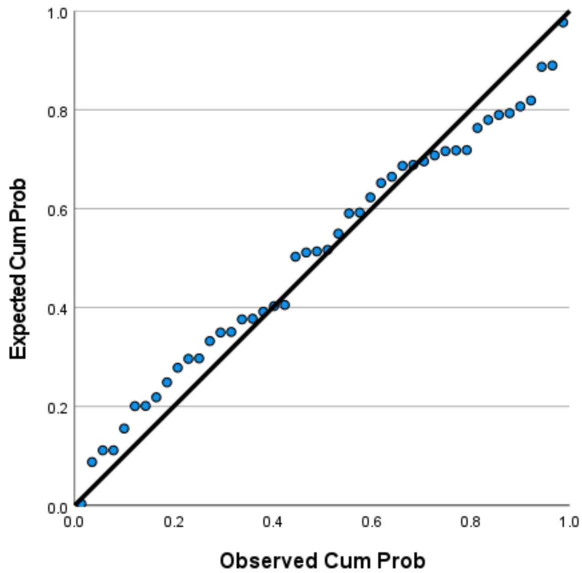
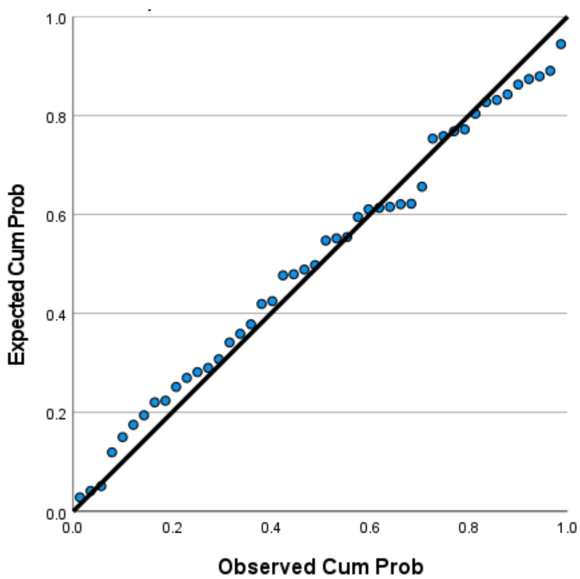



**Figure 4**

*P-P Plot to assess normality for EQ5D-5L Health*



The residuals were considered normally distributed if the dots lie closer to the diagonal line. Based on the plots above, the assumption of normality was violated. However, as only extreme deviations were likely to impact the findings significantly, the results obtained from the analysis could still be valid. Additionally, the predictor and control variables were also tested for normality using Shapiro-Wilks (Table 1). If the p-value was >0.5 (i.e., significant), the variables were not normally distributed.

**Table 1**

*List of Variables with Shapiro-Wilk Test for Normality*

| Variables | Shapiro-Wilk | | |
|---|---|---|---|
| | Statistic | df | Significance |
| Age | 0.96 | 80 | 0.01 |
| NART | 0.97 | 66 | 0.11 |
| Cattell | 0.99 | 75 | 0.85 |
| AWMA Dot Matrix | 0.99 | 79 | 0.51 |
| AWMA Spatial Recall | 0.97 | 78 | 0.07 |
| EBIQ Motivation | 0.94 | 80 | 0.001 |
| EBIQ Depression | 0.93 | 80 | <0.001 |
| TVA Task Absolute Bias | 0.84 | 78 | <0.001 |
| TVA Variability | 0.91 | 80 | <0.001 |
| ANT Top-Down Control | 0.63 | 80 | <0.001 |
| CRT Variability | 0.61 | 78 | <0.001 |
| Oxbridge Cancellation Task | 0.45 | 78 | <0.001 |
| Digit Span Forward | 0.93 | 64 | 0.001 |
| Digit Span Backward | 0.91 | 64 | <0.001 |

Before the following assumption was tested, AWMA Spatial Recall and Dot Matrix Tasks merged with Digit Span Forward and

Backwards before the following assumption was tested. The merged variables created two new variables: Working Memory (i.e., Spatial Recall and Digit Span Backwards) and Working Memory Capacity (i.e., Dot Matrix and Digit Span Forwards).

***Independence***

The following assumption required variables in the regression not to be correlated. Collinearity was checked for all variables. The variance inflation factor (VIF) and tolerance value were statistically values used to diagnose collinearity. The values were based on R-squared values obtained by regressing one predictor on all the other predictors in the analysis. Tolerance is a reciprocal of VIF. A VIF value of >10 would suggests problematic collinearity, and a tolerance value of <0.2 would suggest a cause for concern.

***Collinearity***

**Table 2**

*Tolerance and VIF values*

| Variables | Collinearity Statistics | |
|---|---|---|
| | **Tolerance** | **VIF** |
| Sex | 0.67 | 1.49 |
| Age | 0.40 | 2.53 |
| Lesion Side | 0.55 | 1.81 |
| NART | 0.55 | 1.83 |
| Cattell | 0.32 | 3.10 |
| EBIQ Motivation | 0.55 | 1.81 |
| EBIQ Depression | 0.49 | 2.05 |
| Top-Down Control | 0.71 | 1.40 |
| Working Memory | 0.41 | 2.44 |
| Working Memory Capacity | 0.44 | 2.28 |
| TVA Absolute Bias | 0.62 | 1.61 |
| Oxbridge Heart Cancellation | 0.58 | 1.72 |
| TVA Variability | 0.54 | 1.85 |
| CRT Variability | 0.55 | 1.82 |

Tolerance and VIF are measures of collinearity. The variables in Table 2, 'Cattell', seemed to have slight collinearity based on the VIF values. This should not be a cause for concern as the variables do not meet the cut-off value. Collinearity would become an issue if both tolerance and VIF cut-off values were simultaneously met. This was not the case for the variable 'Cattell'.

***Skewness and Kurtosis***

Skewness and kurtosis for each variable were assessed for the comparative analysis between 'unprocessed' and 'processed' data.

For skewness, if the value is greater than + 1.0, the distribution is right-skewed. If the value is less than -1.0, the distribution is left-skewed. For kurtosis, if the value is greater than + 1.0, the distribution is leptokurtic. If the value is less than -1.0, the distribution is platykurtic. The following variables were observed to have high values in skewness and kurtosis (Table 3).

**Table 3**

*List of Variables with Skewness and Kurtosis Values*

| Variables | Skewness | | Kurtosis | |
|---|---|---|---|---|
| | Statistic | Std. Error | Statistic | Std. Error |
| Age | -0.71 | 0.27 | 0.44 | 0.53 |
| NART | -0.46 | 0.30 | -0.02 | 0.58 |
| Cattell | -0.02 | 0.28 | -0.57 | 0.55 |
| EBIQ Motivation | 0.30 | 0.27 | -0.85 | 0.53 |
| EBIQ Depression | 0.93 | 0.27 | 0.63 | 0.53 |
| TVA Absolute Bias | 1.47* | 0.27 | 1.90* | 0.54 |
| TVA Variability | 1.35* | 0.27 | 2.61* | 0.53 |
| Top-Down Control | 3.48* | 0.27 | 15.69* | 0.53 |
| CRT Variability | 3.16* | 0.27 | 14.68* | 0.54 |
| Oxbridge Heart Cancellation Task | 5.16* | 0.27 | 32.75* | 0.54 |
| Working Memory | 0.34 | 0.30 | 0.63 | 0.60 |
| Working Memory Capacity | -0.33 | 0.30 | -0.27 | 0.60 |

* Variables that crossed the cut-off value for kurtosis and skewness.

## Data Processing

### *Data Transformation*

Based on the skewness and kurtosis, some variables were transformed using either log, square-root, or inverse transformation to correct skewness and kurtosis for the hierarchical regression.

**Table 4**

*List of Variables and the Type of Data Transformation conducted*

| Variables | Type of data transformation |
|---|---|
| EBIQ Motivation | Inverse Transformation |
| EBIQ Depression | Inverse Transformation |
| TVA Absolute Bias | Square root Transformation |
| Oxbridge Cancellation Task | Square root Transformation |
| TVA Variability | Log Transformation |
| CRT Variability | Inverse Transformation |
| ANT Top-Down Control | Inverse Transformation |

***Corrected Normality***

Two transformed variables (i.e., TVA and CRT variability) were corrected to normal distribution (Table 5). The rest of the transformed data continued to be not normally distributed.

**Table 5**

*Shapiro-Wilk Test for Normality Post-Data Transformation*

| Transformed Variables | Shapiro-Wilk | | |
|---|---|---|---|
| | Statistic | df | Significance |
| EBIQ Motivation | 0.95 | 80 | <0.001 |
| EBIQ Depression | 0.97 | 80 | 0.025 |
| Oxbridge Cancellation Task | 0.79 | 78 | <0.001 |
| TVA Absolute Bias Task | 0.96 | 78 | 0.01 |
| TVA Variability | 0.99 | 80 | 0.72 |
| CRT Variability | 0.99 | 78 | 0.83 |
| Top-Down Control | 0.86 | 80 | 0.001 |

***Corrected Skewness.***

Table 6 showed the skewness and kurtosis after doing transformation for each variable specified above. After transformation, Top-Down Control remained leptokurtic.

**Table 6**

*Skewness and Kurtosis Values of Transformed Variables*

| **Transformed Variables** | **Skewness** | | **Kurtosis** | |
|---|---|---|---|---|
| | **Statistic** | **Std. Error** | **Statistic** | **Std. Error** |
| EBIQ Motivation | 0.52 | 0.27 | -0.76 | 0.53 |
| EBIQ Depression | 0.21 | 0.27 | -0.70 | 0.53 |
| Oxbridge Cancellation Task | 0.81 | 0.27 | 0.62 | 0.54 |
| TVA Absolute Bias | 0.55 | 0.27 | -0.37 | 0.54 |
| TVA Variability | 0.15 | 0.27 | -0.08 | 0.53 |
| CRT Variability | 0.16 | 0.27 | -0.44 | 0.54 |
| Top-Down Control | -0.74 | 0.28 | 2.66 | 0.55 |

***Outliers***

Interquartile ranges were used to determine outliers. Using standard deviation to determine outliers could be affected by skewness and if the data was not normally distributed. Outliers were classified as either a) typical outliers (1st or 3rd quartile + 1.5*interquartile range) or b) extreme outliers (1st or 3rd quartile + 3*interquartile range). An entire data row was removed as the participant scored low on the NART, which suggested reading difficulties. This could potentially impact their performance in other tasks. Additionally, values that were extreme outliers were excluded (Table 7).

**Table 7**

*Extreme Outliers removed from Both Variables.*

| Variables | Data points |
|---|---|
| Oxbridge Heart Cancellation Task | 4, 17, 19, 48 and 61 (high levels of bias) |
| ANT Top-Down Control | 16 (very poor attentional control) \| 12, 25, 37, 38 (very good attentional control) |

**Data Cleaning**

There was a need to process the data to allow a reliable and valid analysis of the data due to the complexity and nature of the data. However, this could potentially impact the external validity of the results. Southworth (2012) suggested that the data point should be included if outliers do not affect study results. Additionally, data obtained in many fields of health, education and social sciences yielded values of skewness and kurtosis that deviated from a normal distribution (Blanca et al., 2013). Micceri (1989) concluded that real data commonly followed a non-normal distribution. This would be particularly true for the present data that contained participants with varying presentations of stroke. Combining this with the various task performances looking at cognitive domains administered, it would not be unusual for some participants' performance to be considered outliers. Removing these data points because they do not fit a Gaussian distribution could potentially impact the data's clinical relevance and external validity. Statistically, data transformation was recommended by many to allow biological data to fit the assumptions of parametric statistical tests (McDonald, 2009). However, the many methods used to manage skewness and correct normality, log-normal distribution, Box-Cox transformation or trimmed means were designed to resolve a specific set of data (Gunver, Senocak & Vehid, 2018). Gunver and colleagues further criticised that the current method for data transformation could deform, damage or disregard the nature of the distribution.

Comparative data analysis of the data with various degrees of 'data cleaning' was carried out. Raw data was compared to the cleaned data (i.e., transformed with outliers removed). Table 8 and Table 9 showed minimal observable differences between the two data types for EBIQ Core and EQ5D-5L. Therefore, retaining the data in its original form could provide better clinical representation. Hence, the present study chose to analyse the raw data without removing outliers or transforming the data.

**Table 8**

*Data Type for EBIQ Core.*

| Stage | Data Type | $R^2$ | $R^2$ Adjusted | $\Delta R^2$ | $\Delta R^2$ Adjusted |
|---|---|---|---|---|---|
| 1 | Raw | .77 | .73 | .77 | .73 |
| | Cleaned | .77 | .73 | .77 | .73 |
| 2 | Raw | .78 | .72 | .01 | -.005 |
| | Cleaned | .78 | .72 | .01 | -.005 |
| 3 | Raw | .79 | .72 | .005 | -.008 |
| | Cleaned | .78 | .71 | .001 | -.01 |
| 4 | Raw | .81 | .73 | .02 | .02 |
| | Cleaned | .80 | .72 | .02 | .01 |

**Table 9**

*Data Type for EQ5D-5L.*

| Stage | Data Type | $R^2$ | $R^2$ Adjusted | $\Delta R^2$ | $\Delta R^2$ Adjusted |
|---|---|---|---|---|---|
| 1 | Raw | .20 | .07 | .20 | 0.07 |
| | Cleaned | .20 | .07 | .20 | 0.07 |
| 2 | Raw | .30 | .12 | .01 | 0.05 |
| | Cleaned | .30 | .12 | .01 | 0.05 |
| 3 | Raw | .30 | .08 | .004 | -0.04 |
| | Cleaned | .30 | .07 | .003 | -0.04 |
| 4 | Raw | .34 | .08 | .04 | -0.001 |
| | Cleaned | .35 | .09 | .05 | 0.02 |

## Chapter 6: Discussion and Critical Appraisal

The current section looked at the findings of both the systematic review and the empirical paper simultaneously and discussed their implications. The systematic review found evidence of small effect size for CCT at improving ADL in MCI individuals. The review identified several methodologies/characteristics used in the RCTs that could contribute to CCT's efficacy. Task adaptiveness was used in the majority of the reviewed studies. Additionally, social and competitive characteristics in CCT might also contribute to CCT efficacy. Looking at the reviewed RCTs that have an effect size above 0.1 (five out of ten), speed of processing and attention seem to be the most frequent cognitive domains that were trained.

In the empirical paper, the hierarchical regression model results found tentative results suggesting the cognitive domain of spatial and non-spatial attention were significant predictors of quality of life (QoL) (EBIQ Core) compared to other domains. However, for both domains to reach significance in the regression model, EBIQ depression and motivation subscales had to be removed as control variables. EBIQ Core was derived from the 34-items of the 63 items across the domains, including the EBIQ depression and motivation. The TVA attention task performance could be accounting for both cognitive and emotional aspects of the EBIQ-Core.

To summarise, the main findings from the two studies suggest two things: 1) there is evidence to suggest a small effect of CCT with improving ADL in MCI and 2) compared to other cognitive domains, non-spatial attention seems to contribute most as a predictor of QoL. As noted in both sections, the results of the two studies are tentative at best. However, the results provide possible avenues for researchers to pursue; the role of social factors such as competitiveness and potentially the contribution of emotional factors.

**Targeting Specific Cognitive Domains**

Bringing back the focus to the thesis aim of identifying cognitive domains that best predict the QoL, the systematic review findings identified speed of processing and attention as the most common among the other domains as targets for intervention. The results of the empirical paper provided tentative evidence that non-spatial attention best predicts an individual’s QoL. Theoretically speaking, the cognitive domains responsible for the QoL/ADL in both papers (i.e., speed of processing and sustained attention) are fundamental domains to which many other perceptual or cognitive functions would be compromised if impaired (Parasuraman, 1998; Salthouse, 1996; Sarter, Givens, & Bruno, 2001; Dickinson, Ramsey & Gold, 2007; Foong et al., 2018). Previous research has provided evidence for pursuing this idea. Ball and colleagues (2007) paper assessed data from six separate studies and found that improvement in processing speed through training was maintained for at least two years, translating to improved everyday abilities.

Sustained attention, a fundamental executive function for achieving complex goals over time, was suggested as a novel objective cognitive marker for progression in frailty and linked to poor physical functioning (O'Halloran et al., 2014). However, the effectiveness of cognitive rehabilitation focusing on attention (i.e., sustained and selective attention) post-stroke was limited to immediate effect post-intervention (Loetscher et al., 2019).

Findings from Blotenberg and Schmidt-Atzert's (2020) study suggested that pre-processing of information is an essential component of performance in sustained attention tasks. The authors posited that performance in sustained attention tasks improved by allowing individuals to learn the information beforehand. Therefore, the study results could suggest that helping individuals learn the tasks beforehand could help reduce the impact impairment of processing speed could have on QoL/ADL.

***Sustained Attention or Speed of Processing?***

The tentative findings of the thesis suggested two cognitive domains that are potential targets for interventions. Assuming a ‘purist’ (i.e., targeting a single domain) intervention perspective for a moment, the existence of the two domains brings into question which domain should be the prime focus for interventions. According to the processing-speed theory, ‘speed of processing’ could be contended as the global or single domain that contributes to cognitive decline (Salthouse, 1996). However, sustained attention could also be argued as the global domain responsible for the declining QoL/ADL (Vallesi et al., 2021), more than processing speed. It is generally understood that everyday tasks are impacted by processing speed (Shultz et al., 2016). However, without the ability to sustain attention on a task, it could be argued that an individual could have more difficulty processing the required information for the successful completion of everyday tasks.

This line of thoughts seems to correlate with the attentional control processes posited by Stuss and Alexander (2007). They put forward three areas of attention: energisation, task setting and monitoring. Two of the processes (i.e., energisation and monitoring) could be impacted by sustained attention deficits. Energisation was defined as the process of initiating and sustaining responses over a period. Monitoring is the process of ‘quality control’ and appropriately adjusting to behaviour to complete a task. In the context of everyday functioning, deficits in sustained attention might impair an individual’s ability to continue with a task over an extended period (i.e., energisation). The same ADL could differ daily, requiring an individual to observe his/her performance and adjust their behaviour accordingly (i.e., monitoring). Deficits in sustained attention could impair the ability to maintain self-observation and thereby impact ADL performance. Therefore, sustained attention as an intervention target might yield better improvements, particularly in measures of ADL.

Some researchers might also argue that the focus needs to be on attention for cognitive training to be effective and achieve far transfer (Greenwood & Parasuraman, 2015). In response to this assertion, a meta-analysis looking at commercially available CCT for older adults showed attention as a cognitive target produced the largest effect size (Tetlow & Edwards, 2017). However, the meta-analysis did not differentiate between the different domains of attention. The scope and findings of the current thesis cannot provide conclusive evidence on which domain to focus on. Hence, more research is warranted to expand on this further.

**Intervention Characteristics**

A point to consider that was not explored further in the systematic review was the frequency/duration of the intervention. Intriguingly, Hampshire and colleagues' (2019) large cross-sectional data analysis found frequency and intensity are independent factors contributing to brain training (CCT) efficacy. The RCTs in the systematic review seem to have a discernible pattern between session frequency and duration with 'between-group effect size. RCTs with sessions that are either infrequent (i.e., less) or has a shorter duration were observed to have a smaller effect size than RCTs with more frequent and longer sessions. Hence, the saying 'practise makes perfects' seems to hold when it comes to CCT. However, more studies are warranted to explore the relationship between session characteristics with efficacy.

Adaptiveness is a common characteristic frequently reported in many cognitive interventions. In the context of CCT, it is an intervention feature of allowing individuals to work/train continuously and optimally (Shute, Ke & Wang, 2017). Adaptiveness was operationalised as the continuous monitoring of task performance at 85% accuracy (Garcia-Perez, 1998). It has been suggested that training gains are maximised when individuals' performance was monitored at 85% accuracy (Wilson et al., 2019). Adaptiveness has become a popular and staple characteristic incorporated into the intervention (Kelly et al., 2014; Lampit, Hallock, & Valenzuela, 2014).

The present review observed that half of the RCTs that adopted adaptiveness showed positive gains. Four of the five (i.e., 80%) non-adaptive studies showed very poor or negative CCT efficacy to improve ADL/QoL. This does suggest that adaptive training might be necessary to improve CCT efficacy, but it is insufficient on its own. Furthermore, the difference in efficacy between adaptive interventions could be explained by the difference in the mechanism of adaptiveness, which is sometimes unexplained in intervention studies. Much like the variability observed in intervention methodologies, more research is warranted to uncover and elaborate on the mechanism of adaptiveness.

**Limitations of the Systematic Review and Empirical paper**

The limitations of the systematic review and empirical paper have been detailed in the respective sections. In summary, the reliability and validity of the evidence for the systematic review were impacted by outcome measures employed by the reviewed studies. The measures used to assess ADL were varied in type and depth. The variability meant that it is difficult to assess if CCT does improve ADL. Aside from variability in outcome measures used, the variation in methodologies adds a layer of confound to the results. Despite the large variation in methodologies, the meta-analysis of the review showed a small positive effects size, suggesting the potential of CCT as interventions to improve ADL.

The empirical paper was a secondary analysis, but the limitations of data affected the generalisability of the findings. As discussed in the empirical paper, the EQ5D-VAS is a standalone item that gives a subjective impression of an individual’s subjective health status. The EQ5D-VAS might not be accurately assessing QoL. Hence, the EQ5D-VAS might be less sensitive and more vulnerable to being influenced by impaired self-awareness, a possible deficit experienced by stroke individuals. Furthermore, possible confounds exists that could potentially impact the results.

The analysis conducted in the empirical paper assumed data linearity. The consensus when handling non-linear data was data transformation and removing outliers. Clinical data are often non-linear (Micceri, 1989), meaning that data transformation is recommended. Throughout the process of data analysis, constant contact with the research team was maintained. However, from the meetings with the research team, concerns were raised about losing data variability observed typically from a clinical population. This highlighted a dilemma to be addressed: 1) the requirement for the data to meet the assumptions to be used in a parametric test and 2) conserving, as much as possible, accurate representation of clinical data. This dilemma was addressed in detail through a series of sensitivity analyses exploring the consequences of removing outliers and transforming non-normal variables (Refer back to 'Extended Results' Chapter). It was apparent from the extended chapter that the influence of data transformation and outlier removal on the planned analyses was minimal. Hence, the raw data was used without any transformation or outliers removed. The parametric assumptions for the raw data were tested. Finally, both systematic review and empirical paper had the shared limitation of low numbers of participants, impacting the accuracy and generalisability of findings.

It is important to note that due to the pandemic, it was not possible to start the original planned empirical study due to restrictions impacting face to face contact. Hence, the original empirical study had to be changed to the secondary data analysis study presented in the thesis. The original study planned a feasibility study of a novel CCT for people with MCI with the methodologies (e.g., intervention characteristics and cognitive targets) informed by the systematic review findings. This could have provided a more coherent and focused narrative for the thesis. That being said, the stroke data analysis and findings have provided additional angles for interpreting the systematic review data and implications for future clinical and research work in the field of CCT.

The main findings of the systematic review and empirical paper can provide some clarity and implications for researchers to pursue in future exploration. Aside from the main findings, the role of social/competitiveness in CCT and potentially the contribution of emotional factors towards QoL/ADL warrants further exploration.

**Social Groups and Competitiveness in Relation to CCT Efficacy**

Within the systematic review, the RCT with the largest effect size compared to other RCTs (Hughes et al., 2014) was set apart from the rest by the social (group setting) and competitive aspects of the intervention. This tentative finding has multiple implications on how CCT can be conducted and possible avenues that researchers can explore further. The original intent of the thesis was to identify cognitive domains that are vital targets for predicting QoL and as targets for CCT to have meaningful outcomes in terms of ADLs and QoL. However, the systematic review findings showed a possible key role for social/competitive aspects within CCT that might mediate or moderate the intervention’s efficacy. Hence, cognitive interventions could consider incorporating secondary targets like social enhancements alongside more established features such as being adaptive. As mentioned in previous sections, past research had shown that social contacts were considered a significant modifiable factor that influenced ADL deterioration and QoL (Chang et al., 2017; Cintra et al., 2017; Ćwirlej-Sozańska et al., 2019). Higher degrees of motivation were associated with better ADL performance among individuals with stroke and increased QoL (Lee & Kim, 2014; Haghgoo et al., 2013).

Social isolation significantly impacts individuals experiencing MCI or stroke (Mukherjee, Levin, & Heller, 2006; Hussenoeder et al., 2020). The isolation could be partly due to cognitive impairment, which might affect an individual's ADL capabilities. As a result, the reduction in ADL capability might negatively impact self-efficacy (Korpershoek van der Bijl & Hafsteinsdottir, 2011), further isolating the individual from social participation (Hosseingholizadeh et al., 2019). The consequence of social isolation influences various aspects of an individual, including depressive/anxiety symptoms (Evans et al., 2019) and increased prevalence of other health comorbidities (Nagarajan et al., 2020). Therefore, the incorporation of social aspects as part of the intervention could reduce the impact of isolation.

A counter-argument for incorporating social elements into interventions is the concept of social facilitation. The concept posited that the performance of a learned behaviour could increase or decrease in the presence of another (Guerin, 2010). However, this performance improvement applies only to well-trained or straightforward tasks (Smelser & Baltes, 2001). Additionally, when observed by another, simple task performance might not improve due to orientation of personality. This is because individuals with a negative orientation (i.e., neuroticism and low self-esteem) might perform poorer compared to those with positive orientation (i.e., extraversion and high self-esteem) when observed by another (Uziel et al., 2007).

A comparison of performance with peers might further reduce an individual's self-efficacy if his/her perceived performance was poorer than their peers. Hence, the inclusion of social/competitive components might further confound the efficacy of the intervention that used an individual's task performance as an indication of improvement. On the other hand, there has been evidence in a healthy population that competitiveness increases performance (Rhea et al., 2003; Plante et al., 2001). Navarro and colleagues' (2020) RCT compared competition between two groups and showed that those who competed showed comparable results to those who completed the intervention alone. Additionally, those who competed reported greater enjoyment than the non-competitive group. However, as mentioned above, positive/negative orientation could still play a role in the intervention efficacy.

The two paragraphs above listed out possible advantages and disadvantages of the inclusion of social elements within interventions. One option to retain the pros while detaching the cons of social elements could be facilitating social contact within the intervention group while separating it from actual cognitive intervention. However, this form of arrangement could mean that social elements could become a confound when assessing the intervention’s efficacy. Alternatively, if self-esteem is indeed an issue, psychological interventions addressing self-esteem before cognitive training could potentially provide the advantages of social elements while minimising the elements’ possible disadvantages.

**Emotional and Motivational Factors**

One highlight of the empirical paper’s findings was that the removal of depression and motivation domain of the EBIQ pushed the contribution of non-spatial attention as cognitive predictors of QoL to significance. Additionally, stage one of the model (i.e., control variables) lost its significant contribution to QoL variance when these two EBIQ domains were removed. The regression model observed that depression and motivation domains were responsible for the bulk of the variance explained. When the two domains were removed, among the cognitive domains that were tested, non-spatial attention was the only cognitive domain that contributed significantly to the QoL model.

Despite the extensive theoretical understanding and evidence of cognitive domains and their associations with QoL, the ‘far’ transfer effects or generalisability of cognitive training to meaningful outcomes are issues researchers have continued to contend with (Gates et al., 2011; Butler et al., 2018). The findings could suggest that emotional factors like depression and motivation are important variables. Therefore, the findings could suggest that emotional factors like depression and motivation are important variables that need to be considered in future research when assessing CCT efficacy in ADLs or QoL. Indeed, Kolanowski and colleagues’ (2011) study reported better engagement, time, and sustained attention on activities in older adults with dementia who self-report better mood.

Over the years, researchers have identified various cognitive domains associated with QoL (Morrison & Chien, 2011; Cantarella et al., 2016; Hindle et al., 2017). However, the tentative results of the empirical paper could also imply that rather than focusing on interventions to improve cognition, integrating reduction of depressive symptoms while increasing motivation of individuals into rehabilitation might be a better approach.

**An Alternative Approach to Cognitive Intervention**

Presently, the findings from the systematic review showed little evidence for the effects of cognitive training on everyday functioning. Additionally, the empirical paper showed weak evidence for specific domains of cognition as predictors of QoL, which could not be attributed to emotional variables. Assuming the thesis findings were accurate, further attempts to improve everyday life by focusing solely on cognition were unlikely to yield much benefit. Furthermore, cognitive interventions could still have some role in the field of rehabilitation. However, the thesis has its limitations needed to be addressed, and more studies were needed before any conclusions can be made.

Past research has shown a near-transfer effect from cognitive training in older adults (Tetlow & Edwards, 2017; Nikravesh et al., 2021). This meant that an individual trained on a specific domain/task would show improved performance in that domain/task. Neurodegenerative conditions, like Alzheimer’s Disease, often result in progressive loss of functions. Therefore, there was a possibility that cognitive training that aided in ‘retraining’ specific skills could potentially slow down deterioration across a range of everyday tasks, especially when the ‘trained’ cognitive domain was fundamental to many tasks (e.g., attention or speed of processing). While this rationale still needs to be tested, it showed a potential benefit of cognitive interventions to improve trained cognitive or everyday tasks.

The findings from the thesis also hinted at the potential interaction between cognition, mood/motivation and everyday functioning. There was a possibility that non-cognitive factors (e.g., emotional or social) could impact the efficacy of cognitive interventions on everyday functioning and, therefore, on QoL. These could indicate that the effects of cognitive interventions might be moderated or mediated by other factors. This could be a possible avenue to consider as individuals with cognitive impairments from neurological conditions, who underwent the interventions, might already be experiencing the various psychosocial impacts of cognitive impairment, such as social isolation and depression.

Social isolation has been associated with decreased cognitive function, to which social participation and maintenance of emotionally supportive relationships were suggested as interventions to prevent cognitive decline (Lara et al., 2019). Like social isolation mentioned earlier, individuals with MCI or stroke experience difficulties with depression (Robinson & Jorge, 2016; Snowden et al., 2015) and apathy (Drijgers et al., 2011; Caeiro et al., 2013). Depression and apathy were also known factors that impact further cognitive decline (Ma, 2020). These impairments might also affect an individual’s motivation and engagement with interventions. This creates a vicious cycle that could perpetuate the difficulties experienced by individuals with MCI or stroke. Hence, targeting the cognitive impairments might address the ‘root’ (e.g. cognitive deficits) of many difficulties experienced, but that might be insufficient as the ‘fruits’ (e.g., social isolation, depression or apathy) of the impairment could still be present. Therefore, instead of focusing on improving cognition, socio-emotional or QOL separately, a combined approach might be the way forward.

Based on what was discussed, future research on interventions might consider adapting cognitive interventions that focus on targeted domains fundamental to everyday functioning (e.g., attention or speed of processing) while considering the roles and impacts emotional and social factors have on the individual. For example, older adults with dementia might undergo cognitive training might set individualised and meaningful goals, commonly used in neurological rehabilitation (Knutti et al., 2020). Additionally, the interventions could be delivered to the individual combined with a social component (e.g., task cooperation) with a possible leaderboard to drive competition. This could enhance existing cognitive rehabilitation/interventions and tackle the aforementioned emotional issues like depression and apathy that could perpetuate cognitive and non-cognitive difficulties among individuals with stroke or MCI.

***From Symptom Reduction to Individualised Goals***

In psychotherapy research, the most common focus on outcome research was symptom reduction (Cuijpers, 2019). This approach in outcome research is similar to the current stroke and MCI intervention study approach in which interventions would attempt to reduce the ‘symptom’ of cognitive impairment observed in

MCI and stroke. Considering the difficulties of constructing an intervention with strong ‘far’ transfer effects to outcomes related to QoL, it might be worth considering shifting the focus from interventions focusing on simply training cognition to meaningful targets to the individual.

In recent years, psychotherapy has shifted to focus more on treatment targets that patients would like to achieve (i.e., patient-defined outcomes) (Wampold, 2015; Kealy et al., 2019). Therefore, MCI and stroke interventions might benefit from using a ‘two steps’ approach, where the ‘root’ and ‘fruits’ of the impairments are addressed simultaneously through cognitive intervention and individually-focused goals, respectively.

The concept of individualised goals is not a novel idea in cognitive rehabilitation. According to the World Health Organisation (WHO), rehabilitation aims to support individuals to be as independent as possible in everyday activities and enable meaningful activities important to the individuals (WHO, 2020). Guidance from other health organisations stated similar reasoning and recommended for rehabilitation to be trained in accordance with patient’s strengths, wishes and participation goals (New Zealand’s Ministry of Health, 2006; Scottish Intercollegiate Guidelines Network, 2013). This provides a more holistic approach as many consider it impossible to separate the cognitive, social, emotional, and functional aspects of brain injury (Wilson et al., 2017).

**Clinical Implications of the Thesis**

Several clinical implications can be unpacked from the current thesis. Firstly, considering the rehabilitation stance that cognitive intervention studies should adopt to improve QoL/ADL. Zangwill (1947) referred to three main approaches to brain rehabilitation: compensation, substitution, and direct retraining (i.e., restoration). The current methodology for CCT seems to be adopting the stance of 'direct retraining', which posits that 'damaged'/impaired brain functions could be restored through training, with its use of training protocols that aim to enhance the impaired cognitive domain. Alternatively, CCT or cognitive interventions could consider compensation, defined as the reorganisation of psychological function to reduce or bypass the impact of a specific disability, as a different approach to rehabilitation. Researchers might also consider integrating both restoration and compensation approaches in cognitive interventions moving forward.

Another implication observed from the findings was incorporating computerisation to target the cognitive domain responsible for QoL/ADL. Like medication, where different dosages are required depending on the requirement of the individual, computerisation could potentially allow interventions to be fine-tuned/personalised to the individual's needs, as achieved through adaptive training protocols of cognitive training tasks.

The concept of 'Gamification' (i.e., incorporating game-like features into mundane tasks) could be the answer to 'computerisation' of the intervention. Cognitive interventions could be designed as mobile applications easily accessed by individuals using mobile devices (e.g., phones or tablets). The use of applications could encourage social connection among individuals. Hourcade and colleagues' (2013) designed a novel intervention for children with Autism. The intervention was designed to encourage children to complete tasks together using a tablet collaboratively. The same concept could be employed in CCT, which could simultaneously improve cognition and enhance social engagement between individuals.

As mentioned, computerisation of the intervention could help with the facilitation of socio/emotional factors, which are known factors that could impact cognition and QoL. Features like a ‘leader board’ or ‘achievements medals’, common game elements, could encourage engagement and prosocial behaviours (Lumsden et al., 2016). These features are not foreign concepts in health technology as fitness devices like FitBit use these features to encourage users to engage in more physical activities. Hence, using these features could therefore motivate individuals to engage more with the intervention.

Social facilitation, as mentioned, posits that performance could decrease in the presence of another. The use of virtual space and the absence of a physical observer could retain the sense of competition among individuals while reducing the negative impact social facilitation could have on task performance. Likewise, the accessibility of the application is an advantage that cannot be ignored. Traditional cognitive training, including laboratory computerised training, confines individuals to specific locations for the interventions to be carried out. Individuals with stroke or MCI are at risk of apathy. The added requirement adds another layer of obstacle for intervention engagement for individuals who are already experiencing low motivation. Hence, computerisation, and to a certain extent ‘gamification’, allows incorporating and further expanding competitive, social, and emotional elements into cognitive training, more than what traditional cognitive training can offer. However, current evidence of CCT efficacy in improving quality QoL/ADL is inconclusive.

**Research Implications**

From the findings and discussions laid out in the current thesis, several research implications can be inferred for future research. The systematic review results suggested that more research should be carried out differentiating the mechanisms of adaptiveness used in interventions. The unknown mechanisms of some features in CCT methodology presently do not help determine which parameters contribute to or improve the interventions’ efficacy. Furthermore, session frequency and intensity require further consideration as well. Hence, future research is still warranted to explore the features and characteristics identified from the review further.

The tentativeness of the empirical paper's results means that replication of the study is warranted. As mentioned above, it could be vital to re-operationalise the dependent variables and ensure the predictors or demographic variables are not related to the dependent variables (i.e., not derived from the same questionnaire or domains). Additionally, emotional and social factors need to be accounted for as previous research has found a strong association between those factors with cognitive task performance and QoL. Additionally, the finding of the two papers suggested two cognitive domains that might influence the QoL/ADL (i.e., spatial/non-spatial attention and speed of processing). Future trials could consider teasing out the relationship, if it exists, between the two domains or look into determining the 'main' domain that underpins it all.

The thesis results might be a 'waking call' to shift focus from cognitive interventions away from 'near transfer' outcomes to targeting and supporting individual goals or everyday life difficulties of people with stroke or MCI. Future research could compare cognitive training with interventions that focused more on individualised goals. Further research is warranted on integrating social, emotional and motivation features into interventions that could potentially enhance learning and far transfer effects.

**Thesis Reference**

Albert, M. S., DeKosky, S. T., Dickson, D., Dubois, B., Feldman, H. H., Fox, N. C., ... & Phelps, C. H. (2011). The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's & dementia, 7(3), 270-279.

Alloway, T. P. (2007). *Automated Working: Memory Assessment: Manual*. Pearson.

Alvarez, J., & Djaouti, D. (2012). Serious games: an introduction. *Limoges, France: Questions Théoriques*.

Andersen, C. K., Wittrup-Jensen, K. U., Lolk, A., Andersen, K., & Kragh-Sørensen, P. (2004). Ability to perform activities of daily living is the main factor affecting quality of life in patients with dementia. *Health and quality of life outcomes*, *2*(1), 1-7.

Anderson-Hanley, C., Snyder, A. L., Nimon, J. P., & Arciero, P. J. (2011). Social facilitation in virtual reality-enhanced exercise:

competitiveness moderates exercise effort of older adults. *Clinical interventions in aging*, *6*, 275.

Artola A, Singer W. 1987. Long-term potentiation and NMDA receptors in rat visual cortex. Nature 330: 649–52

Azouvi, P., Jacquin-Courtois, S., & Luauté, J. (2017). Rehabilitation of unilateral neglect: Evidence-based medicine. *Annals of physical and rehabilitation medicine*, *60*(3), 191-197.

Ball, K., Edwards, J. D., & Ross, L. A. (2007). The impact of speed of processing training on cognitive and everyday functions. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *62*(Special_Issue_1), 19-31.

Ball, K., Edwards, J. D., & Ross, L. A. (2007). The impact of speed of processing training on cognitive and everyday functions. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *62*(Special_Issue_1), 19-31.

Barker-Collo, S. L., Feigin, V. L., Lawes, C. M. M., Parag, V., & Senior, H. (2010). Attention deficits after incident stroke in the acute period: Frequency across types of attention and relationships to patient characteristics and functional outcomes. Topics in Stroke Rehabilitation, 17(6), 463–476. doi:10.1310/tsr1706-463

Barnett, S. M., & Ceci, S. J. (2002). When and where do we apply what we learn?: A taxonomy for far transfer. *Psychological bulletin*, *128*(4), 612.

Bateman, A., Teasdale, T. W., & Willmes, K. (2009). Assessing construct validity of the self-rating version of the European Brain Injury Questionnaire (EBIQ) using Rasch analysis. *Neuropsychological rehabilitation*, *19*(6), 941-954.

Béjot, Y., Bailly, H., Durier, J., & Giroud, M. (2016). Epidemiology of stroke in Europe and trends for the 21st century. *La Presse Médicale*, *45*(12), e391-e398.

Béjot, Y., Bailly, H., Graber, M., Garnier, L., Laville, A., Dubourget, L., ... & Giroud, M. (2019). Impact of the ageing population on the burden of stroke: the Dijon Stroke Registry. *Neuroepidemiology*, *52*(1-2), 78-85.

Belleville, S. (2008). Cognitive training for persons with mild cognitive impairment. *International Psychogeriatrics*, *20*(1), 57.

Belleville, S., Hudon, C., Bier, N., Brodeur, C., Gilbert, B., Grenier, S., ... & Gauthier, S. (2018). MEMO+: efficacy, durability and effect of cognitive training and psychosocial intervention in individuals with mild cognitive impairment. *Journal of the American Geriatrics Society*, *66*(4), 655-663.

Bickerton, W. L., Demeyere, N., Francis, D., Kumar, V., Remoundou, M., Balani, A., ... & Humphreys, G. W. (2015). The BCoS cognitive profile screen: Utility and predictive value for stroke. *Neuropsychology*, *29*(4), 638.

Birren, J. E. (1974). Translations in gerontology: From lab to life: Psychophysiology and speed of response. *American Psychologist*, *29*(11), 808.

Blanca, M. J., Arnau, J., López-Montiel, D., Bono, R., & Bendayan, R. (2013). Skewness and kurtosis in real data samples. *Methodology*.

Bliss, T. V., & Lømo, T. (1973). Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the perforant path. *The Journal of physiology*, *232*(2), 331-356.

Blotenberg, I., & Schmidt-Atzert, L. (2019). On the locus of the practice effect in sustained attention tests. *Journal of intelligence*, *7*(2), 12.

Bo, W., Lei, M., Tao, S., Jie, L. T., Qian, L., Lin, F. Q., & Ping, W. X. (2019). Effects of combined intervention of physical exercise and cognitive training on cognitive function in stroke survivors with vascular cognitive impairment: a randomized controlled trial. *Clinical rehabilitation*, *33*(1), 54-63.

Bonell, C., Oakley, A., Hargreaves, J., Strange, V., & Rees, R. (2006). Assessment of generalisability in trials of health interventions: suggested framework and systematic review. *Bmj*, *333*(7563), 346-349.

Borges, S. D. M., Radanovic, M., & Forlenza, O. V. (2015). Fear of falling and falls in older adults with mild cognitive impairment and Alzheimer's disease. *Aging, Neuropsychology, and Cognition*, *22*(3), 312-321.

Bour, A., Rasquin, S., Aben, I., Boreas, A., Limburg, M., & Verhey, F. (2010). A one-year follow-up study into the course of depression after stroke. *The journal of nutrition, health & aging*, *14*(6), 488-493.

Bowen, A., Hazelton, C., Pollock, A., & Lincoln, N. B. (2013). Cognitive rehabilitation for spatial neglect following stroke. *Cochrane Database of Systematic Reviews*, (7).

Brown, D. S., Thompson, W. W., Zack, M. M., Arnold, S. E., & Barile, J. P. (2015). Associations between health-related quality of life and mortality in older adults. *Prevention Science*, *16*(1), 21-30.

Burckhardt, C. S., & Anderson, K. L. (2003). The Quality of Life Scale (QOLS): reliability, validity, and utilization. *Health and quality of life outcomes*, *1*(1), 1-7.

Burge, W. K., Ross, L. A., Amthor, F. R., Mitchell, W. G., Zotov, A., & Visscher, K. M. (2013). Processing speed training increases the efficiency of attentional resource allocation in young adults. *Frontiers in Human Neuroscience*, *7*, 684.

Butler, M., McCreedy, E., Nelson, V. A., Desai, P., Ratner, E., Fink, H. A., ... & Kane, R. L. (2018). Does cognitive training prevent cognitive decline? A systematic review. *Annals of internal medicine*, *168*(1), 63-68.

Caeiro, L., Ferro, J. M., e Melo, T. P., Canhão, P., & Figueira, M. L. (2013). Post-stroke apathy: an exploratory longitudinal study. *Cerebrovascular Diseases*, *35*(6), 507-513.

Cantarella, A., Borella, E., Carretti, B., Kliegel, M., & de Beni, R. (2017). Benefits in tasks related to everyday life competences after a working memory training in older adults. *International journal of geriatric psychiatry*, *32*(1), 86-93.

Caporale, N., & Dan, Y. (2008). Spike timing–dependent plasticity: a Hebbian learning rule. *Annu. Rev. Neurosci.*, *31*, 25-46.

Carod-Artal, F. J., & Egido, J. A. (2009). Quality of life after stroke: the importance of a good recovery. *Cerebrovascular diseases*, *27*(Suppl. 1), 204-214.

Carod-Artal, F. J., González-Gutiérrez, J. L., Herrero, J. A. E., Horan, T., & Seijas, E. V. D. (2002). Functional recovery and instrumental activities of daily living: follow-up 1-year after treatment in a stroke unit. *Brain injury*, *16*(3), 207-216.

Cations, M., Radisic, G., Crotty, M., & Laver, K. E. (2018). What does the general public understand about prevention and treatment of dementia? A systematic review of population-based surveys. *PLoS One*, *13*(4), e0196085.

Cattell, R. B. (1978). *Use of factor analysis in the behavioral and life sciences*. New York: Plenum

Chang, C. F., Yang, R. J., Chang, S. F., Chou, Y. H., & Huang, E. W. (2017). The effects of quality of life and ability to perform activities of daily living on mild cognitive impairment in older people living in publicly managed congregate housing. *journal of nursing research*, *25*(3), 187-197.

Chen, C., Hu, Z., Jiang, Z., & Zhou, F. (2018). Prevalence of anxiety in patients with mild cognitive impairment: a systematic review and meta-analysis. *Journal of affective disorders*, *236*, 211-221.

Chen, H.-C., Koh, C.-L., Hsieh, C.-L., & Hsueh, I. P. (2009). Test–re-test reliability of two sustained attention tests in persons with chronic stroke. Brain Injury, 23(9), 715–722. doi:10.1080/02699050903013602

Cicerone, K. D., Goldin, Y., Ganci, K., Rosenbaum, A., Wethe, J. V., Langenbahn, D. M., ... & Harley, J. P. (2019). Evidence-based cognitive rehabilitation: systematic review of the literature from 2009 through 2014. *Archives of physical medicine and rehabilitation*, *100*(8), 1515-1533.

Cicerone, K. D., Langenbahn, D. M., Braden, C., Malec, J. F., Kalmar, K., Fraas, M., ... & Ashman, T. (2011). Evidence-based cognitive rehabilitation: updated review of the literature from 2003 through 2008. *Archives of physical medicine and rehabilitation*, *92*(4), 519-530.

Cintra, F. C. M. D. C., Cintra, M. T. G., Nicolato, R., Bertola, L., Ávila, R. T., Malloy-Diniz, L. F., ... & Bicalho, M. A. C. (2017). Functional decline in the elderly with MCI: Cultural adaptation of the ADCS-ADL scale. *Revista da Associação Médica Brasileira*, *63*(7), 590-599.

Cipriani, G., Lucetti, C., Carlesi, C., Danti, S., & Nuti, A. (2015). Depression and dementia. A review. *European Geriatric Medicine*, *6*(5), 479-486.

Claesson, L., Lindén, T., Skoog, I., & Blomstrand, C. (2005). Cognitive impairment after stroke–impact on activities of daily living and costs of care for elderly people. *Cerebrovascular Diseases*, *19*(2), 102-109.

Clugnet, M. C., & LeDoux, J. E. (1990). Synaptic plasticity in fear conditioning circuits: induction of LTP in the lateral nucleus of the amygdala by stimulation of the medial geniculate body. *Journal of Neuroscience, 10*(8), 2818-2824.

Colom, R., Román, F. J., Abad, F. J., Shih, P. C., Privado, J., Froufe, M., ... & Jaeggi, S. M. (2013). Adaptive n-back training does not improve fluid intelligence at the construct level: Gains on individual tests suggest that training may enhance visuospatial processing. *Intelligence*, *41*(5), 712-727.

Cuijpers, P. (2019). Targets and outcomes of psychotherapies for mental disorders: an overview. *World Psychiatry, 18*(3), 276-285.

Cumming, T. B., Marshall, R. S., & Lazar, R. M. (2013). Stroke, cognitive deficits, and rehabilitation: still an incomplete picture. *International Journal of stroke*, *8*(1), 38-45.

Ćwirlej-Sozańska, A., Wiśniowska-Szurlej, A., Wilmowska-Pietruszyńska, A., & Sozański, B. (2019). Determinants of ADL and IADL disability in older adults in southeastern Poland. *BMC geriatrics*, *19*(1), 1-13.

de Haan, R. D., Aaronson, N., Limburg, M., Hewer, R. L., & Van Crevel, H. (1993). Measuring quality of life in stroke. *stroke*, *24*(2), 320-327.

de Haan, R. D., Aaronson, N., Limburg, M., Hewer, R. L., & Van Crevel, H. (1993). Measuring QoL in stroke. *stroke*, *24*(2), 320-327.

De Wit, L., Theuns, P., Dejaeger, E., Devos, S., Gantenbein, A. R., Kerckhofs, E., ... & Putman, K. (2017). Long-term impact of stroke on patients' health-related quality of life. *Disability and rehabilitation*, *39*(14), 1435-1440.

Del Zotto, E., Costa, P., Morotti, A., Poli, L., de Giuli, V., Giossi, A., ... & Pezzini, A. (2014). Stroke and depression: A bidirectional link. *World Journal of Meta-Analysis*, *2*(3), 49-63.

Dementia Statistics Hub (2018). *Prevalence by age in the UK.* Retrieved 23rd May 2021 from https://www.dementiastatistics.org/statistics/prevalence-by-age-in-the-uk/.

Dementia Statistics Hub (2021) *Global Prevalence*. Retrieved 23rd May 2021 from https://www.dementiastatistics.org/statistics/global-prevalence/

Demeyere, N., Riddoch, M. J., Slavkova, E. D., Bickerton, W. L., & Humphreys, G. W. (2015). The Oxford Cognitive Screen (OCS): validation of a stroke-specific short cognitive screening tool. *Psychological assessment*, *27*(3), 883.

Di Iulio, F., Palmer, K., Blundo, C., Casini, A. R., Gianni, W., Caltagirone, C., & Spalletta, G. (2010). Occurrence of neuropsychiatric symptoms and psychiatric disorders in mild Alzheimer's disease and mild cognitive impairment subtypes. *International Psychogeriatrics*, *22*(4), 629-640.

Dickinson, D., Ramsey, M. E., & Gold, J. M. (2007). Overlooking the obvious: a meta-analytic comparison of digit symbol coding tasks and other cognitive measures in schizophrenia. *Archives of general psychiatry*, *64*(5), 532-542.

Djabelkhir, L., Wu, Y. H., Vidal, J. S., Cristancho-Lacroix, V., Marlats, F., Lenoir, H., ... & Rigaud, A. S. (2017). Computerised cognitive stimulation and engagement programs in older adults with mild cognitive impairment: comparing feasibility, acceptability, and cognitive and psychosocial effects. *Clinical interventions in aging*, *12*, 1967.

Drijgers, R. L., Verhey, F. R., Leentjens, A. F., Köhler, S., & Aalten, P. (2011). Neuropsychological correlates of apathy in mild cognitive impairment and Alzheimer's disease: the role of executive functioning. *International Psychogeriatrics*, *23*(8), 1327.

Duara, R., Loewenstein, D. A., Potter, E., Barker, W., Raj, A., Schoenberg, M., ... & Borenstein, A. (2011). Pre-MCI and MCI: neuropsychological, clinical, and imaging features and progression rates. *The American Journal of Geriatric Psychiatry*, *19*(11), 951-960.

Dunlosky, J., Kubat-Silman, A. K., & Hertzog, C. (2003). Training monitoring skills improves older adults' self-paced associative learning. *Psychology and aging*, *18*(2), 340.

Easton, J. D., Saver, J. L., Albers, G. W., Alberts, M. J., Chaturvedi, S., Feldmann, E., ... & Sacco, R. L. (2009). Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on

Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease: the American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. *Stroke*, *40*(6), 2276-2293.

Edemekong, P. F., Bomgaars, D. L., & Levy, S. B. (2017). Activities of daily living (ADLs).

Edemekong, P. F., Bomgaars, D., Sukumaran, S., & Levy, S. B. (2019). Activities of daily living.

Espinosa, A. N. A., Alegret, M., Boada, M., Vinyes, G., Valero, S., Martínez-Lage, P., ... & Tárraga, L. (2009). Ecological assessment of executive functions in mild cognitive impairment and mild Alzheimer's disease. *Journal of the International Neuropsychological Society*, *15*(5), 751-757.

Evans, I. E., Llewellyn, D. J., Matthews, F. E., Woods, R. T., Brayne, C., & Clare, L. (2019). Social isolation, cognitive reserve, and cognition in older people with depression and anxiety. *Aging & mental health*, *23*(12), 1691-1700.

Fakoya, O. A., McCorry, N. K., & Donnelly, M. (2020). Loneliness and social isolation interventions for older adults: a scoping review of reviews. BMC public health, 20(1), 1-14.

Falck, R. S., Best, J. R., Davis, J. C., Eng, J. J., Middleton, L. E., Hall, P. A., & Liu-Ambrose, T. (2019). Sleep and cognitive function in chronic stroke: a comparative cross-sectional study. *Sleep*, *42*(5), zsz040.

Feigin, V. L., Abajobir, A. A., Abate, K. H., Abd-Allah, F., Abdulle, A. M., Abera, S. F., ... & Nguyen, G. (2017). Global, regional, and national burden of neurological disorders during 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet Neurology*, *16*(11), 877-897.

Feng, Y., Parkin, D., & Devlin, N. J. (2014). Assessing the performance of the EQ-VAS in the NHS PROMs programme. *Quality of Life Research*, *23*(3), 977-989.

Foong, H. F., Hamid, T. A., Ibrahim, R., & Haron, S. A. (2018). Information processing speed as a mediator between psychosocial stress and global cognition in older adults. *Psychogeriatrics*, *18*(1), 21-29.

Fortenbaugh, F. C., DeGutis, J., & Esterman, M. (2017). Recent theoretical, neural, and clinical advances in sustained attention research. *Annals of the New York Academy of Sciences*, *1396*(1), 70.

Fragkiadaki, S., Kontaxopoulou, D., Beratis, I. N., Andronas, N., Economou, A., Yannis, G., ... & Papageorgiou, S. G. (2016). Self-awareness of cognitive efficiency: differences between healthy elderly and patients with mild cognitive impairment (MCI). *Journal of clinical and experimental neuropsychology*, *38*(10), 1144-1157.

Franceschini, M., La Porta, F., Agosti, M., & Massucci, M. (2010). Is health-related-quality of life of stroke patients influenced by neurological impairments at one year after stroke?. *European journal of physical and rehabilitation medicine*, *46*(3), 389-399.

Fukuda, K., Vogel, E., Mayr, U., & Awh, E. (2010). Quantity, not quality: The relationship between fluid intelligence and working memory capacity. *Psychonomic bulletin & review*, *17*(5), 673-679.

Fulk, G., Duncan, P., & Klingman, K. J. (2020). Sleep problems worsen health-related quality of life and participation during the first 12 months of stroke rehabilitation. *Clinical Rehabilitation*, *34*(11), 1400-1408.

Gagnon, L. G., & Belleville, S. (2012). Training of attentional control in mild cognitive impairment with executive deficits: results from a double-blind randomised controlled study. *Neuropsychological rehabilitation*, *22*(6), 809-835.

Gamir-Morralla, A., López-Menéndez, C., Medina, M., & Iglesias, T. (2017). A novel neuroprotection target with distinct regulation in stroke and Alzheimer’s disease. In *Neuroprotection in Alzheimer's Disease* (pp. 123-147). Academic Press.

Gamito, P., Oliveira, J., Coelho, C., Morais, D., Lopes, P., Pacheco, J., ... & Barata, A. F. (2017). Cognitive training on stroke patients via virtual reality-based serious games. *Disability and rehabilitation*, *39*(4), 385-388.

García-Casal, J. A., Loizeau, A., Csipke, E., Franco-Martín, M., Perea-Bartolomé, M. V., & Orrell, M. (2017). Computer-based cognitive interventions for people living with dementia: a systematic literature review and meta-analysis. *Aging & mental health*, *21*(5), 454-467.

Garcıa-Pérez, M. A. (1998). Forced-choice staircases with fixed step sizes: asymptotic and small-sample properties. *Vision research*, *38*(12), 1861-1881

Gates, N. J., Rutjes, A. W., Di Nisio, M., Karim, S., Chong, L. Y., March, E., ... & Vernooij, R. W. (2019). Computerised cognitive training for maintaining cognitive function in cognitively healthy people in late life. *Cochrane database of systematic reviews*, (3).

Gates, N. J., Sachdev, P. S., Singh, M. A. F., & Valenzuela, M. (2011). Cognitive and memory training in adults at risk of dementia: a systematic review. *BMC geriatrics*, *11*(1), 1-14.

Gates, N. J., Vernooij, R. W., Di Nisio, M., Karim, S., March, E., Martinez, G., & Rutjes, A. W. (2019). Computerised cognitive training for preventing dementia in people with mild cognitive impairment. *Cochrane database of systematic reviews*, (3).

Gates, N., & Valenzuela, M. (2010). Cognitive exercise and its role in cognitive function in older adults. *Current psychiatry reports*, *12*(1), 20-27.

Gbiri, C. A., Akinpelu, A. O., & Odole, A. C. (2010). Prevalence, pattern and impact of depression on quality of life of stroke survivors. *International Journal of Psychiatry in Clinical Practice*, *14*(3), 198-203.

Golicki, D., Niewada, M., Buczek, J., Karlińska, A., Kobayashi, A., Janssen, M. F., & Pickard, A. S. (2015). Validity of EQ-5D-5L in stroke. *Quality of Life Research, 24*(4), 845-850.

Golicki, D., Niewada, M., Karlińska, A., Buczek, J., Kobayashi, A., Janssen, M. F., & Pickard, A. S. (2015). Comparing responsiveness of the EQ-5D-5L, EQ-5D-3L and EQ VAS in stroke patients. *Quality of Life Research, 24*(6), 1555-1563.

Goodwin, R. A., Lincoln, N. B., das Nair, R., & Bateman, A. (2020). Evaluation of NeuroPage as a memory aid for people with multiple sclerosis: a randomised controlled trial. *Neuropsychological rehabilitation*, *30*(1), 15-31.

Goverover, Y., Chiaravalloti, N. D., O'Brien, A. R., & DeLuca, J. (2018). Evidenced-based cognitive rehabilitation for persons with multiple sclerosis: an updated review of the literature from 2007 to 2016. *Archives of physical medicine and rehabilitation*, *99*(2), 390-407.

Greenwood, P. M., & Parasuraman, R. (2016). The mechanisms of far transfer from cognitive training: Review and hypothesis. *Neuropsychology*, *30*(6), 742.

Guerin, B. (2010). Social facilitation. *The Corsini encyclopedia of psychology*, 1-2.

Gunver, M. G., Senocak, M. S., & Vehid, S. (2018). To determine skewness, mean and deviation with a new approach on continuous data. *Int. J. Sci. Res, 74*, 64-79.

Habekost, T. (2015). Clinical TVA-based studies: a general review. *Frontiers in psychology, 6*, 290.

Hackett, M. L., Anderson, C. S., House, A., & Xia, J. (2008). Interventions for treating depression after stroke. *Cochrane Database of Systematic Reviews*, (4).

Haghgoo, H. A., Pazuki, E. S., Hosseini, A. S., & Rassafiani, M. (2013). Depression, activities of daily living and quality of life in patients with stroke. Journal of the neurological sciences, 328(1-2), 87-91.

Hagovska, M., & Nagyova, I. (2017). The transfer of skills from cognitive and physical training to activities of daily living: a randomised controlled study. *European journal of ageing, 14*(2), 133-142.

Halligan, P. W., & Marshall, J. C. (1998). Neglect of awareness. *Consciousness and cognition*, *7*(3), 356-380.

Hampshire, A., Sandrone, S., & Hellyer, P. J. (2019). A large-scale, cross-sectional investigation into the efficacy of brain training. *Frontiers in human neuroscience*, *13*, 221.

Hebb, D. O. (1949). The first stage of perception: growth of the assembly. *The Organization of Behavior*, *4*, 60-78.

Heiberg, G., Pedersen, S. G., Friborg, O., Nielsen, J. F., Holm, H. S., Arntzen, C., & Anke, A. (2018). Can the health related quality of life measure QOLIBRI-overall scale (OS) be of use after stroke? A validation study. *BMC neurology*, *18*(1), 1-10.

Herdman, M., Gudex, C., Lloyd, A., Janssen, M. F., Kind, P., Parkin, D., ... & Badia, X. (2011). Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of life research*, *20*(10), 1727-1736.

Higgins, J. P., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., ... & Sterne, J. A. (2011). The Cochrane Collaboration’s tool for assessing risk of bias in randomised trials. *Bmj*, *343*.

Hindle, J. V., Martin-Forbes, P. A., Martyr, A., Bastable, A. J., Pye, K. L., Mueller Gathercole, V. C., ... & Clare, L. (2017). The effects of lifelong cognitive lifestyle on executive function in older people with Parkinson's disease. *International journal of geriatric psychiatry*, *32*(12), e157-e165.

Hooshyar, D., Yousefi, M., & Lim, H. (2019). A systematic review of data-driven approaches in player modeling of educational games. *Artificial Intelligence Review*, *52*(3), 1997-2017.

Hosseingholizadeh, N., Sadeghi, R., Ardebili, H. E., Foroushani, A. R., & Taghdisi, M. H. (2019). The correlation of self-efficacy and social support with social participation: A cross sectional study among the elderly. *Journal of medicine and life*, *12*(3), 239.

Hourcade, J. P., Williams, S. R., Miller, E. A., Huebner, K. E., & Liang, L. J. (2013, April). Evaluation of tablet apps to encourage social interaction in children with autism spectrum disorders. In *Proceedings of the SIGCHI conference on human factors in computing systems* (pp. 3197-3206).

Hughes, T. F., Flatt, J. D., Fu, B., Butters, M. A., Chang, C. C. H., & Ganguli, M. (2014). Interactive video gaming compared with health education in older adults with mild cognitive impairment: a feasibility study. *International journal of geriatric psychiatry*, *29*(9), 890-898.

Hurst, F. G., Ownsworth, T., Beadle, E., Shum, D. H., & Fleming, J. (2020). Domain-specific deficits in self-awareness and relationship to psychosocial outcomes after severe traumatic brain injury. *Disability and rehabilitation*, *42*(5), 651-659.

Husain, M., & Rorden, C. (2003). Non-spatially lateralized mechanisms in hemispatial neglect. *Nature Reviews Neuroscience*, *4*(1), 26-36.

Hussenoeder, F. S., Conrad, I., Roehr, S., Fuchs, A., Pentzek, M., Bickel, H., ... & Riedel-Heller, S. G. (2020). Mild cognitive impairment and quality of life in the oldest old: a closer look. *Quality of Life Research*, *29*(6), 1675-1683.

Huygelier, H., Schraepen, B., Lafosse, C., Vaes, N., Schillebeeckx, F., Michiels, K., ... & Gillebert, C. R. (2020). An immersive virtual reality game to train spatial attention orientation after stroke: A feasibility study. *Applied Neuropsychology: Adult*, 1-21.

Hyer, L., Scott, C., Atkinson, M. M., Mullen, C. M., Lee, A., Johnson, A., & Mckenzie, L. C. (2016). Cognitive training program to improve working memory in older adults with MCI. *Clinical Gerontologist*, *39*(5), 410-427.

Imanishi, M., Tomohisa, H., & Higaki, K. (2017). Impact of continuous in-home rehabilitation on quality of life and activities of daily living in elderly clients over 1 year. *Geriatrics & gerontology international*, *17*(11), 1866-1872.

Ismail, Z., Elbayoumi, H., Fischer, C. E., Hogan, D. B., Millikin, C. P., Schweizer, T., ... & Fiest, K. M. (2017). Prevalence of depression in patients with mild cognitive impairment: a systematic review and meta-analysis. *JAMA psychiatry*, *74*(1), 58-67.

Ito M. 2005. Bases and implications of learning in the cerebellum—adaptive control and internal model mechanism. Prog. Brain Res. 148: 95–109

Jefferson, A. L., Byerly, L. K., Vanderhill, S., Lambe, S., Wong, S., Ozonoff, A., & Karlawish, J. H. (2008). Characterization of activities of daily living in individuals with mild cognitive impairment. *The American journal of geriatric psychiatry*, *16*(5), 375-383.

Jenkins, W. M., & Merzenich, M. M. (1987). Reorganization of neocortical representations after brain injury: a neurophysiological model of the bases of recovery from stroke. In *Progress in brain research* (Vol. 71, pp. 249-266). Elsevier.

Jeong, B. O., Kang, H. J., Bae, K. Y., Kim, S. W., Kim, J. M., Shin, I. S., ... & Yoon, J. S. (2012). Determinants of quality of life in the acute stage following stroke. *Psychiatry Investigation*, *9*(2), 127.

Johnstone, E. C., Owens, D. C., & Lawrie, S. M. (2010). *Companion to psychiatric studies e-book*. Elsevier Health Sciences.

Karnath, H. O., Rorden, C., & Ticini, L. F. (2009). Damage to white matter fiber tracts in acute spatial neglect. *Cerebral Cortex*, *19*(10), 2331-2337.

Kealy, D., Joyce, A. S., Weber, R., Ehrenthal, J. C., & Ogrodniczuk, J. S. (2019). What the patient wants: Addressing patients' treatment targets in an integrative group psychotherapy programme. *Psychology and Psychotherapy: Theory, Research and Practice*, *92*(1), 20-38.

Kelly, M. E., Loughrey, D., Lawlor, B. A., Robertson, I. H., Walsh, C., & Brennan, S. (2014). The impact of cognitive training and mental stimulation on cognitive and everyday functioning of healthy older adults: a systematic review and meta-analysis. *Ageing research reviews*, *15*, 28-43.

Khot, S. P., & Morgenstern, L. B. (2019). Sleep and stroke. *Stroke*, *50*(6), 1612-1617.

Kim, B. J., Liu, L., Nakaoka, S., Jang, S., & Browne, C. (2018). Depression among older Japanese Americans: The impact of functional (ADL & IADL) and cognitive status. *Social work in health care, 57*(2), 109-125.

Knapen, J., Vancampfort, D., Schoubs, B., Probst, M., Sienaert, P., Haake, P., ... & Pieters, G. (2009). Exercise for the treatment of depression. *The Open Complementary Medicine Journal*, *1*(1).

Knapp, P., Burton, C. A. C., Holmes, J., Murray, J., Gillespie, D., Lightbody, C. E., ... & Lewis, S. R. (2017). Interventions for treating anxiety after stroke. *Cochrane Database of Systematic Reviews*, (5).

Knutti, K., Björklund Carlstedt, A., Clasen, R., & Green, D. (2020). Impacts of goal setting on engagement and rehabilitation outcomes following acquired brain injury: a systematic review of reviews. *Disability and Rehabilitation*, 1-10.

Koepsell, T. D., & Monsell, S. E. (2012). Reversion from mild cognitive impairment to normal or near-normal cognition: risk factors and prognosis. *Neurology*, *79*(15), 1591-1598.

Kolanowski, A., Bossen, A., Hill, N., Guzman-Velez, E., & Litaker, M. (2012). Factors associated with sustained attention during an activity intervention in persons with dementia. *Dementia and geriatric cognitive disorders*, *33*(4), 233-239.

Korpershoek, C., Van der Bijl, J., & Hafsteinsdóttir, T. B. (2011). Self-efficacy and its influence on recovery of patients with stroke: a systematic review. *Journal of advanced nursing*, *67*(9), 1876-1894.

Kueider, A. M., Parisi, J. M., Gross, A. L., & Rebok, G. W. (2012). Computerized cognitive training with older adults: a systematic review. *PloS one*, *7*(7), e40588.

Kumar, M. P., Packer, B., & Koller, D. (2010). Self-Paced Learning for Latent Variable Models. In *NIPS* (Vol. 1, p. 2).

Lampit, A., Hallock, H., & Valenzuela, M. (2014). Computerized cognitive training in cognitively healthy older adults: a systematic review and meta-analysis of effect modifiers. *PLoS medicine*, *11*(11), e1001756.

Lara, E., Caballero, F. F., Rico-Uribe, L. A., Olaya, B., Haro, J. M., Ayuso-Mateos, J. L., & Miret, M. (2019). Are loneliness and social isolation associated with cognitive decline?. *International journal of geriatric psychiatry*, *34*(11), 1613-1622.

Lara, E., Koyanagi, A., Caballero, F., Domènech-Abella, J., Miret, M., Olaya, B., ... & Haro, J. M. (2017). Cognitive reserve is associated with QoL: A population-based study. *Experimental gerontology*, *87*, 67-73.

Law, L. L., Mok, V. C., & Yau, M. M. (2019). Effects of functional tasks exercise on cognitive functions of older adults with mild cognitive impairment: a randomized controlled pilot trial. *Alzheimer's research & therapy*, *11*(1), 1-10.

Law, M., Polatajko, H., Baptiste, S., & Townsend, E. (1997). Core concepts of occupational therapy. *Enabling occupation: An occupational therapy perspective*, 29-56.

Lee, J. Y., & Kim, H. S. (2014). Influences of social support, self-esteem and motivation for rehabilitation on the activities of daily living in stroke patients. *Journal of East-West Nursing Research*, *20*(2), 145-153.

Leifer, B. P. (2003). Early diagnosis of Alzheimer's disease: clinical and economic benefits. *Journal of the American Geriatrics Society*, *51*(5s2), S281-S288.

Leng, M., Yin, H., Zhang, P., Jia, Y., Hu, M., Li, G., ... & Chen, L. (2020). Sleep quality and health-related quality of life in older people with subjective cognitive decline, mild cognitive impairment, and Alzheimer disease. *The Journal of nervous and mental disease*, *208*(5), 387-396.

Leyhe, T., Reynolds III, C. F., Melcher, T., Linnemann, C., Klöppel, S., Blennow, K., ... & Hampel, H. (2017). A common challenge in older adults: Classification, overlap, and therapy of depression and dementia. *Alzheimer's & dementia*, *13*(1), 59-71.

Leys, D., Hénon, H., Mackowiak-Cordoliani, M. A., & Pasquier, F. (2005). Poststroke dementia. *The Lancet Neurology*, *4*(11), 752-759.

Lezak, M. D., Howieson, D. B., Loring, D. W., & Fischer, J. S. (2004). *Neuropsychological assessment*. Oxford University Press, USA.

Liao, Y. Y., Tseng, H. Y., Lin, Y. J., Wang, C. J., & Hsu, W. C. (2019). Using virtual reality-based training to improve cognitive function, instrumental activities of daily living and neural efficiency in older adults with mild cognitive impairment. *European journal of physical and rehabilitation medicine*, *56*(1), 47-57.

Lin, F., Heffner, K. L., Ren, P., Tivarus, M. E., Brasch, J., Chen, D. G., ... & Tadin, D. (2016). Cognitive and neural effects of vision-based speed-of-processing training in older adults with amnestic mild cognitive impairment: A pilot study. *Journal of the American Geriatrics Society*, *64*(6), 1293-1298.

Lin, J. H., Huang, M. W., Wang, D. W., Chen, Y. M., Lin, C. S., Tang, Y. J., ... & Lane, H. Y. (2014). Late-life depression and quality of life in a geriatric evaluation and management unit: an exploratory study. *BMC geriatrics*, *14*(1), 1-7.

Lindenberger, U., Wenger, E., & Lövdén, M. (2017). Towards a stronger science of human plasticity. *Nature Reviews Neuroscience*, *18*(5), 261-262.

Lipnicki, D. M., Crawford, J., Kochan, N. A., Trollor, J. N., Draper, B., Reppermund, S., ... & Wong, S. (2017). Risk factors for mild cognitive impairment, dementia and mortality: The sydney memory and ageing study. *Journal of the American Medical Directors Association*, *18*(5), 388-395.

Lipskaya-Velikovsky, L., Zeilig, G., Weingarden, H., Rozental-Iluz, C., & Rand, D. (2018). Executive functioning and daily living of individuals with chronic stroke: measurement and implications. *International journal of rehabilitation research*, *41*(2), 122-127.

Livingston, G., Sommerlad, A., Orgeta, V., Costafreda, S. G., Huntley, J., Ames, D., ... & Mukadam, N. (2017). Dementia prevention, intervention, and care. *The Lancet*, *390*(10113), 2673-2734.

Loetscher, T., Potter, K. J., Wong, D., & das Nair, R. (2019). Cognitive rehabilitation for attention deficits following stroke. *Cochrane Database of Systematic Reviews*, (11).

Lumsden, J., Edwards, E. A., Lawrence, N. S., Coyle, D., & Munafò, M. R. (2016). Gamification of cognitive assessment and cognitive training: a systematic review of applications and efficacy. *JMIR serious games*, *4*(2), e11.

Ma, L. (2020). Depression, anxiety, and apathy in mild cognitive impairment: current perspectives. *Frontiers in aging neuroscience*, *12*, 9.

MacIntosh, B. J., Edwards, J. D., Kang, M., Cogo-Moreira, H., Chen, J. L., Mochizuki, G., ... & Swardfager, W. (2017). Post-stroke fatigue and depressive symptoms are differentially related to mobility and cognitive performance. *Frontiers in aging neuroscience*, *9*, 343.

Mahesh, P. K. B., Gunathunga, M. W., Jayasinghe, S., Arnold, S. M., & Liyanage, S. N. (2018). Factors influencing pre-stroke and post-stroke QoL among stroke survivors in a lower middle-income country. *Neurological Sciences*, *39*(2), 287-295.

Manenti, R., Gobbi, E., Baglio, F., Macis, A., Ferrari, C., Pagnoni, I., ... & Cotelli, M. (2020). Effectiveness of an Innovative Cognitive Treatment and Telerehabilitation on Subjects With Mild Cognitive Impairment: A Multicenter, Randomized, Active-Controlled Study. *Frontiers in Aging Neuroscience*, *12*, 400.

Marshall, G. A., Rentz, D. M., Frey, M. T., Locascio, J. J., Johnson, K. A., Sperling, R. A., & Alzheimer's Disease Neuroimaging

Initiative. (2011). Executive function and instrumental activities of daily living in mild cognitive impairment and Alzheimer's disease. *Alzheimer's & Dementia, 7*(3), 300-308.

McDonald, J. H. (2009). *Handbook of biological statistics* (Vol. 2, pp. 6-59). Baltimore, MD: sparky house publishing.

Merzenich, M. M., Kaas, J. H., Wall, J., Nelson, R. J., Sur, M., & Felleman, D. (1983). Topographic reorganization of somatosensory cortical areas 3b and 1 in adult monkeys following restricted deafferentation. *Neuroscience, 8*(1), 33-55.

Merzenich, M. M., Van Vleet, T. M., & Nahum, M. (2014). Brain plasticity-based therapeutics. *Frontiers in human neuroscience, 8*, 385.

Micceri, T. (1989). The unicorn, the normal curve, and other improbable creatures. *Psychological bulletin, 105*(1), 156.

Michael, D. R., & Chen, S. L. (2005). *Serious games: Games that educate, train, and inform*. Muska & Lipman/Premier-Trade.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., Antes, G., Atkins, D., Barbour, V., Barrowman, N., Berlin, J. A., Clark, J., Clarke, M., Cook, D., D'Amico, R., Deeks, J. J., Devereaux, P. J., Dickersin, K., Egger, M., Ernst, E., Gøtzsche, P. C., ... Tugwell, P. (2014). Ítems de referencia para publicar Revisiones Sistemáticas y Metaanálisis: La Declaración PRISMA. *Revista Espanola de Nutricion Humana y Dietetica*, *18*(3), 172-181.

Morrison, A. B., & Chein, J. M. (2011). Does working memory training work? The promise and challenges of enhancing cognition by training working memory. *Psychonomic bulletin & review*, *18*(1), 46-60.

Mrakic-Sposta, S., Di Santo, S. G., Franchini, F., Arlati, S., Zangiacomi, A., Greci, L., ... & Vezzoli, A. (2018). Effects of combined physical and cognitive virtual reality-based training on cognitive impairment and oxidative stress in MCI patients: a pilot study. *Frontiers in aging neuroscience*, *10*, 282.

Mukherjee, D., Levin, R. L., & Heller, W. (2006). The cognitive, emotional, and social sequelae of stroke: psychological and ethical concerns in post-stroke adaptation. *Topics in stroke rehabilitation*, *13*(4), 26-35.

Nagarajan, D., Lee, D. C. A., Robins, L. M., & Haines, T. P. (2020). Risk factors for social isolation in post-hospitalized older adults. *Archives of gerontology and geriatrics*, *88*, 104036.

Naghavi, M., Abajobir, A. A., Abbafati, C., Abbas, K. M., Abd-Allah, F., Abera, S. F., ... & Fischer, F. (2017). Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*, *390*(10100), 1151-1210.

Navarro, M. D., Llorens, R., Borrego, A., Alcañiz, M., Noé, E., & Ferri, J. (2020). Competition enhances the effectiveness and motivation of attention rehabilitation after stroke. A randomized controlled trial. *Frontiers in human neuroscience*, *14*, 385.

Nelson, H. E., & O'Connell, A. (1978). Dementia: the estimation of premorbid intelligence levels using the New Adult Reading Test. *Cortex*, *14*(2), 234-244.

New Zealand Guidelines Group Incorporated (2006) *Traumatic Brain Injury: Diagnosis, Acute Management and Rehabilitation*. Retrived from https://www.moh.govt.nz/NoteBook/nbbooks.nsf/0/B8738C3605889A6ACC257A6D00809243/$file/traumatic-brain-injury-acc.pdf.

Nguyen, C. M., Copeland, C. T., Lowe, D. A., Heyanka, D. J., & Linck, J. F. (2020). Contribution of executive functioning to instrumental activities of daily living in older adults. *Applied Neuropsychology: Adult*, *27*(4), 326-333.

Nichol, A. D., Higgins, A. M., Gabbe, B. J., Murray, L. J., Cooper, D. J., & Cameron, P. A. (2011). Measuring functional and quality of life outcomes following major head injury: common scales and checklists. *Injury*, *42*(3), 281-287.

Nikravesh, M., Aghajanzadeh, M., Maroufizadeh, S., Saffarian, A., & Jafari, Z. (2021). Working memory training in post-stroke aphasia: Near and far transfer effects. *Journal of communication disorders*, *89*, 106077.

Nunnari, D., Bramanti, P., & Marino, S. (2014). Cognitive reserve in stroke and traumatic brain injury patients. *Neurological Sciences*, *35*(10), 1513-1518.

Nys, G. M. S., Van Zandvoort, M. J. E., Van Der Worp, H. B., De Haan, E. H. F., De Kort, P. L. M., Jansen, B. P. W., &

Kappelle, L. J. (2006). Early cognitive impairment predicts long-term depressive symptoms and QoL after stroke. *Journal of the neurological sciences*, *247*(2), 149-156.

O'Halloran, A. M., Finucane, C., Savva, G. M., Robertson, I. H., & Kenny, R. A. (2014). Sustained attention and frailty in the older adult population. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *69*(2), 147-156.

Oh, S. J., Seo, S., Lee, J. H., Song, M. J., & Shin, M. S. (2018). Effects of smartphone-based memory training for older adults with subjective memory complaints: a randomized controlled trial. *Aging & mental health*, *22*(4), 526-534.

Owsley, C., Sloane, M., McGwin Jr, G., & Ball, K. (2002). Timed instrumental activities of daily living tasks: relationship to cognitive function and everyday performance assessments in older adults. *Gerontology*, *48*(4), 254-265.

Page, M. J., McKenzie, J., Bossuyt, P., Boutron, I., Hoffmann, T., & Mulrow, C. D. (2020). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. MetaArXiv. 2020.

Parasuraman, R. (Ed.). (2000). *The attentive brain*. Mit Press.

Park, J. H., & Park, J. H. (2018). Does cognition-specific computer training have better clinical outcomes than non-specific computer training? A single-blind, randomized controlled trial. *Clinical rehabilitation*, *32*(2), 213-222.

Pasi, M., Poggesi, A., Salvadori, E., & Pantoni, L. (2012). Post-stroke dementia and cognitive impairment. *Manifestations of Stroke*, *30*, 65-69.

Pedullà, L., Brichetto, G., Tacchino, A., Vassallo, C., Zaratin, P., Battaglia, M. A., ... & Bove, M. (2016). Adaptive vs. non-adaptive cognitive training by means of a personalized App: a randomized trial in people with multiple sclerosis. *Journal of neuroengineering and rehabilitation*, *13*(1), 1-10.

Peers, P. V., Astle, D. E., Duncan, J., Murphy, F., Hampshire, A., Das, T., & Manly, T. (2018). A randomised exploratory investigation of the effects of Attention vs Working Memory Training on cognitive performance and everyday functioning following stroke. *BioRxiv*, 296723.

Peers, P. V., Punton, S. F., Murphy, F. C., Watson, P., Bateman, A., Duncan, J., ... & Manly, T. (2021). A randomised control trial of the effects of home-based online attention training and working memory training on cognition and everyday function in a community stroke sample. *medRxiv*.

Pereira, F. S., Yassuda, M. S., Oliveira, A. M., Diniz, B. S., Radanovic, M., Talib, L. L., ... & Forlenza, O. V. (2010). Profiles of functional deficits in mild cognitive impairment and dementia: benefits from objective measurement. *Journal of the International Neuropsychological Society*, *16*(2), 297-305.

Petersen, R. C. (2004). Mild cognitive impairment as a diagnostic entity. *Journal of internal medicine*, *256*(3), 183-194.

Petersen, R. C., Smith, G. E., Waring, S. C., Ivnik, R. J., Kokmen, E., & Tangelos, E. G. (1997). Aging, memory, and mild cognitive impairment. *International psychogeriatrics*, *9*(S1), 65-69.

Plante, T. G., Coscarelli, L., & Ford, M. (2001). Does exercising with another enhance the stress-reducing benefits of exercise?. *International Journal of Stress Management*, *8*(3), 201-213.

Plante, T. G., Madden, M., Mann, S., & Lee, G. (2010). Effects of perceived fitness level of exercise partner on intensity of exertion.

Pohjasvaara, T., Leppavuori, A., Siira, I., Vataja, R., Kaste, M., & Erkinjuntti, T. (1998). Frequency and clinical determinants of poststroke depression. *stroke*, *29*(11), 2311-2317.

Pollock, A., Farmer, S. E., Brady, M. C., Langhorne, P., Mead, G. E., Mehrholz, J., & van Wijck, F. (2014). Interventions for improving upper limb function after stroke. *Cochrane Database of Systematic Reviews*, (11).

Prince M, Albanese E, Guerchet M, Prina M. World Alzheimer Report 2014. Dementia and risk reduction: an analysis of protective and modifiable risk factors. London: Alzheimer's Disease International; 2014 (https://www.alzint.org/u/WorldAlzheimerReport2014.pdf, accessed 11 May 2021).

Puente, A. N., Terry, D. P., Faraco, C. C., Brown, C. L., & Miller, L. S. (2014). Functional impairment in mild cognitive impairment evidenced using performance-based measurement. *Journal of geriatric Psychiatry and Neurology*, *27*(4), 253-258.

Rasquin, S. M. C., Lodder, J., & Verhey, F. R. J. (2005). Predictors of reversible mild cognitive impairment after stroke: a 2-year follow-up study. *Journal of the neurological sciences*, *229*, 21-25.

Reijnders, J., van Heugten, C., & van Boxtel, M. (2013). Cognitive interventions in healthy older adults and people with mild cognitive impairment: a systematic review. *Ageing research reviews*, *12*(1), 263-275.

Remsik, A., Young, B., Vermilyea, R., Kiekhoefer, L., Abrams, J., Evander Elmore, S., ... & Prabhakaran, V. (2016). A review of the progression and future implications of brain-computer interface therapies for restoration of distal upper extremity motor function after stroke. *Expert review of medical devices*, *13*(5), 445-454.

Rhea, M. R., Landers, D. M., Alvar, B. A., & Arent, S. M. (2003). The effects of competition and the presence of an audience on weight lifting performance. *Journal of Strength and Conditioning Research*, *17*(2), 303-306.

Richardson, C., Stephan, B. C., Robinson, L., Brayne, C., & Matthews, F. E. (2019). Two-decade change in prevalence of cognitive impairment in the UK. *European journal of epidemiology, 34*(11), 1085-1092.

Roberts, R., & Knopman, D. S. (2013). Classification and epidemiology of MCI. *Clinics in geriatric medicine*, *29*(4), 753-772.

Robertson, I. H., Ridgeway, V., Greenfield, E., & Parr, A. (1997). Motor recovery after stroke depends on intact sustained attention: a 2-year follow-up study. *Neuropsychology*, *11*(2), 290.

Robinson, R. G., & Jorge, R. E. (2016). Post-stroke depression: a review. *American Journal of Psychiatry*, *173*(3), 221-231.7

Rosenich, E., Hordacre, B., Paquet, C., Koblar, S. A., & Hillier, S. L. (2020). Cognitive reserve as an emerging concept in stroke recovery. *Neurorehabilitation and neural repair*, *34*(3), 187-199.

Rubio, E., Lázaro, A., & Sánchez-Sánchez, A. (2009). Social participation and independence in activities of daily living: a cross sectional study. *BMC geriatrics*, *9*(1), 1-11.

Russ, T. C., & Morling, J. R. (2012). Cholinesterase inhibitors for mild cognitive impairment. *Cochrane Database of Systematic Reviews*, (9).

Sachdev, P. S., Brodaty, H., Valenzuela, M. J., Lorentz, L., Looi, J. C. L., Berman, K., ... & Zagami, A. S. (2006). Clinical determinants of dementia and mild cognitive impairment following ischaemic stroke: the Sydney Stroke Study. *Dementia and geriatric cognitive disorders*, *21*(5-6), 275-283.

Sachdev, P. S., Chen, X., Brodaty, H., Thompson, C., Altendorf, A., & Wen, W. (2009). The determinants and longitudinal course of post-stroke mild cognitive impairment. *Journal of the International Neuropsychological Society: JINS*, *15*(6), 915.

Salehi, S., Tahan, N., Bagheban, A. A., & Monfared, M. E. (2019). Quality of Life Within Three Months After Stroke: A Study in the City of Arak, Iran. *Journal of the National Medical Association*, *111*(5), 475-480.

Salter, K. L., Moses, M. B., Foley, N. C., & Teasell, R. W. (2008). Health-related quality of life after stroke: what are we measuring?. *International Journal of Rehabilitation Research*, *31*(2), 111-117.

Salthouse, T. A. (1996). The processing-speed theory of adult age differences in cognition. *Psychological review*, *103*(3), 403.

Sánchez-Rodríguez, J. L., Torrellas-Morales, C., Fernández-Gómez, M. J., & Martín-Vallejo, J. (2013). Influencia de la reserva cognitiva en la calidad de vida en sujetos con enfermedad de Alzheimer. *Anales de Psicología/Annals of Psychology*, *29*(3), 762-771.

Sarter, M., Givens, B., & Bruno, J. P. (2001). The cognitive neuroscience of sustained attention: where top-down meets bottom-up. *Brain research reviews*, *35*(2), 146-160.

Savva, G. M., Stephan, B. C., & Alzheimer's Society Vascular Dementia Systematic Review Group. (2010). Epidemiological studies of the effect of stroke on incident dementia: a systematic review. *Stroke*, *41*(1), e41-e46.

Schöttke, H., & Giabbiconi, C. M. (2015). Post-stroke depression and post-stroke anxiety: prevalence and predictors. *International Psychogeriatrics*, *27*(11), 1805-1812.

Schubert, T., Strobach, T., & Karbach, J. (2014). New directions in cognitive training: on methods, transfer, and application.

Scottish Intercollegiate Guidelines Network (SIGN). Brain injury rehabilitation in adults. Edinburgh: SIGN; 2013. (SIGN publication no. 130). [March 2013]. Available from URL: http://www.sign.ac.uk

Shea-Shumsky, N. B., Schoeneberger, S., & Grigsby, J. (2019). Executive functioning as a predictor of stroke rehabilitation outcomes. *The Clinical Neuropsychologist*, *33*(5), 854-872.

Shulman, G. L., Pope, D. L., Astafiev, S. V., McAvoy, M. P., Snyder, A. Z., & Corbetta, M. (2010). Right hemisphere dominance during spatial selective attention and target detection occurs outside the dorsal frontoparietal network. *Journal of Neuroscience*, *30*(10), 3640-3651.

Shultz, E. L., Hoskinson, K. R., Keim, M. C., Dennis, M., Taylor, H. G., Bigler, E. D., ... & Yeates, K. O. (2016). Adaptive functioning following pediatric traumatic brain injury: Relationship to executive function and processing speed. *Neuropsychology*, *30*(7), 830.

Shute, V., Ke, F., & Wang, L. (2017). Assessment and adaptation in games. In *Instructional techniques to facilitate learning and motivation of serious games* (pp. 59-78). Springer, Cham.

Simons, D. J., Boot, W. R., Charness, N., Gathercole, S. E., Chabris, C. F., Hambrick, D. Z., & Stine-Morrow, E. A. (2016). Do “brain-training” programs work?. *Psychological Science in the Public Interest*, *17*(3), 103-186.

Smelser, N. J., & Baltes, P. B. (Eds.). (2001). *International encyclopedia of the social & behavioral sciences* (Vol. 11). Amsterdam: Elsevier.

Smith, G. E., Housen, P., Yaffe, K., Ruff, R., Kennison, R. F., Mahncke, H. W., & Zelinski, E. M. (2009). A cognitive training program based on principles of brain plasticity: results from the Improvement in Memory with Plasticity-based Adaptive Cognitive Training (IMPACT) Study. *Journal of the American Geriatrics Society*, *57*(4), 594-603.

Snowden, M. B., Atkins, D. C., Steinman, L. E., Bell, J. F., Bryant, L. L., Copeland, C., & Fitzpatrick, A. L. (2015). Longitudinal association of dementia and depression. *The American Journal of Geriatric Psychiatry*, *23*(9), 897-905.

Sood, P., Kletzel, S. L., Krishnan, S., Devos, H., Negm, A., Hoffecker, L., ... & Heyn, P. C. (2019). Nonimmersive brain gaming for older adults with cognitive impairment: A scoping review. *The Gerontologist*, *59*(6), e764-e781.

Sopena, S., Dewar, B. K., Nannery, R., Teasdale, T. W., & Wilson, B. A. (2007). The European Brain Injury Questionnaire (EBIQ) as a reliable outcome measure for use with people with brain injury. *Brain Injury*, *21*(10), 1063-1068.

Southworth, C. (2012). Making Sense of Biostatistics: Outliers in Clinical Data. *Clinical research Journal*, *6*(1), 2-3.

Steward, K. A., Bull, T. P., & Wadley, V. G. (2019). Differences in self-awareness of functional deficits between amnestic single- and multidomain mild cognitive impairment. *Journal of clinical and experimental neuropsychology*, *41*(5), 544-553.

Stites, S. D., Harkins, K., Rubright, J. D., & Karlawish, J. (2018). Relationships between Cognitive Complaints and Quality of Life in Older Adults with Mild Cognitive Impairment, Mild Alzheimer's Disease Dementia, and Normal Cognition. *Alzheimer disease and associated disorders*, *32*(4), 276.

Sturm, J. W., Donnan, G. A., Dewey, H. M., Macdonell, R. A., Gilligan, A. K., Srikanth, V., & Thrift, A. G. (2004). Quality of life after stroke: the North East Melbourne stroke incidence study (NEMESIS). *Stroke*, *35*(10), 2340-2345.

Sturm, W., & Willmes, K. (2001). On the functional neuroanatomy of intrinsic and phasic alertness. *Neuroimage, 14*(1), S76-S84.

Stuss, D. T., & Alexander, M. P. (2007). Is there a dysexecutive syndrome?. *Philosophical Transactions of the Royal Society B: Biological Sciences, 362*(1481), 901-915.

Stuss, D. T., Stethem, L. L., Hugenholtz, H., Picton, T., Pivik, J., & Richard, M. T. (1989). Reaction time after head injury: fatigue, divided and focused attention, and consistency of performance. *Journal of Neurology, Neurosurgery & Psychiatry*, *52*(6), 742-748.

Sun, J. H., Tan, L., & Yu, J. T. (2014). Post-stroke cognitive impairment: epidemiology, mechanisms and management. *Annals of translational medicine*, *2*(8).

Tabert, MH, Albert, SM, Borukhova-Milov, L. Functional deficits in patients with mild cognitive impairment: prediction of AD. Neurology. 2002;58(5):758–764.

Takeuchi, N., & Izumi, S. I. (2013). Rehabilitation with poststroke motor recovery: a review with a focus on neural plasticity. *Stroke research and treatment, 2013*.

Tatemichi, T. K., Desmond, D. W., Paik, M., Figueroa, M., Gropen, T. I., Stern, Y., ... & Mayeux, R. (1993). Clinical determinants of dememtia related to stroke. *Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society*, *33*(6), 568-575.

Tetlow, A. M., & Edwards, J. D. (2017). Systematic literature review and meta-analysis of commercially available computerized cognitive training among older adults. *Journal of Cognitive Enhancement, 1*(4), 559-575.

Tetlow, A. M., & Edwards, J. D. (2017). Systematic literature review and meta-analysis of commercially available computerized cognitive training among older adults. *Journal of Cognitive Enhancement, 1*(4), 559-575.

Tomaszewski Farias, S., Cahn-Weiner, D. A., Harvey, D. J., Reed, B. R., Mungas, D., Kramer, J. H., & Chui, H. (2009). Longitudinal changes in memory and executive functioning are associated with longitudinal change in instrumental activities of daily living in older adults. *The Clinical Neuropsychologist*, *23*(3), 446-461.

Truelsen, T., Begg, S., & Mathers, C. (2006). The global burden of cerebrovascular. In *Who Int*.

Tschanz, J. T., Welsh-Bohmer, K. A., Lyketsos, C. G., Corcoran, C., Green, R. C., Hayden, K., ... & Cache County Investigators. (2006). Conversion to dementia from mild cognitive disorder: the Cache County Study. *Neurology*, *67*(2), 229-234.

Tünnermann, J., Petersen, A., & Scharlau, I. (2015). Does attention speed up processing? Decreases and increases of processing rates in visual prior entry. *Journal of vision*, *15*(3), 1-1.

Urwyler, P., Stucki, R., Rampa, L., Müri, R., Mosimann, U. P., & Nef, T. (2017). Cognitive impairment categorized in community-dwelling older adults with and without dementia using in-home sensors that recognise activities of daily living. *Scientific reports*, *7*(1), 1-9.

Uziel, L. (2007). Individual differences in the social facilitation effect: A review and meta-analysis. *Journal of Research in Personality*, *41*(3), 579-601.

Valdés, E. G., Andel, R., Lister, J. J., Gamaldo, A., & Edwards, J. D. (2019). Can Cognitive Speed of Processing Training Improve Everyday Functioning Among Older Adults With Psychometrically Defined Mild Cognitive Impairment?. *Journal of aging and health*, *31*(4), 595-610.

Vallesi, A., Tronelli, V., Lomi, F., & Pezzetta, R. (2021). Age differences in sustained attention tasks: A meta-analysis. *Psychonomic Bulletin & Review*, 1-21.

van de Port, I. G., Kwakkel, G., Schepers, V. P., Heinemans, C. T., & Lindeman, E. (2007). Is fatigue an independent factor associated with activities of daily living, instrumental activities of daily living and health-related quality of life in chronic stroke?. *Cerebrovascular Diseases*, *23*(1), 40-45.

van de Ven, R. M., Murre, J. M., Veltman, D. J., & Schmand, B. A. (2016). Computer-based cognitive training for executive functions after stroke: a systematic review. *Frontiers in human neuroscience*, *10*, 150.

Van der Kuil, M. N., Visser-Meily, J., Evers, A. W., & Van der Ham, I. J. (2018). A usability study of a serious game in cognitive rehabilitation: a compensatory navigation training in acquired brain injury patients. *Frontiers in psychology*, *9*, 846.

Vijayan, M., & Reddy, P. H. (2016). Stroke, vascular dementia, and Alzheimer’s disease: molecular links. *Journal of Alzheimer's Disease*, *54*(2), 427-443.

Vogt, A., Kappos, L., Calabrese, P., Stöcklin, M., Gschwind, L., Opwis, K., & Penner, I. K. (2009). Working memory training in patients with multiple sclerosis–comparison of two different training schedules. *Restorative neurology and neuroscience*, *27*(3), 225-235.

von Steinbuechel, N., Petersen, C., Bullinger, M., & QoLIBRI Group. (2005). Assessment of health-related quality of life in persons after traumatic brain injury—development of the Qolibri, a specific measure. *Re-Engineering of the Damaged Brain and Spinal Cord*, 43-49.

Von Steinbuechel, N., Wilson, L., Gibbons, H., Muehlan, H., Schmidt, H., Schmidt, S., ... & Truelle, J. L. (2012). QOLIBRI overall scale: a brief index of health-related quality of life after traumatic brain injury. *Journal of Neurology, Neurosurgery & Psychiatry*, *83*(11), 1041-1047.

Wampold, B. E. (2015). How important are the common factors in psychotherapy? An update. *World Psychiatry*, *14*(3), 270-277.

Wang, R., & Langhammer, B. (2018). Predictors of quality of life for chronic stroke survivors in relation to cultural differences: a literature review. *Scandinavian journal of caring sciences*, *32*(2), 502-514.

Wang, Y., Song, M., Yu, L., Wang, L., An, C., Xun, S., ... & Wang, X. (2015). Mild cognitive impairment: vascular risk factors in community elderly in four cities of Hebei Province, China. *PloS one*, *10*(5), e0124566.

Watson, R., Bryant, J., Sanson-Fisher, R., Mansfield, E., & Evans, T. J. (2018). What is a 'timely'diagnosis? Exploring the preferences of Australian health service consumers regarding when a diagnosis of dementia should be disclosed. *BMC health services research*, *18*(1), 1-9.

Weng, W., Liang, J., Xue, J., Zhu, T., Jiang, Y., Wang, J., & Chen, S. (2019). The transfer effects of cognitive training on working memory among Chinese older adults with mild cognitive impairment: a randomized controlled trial. *Frontiers in aging neuroscience*, *11*, 212.

Whalley, L. J., Deary, I. J., Appleton, C. L., & Starr, J. M. (2004). Cognitive reserve and the neurobiology of cognitive aging. *Ageing research reviews*, *3*(4), 369-382.

Whoqol Group. (1995). The World Health Organization quality of life assessment (WHOQOL): position paper from the World Health Organization. *Social science & medicine*, *41*(10), 1403-1409.

Whoqol Group. (1998). Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychological medicine*, *28*(3), 551-558.

Williams, L. S., Weinberger, M., Harris, L. E., Clark, D. O., & Biller, J. (1999). Development of a stroke-specific QoL scale. *Stroke*, *30*(7), 1362-1369.

Williams, O. E., Elghenzai, S., Subbe, C., Wyatt, J. C., & Williams, J. (2017). The use of telemedicine to enhance secondary care: some lessons from the front line. *Future healthcare journal*, *4*(2), 109.

Williams, P. G., Tinajero, R., & Suchy, Y. (2017). Executive functioning and health. *Oxford Handbooks Online*.

Wilson, B. A., Winegardner, J., van Heugten, C. M., & Ownsworth, T. (Eds.). (2017). *Neuropsychological rehabilitation: The international handbook*. Psychology Press.

Wilson, R. C., Shenhav, A., Straccia, M., & Cohen, J. D. (2019). The eighty five percent rule for optimal learning. *Nature communications*, *10*(1), 1-9.

Winblad, B, Palmer, K, Kivipelto. Mild cognitive impairment--beyond controversies, towards a consensus: report of the international working group on mild cognitive impairment. J Intern Med. 2004;256(3):240–246.

Wolters, F. J., & Ikram, M. A. (2018). Epidemiology of dementia: the burden on society, the challenges for research. In *Biomarkers for Alzheimer's Disease Drug Development* (pp. 3-14). Humana Press, New York, NY.

Woodworth, R. S., & Thorndike, E. L. (1901). The influence of improvement in one mental function upon the efficiency of other functions.(I). *Psychological review*, *8*(3), 247.

World Health Organisation (2019) *Global Health Estimates: Life expectancy and leading causes of death and disability*.

https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates

World Health Organisation (2020) *GHE: Life expectancy and healthy life expectancy*. https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-life-expectancy-and-healthy-life-expectancy#:~:text=Globally%2C%20life%20expectancy%20has%20increased,reduced%20years%20lived%20with%20disability.

World Health Organization. (1978). *International classification of procedures in medicine* (Vol. 1). World Health Organization.

World Health Organization. (2008). "Social participation." Retrieved May 23 2021 from https://www.who.int/social_determinants/thecommission/countrywork/within/socialparticipation/en/

World Health Organization. (2021). *Rehabilitation*. https://www.who.int/news-room/fact-sheets/detail/rehabilitation/

Yates, J. A., Clare, L., & Woods, R. T. (2017). “You’ve got a friend in me”: can social networks mediate the relationship between mood and MCI?. *BMC geriatrics*, *17*(1), 1-7.

Zangwill, O. L. (1947). Psychological aspects of rehabilitation in cases of brain injury. *British Journal of Psychology, 37*(2), 60.

Zatorre, R. J., Fields, R. D., & Johansen-Berg, H. (2012). Plasticity in gray and white: neuroimaging changes in brain structure during learning. *Nature neuroscience*, *15*(4), 528-536.

Zboralski1ABCD, K., Florkowski1G, A., Talarowska-Bogusz1BCDE, M., Macander2B, M., & Gałecki1F, P. (2008). Quality of life and emotional functioning in selected psychosomatic diseases Jakość życia i funkcjonowanie emocjonalne w wybranych schorzeniach psychosomatycznych. *Postepy Hig Med Dosw.(online)*, *62*, 36-41.

Zhang, H., Huntley, J., Bhome, R., Holmes, B., Cahill, J., Gould, R. L., ... & Howard, R. (2019). Effect of computerised cognitive training on cognitive outcomes in mild cognitive impairment: a systematic review and meta-analysis. *BMJ open*, *9*(8), e027062.

Zygouris, S., Ntovas, K., Giakoumis, D., Votis, K., Doumpoulakis, S., Segkouli, S., ... & Tsolaki, M. (2017). A preliminary study on the feasibility of using a virtual reality cognitive training application for remote detection of mild cognitive impairment. *Journal of Alzheimer's Disease*, *56*(2), 619-627.

# Appendix A

## Data Sharing Agreement

Data Sharing Agreement

This agreement has been set up to share data between the University of Cambridge MRC Cognition and Brain Sciences Unit (Polly Peers, Fionnuala Murphy and Tom Manly) and University of East Anglia (Fergus Gracey and Grant Chai).

Researchers from the MRC Cognition and Brain Sciences Unit have agreed to make available a fully anonymised dataset arising from the study "Progressive home-based Working Memory and Attention Training following Stroke; implications for spatial bias: A preliminary Study." (Cambridge NRES ref 14/EE/0149) for the purposes of a particular analysis relating to the effects of executive functioning, and patient/carer insight on everyday functioning in stroke patients that will be completed by Grant Chai as part of his Clinical Psychology Doctoral Research thesis. In accepting the dataset, Grant Chai and Fergus Gracey agree to

- Keep the data securely and not distribute the data further without new explicit permission from MRC CBU researchers
- Make no attempt to re-identify participants
- Make the MRC CBU researchers aware of any errors in the data
- If new variables are created (e.g. by calculation from existing scores) the UEA researchers will return a fully annotated version of the revised dataset to the MRC CBU with sufficient explanation of how the new variables were defined.
- Consult with MRC CBU researchers before submission of any manuscript, including whether a condition of submission is making data open.
- Include CBU researchers on any publication arising from the analysis

| | | |
|---|---|---|
| Polly Peers<br>(on behalf of the MRC-CBU) | Fergus Gracey<br>(UEA)<br>24/7/2020 | Grant Chai<br>(UEA)<br>24/07/2020 |

Medical Research Council Cognition and Brain Sciences Unit
University of Cambridge, 15 Chaucer Road, Cambridge CB2 7EF
www.mrc-cbu.cam.ac.uk

# Appendix B

## Instructions for submission to Neuroscience & Biobehavioral Reviews

### Submission checklist

You can use this list to carry out a final check of your submission before you send it to the journal for review. Please check the relevant section in this Guide for Authors for more details.

**Ensure that the following items are present:**

One author has been designated as the corresponding author with contact details:

• E-mail address

• Full postal address

All necessary files have been uploaded:

*Manuscript*:

• Include keywords

• All figures (include relevant captions)

• All tables (including titles, description, footnotes)

• Ensure all figure and table citations in the text match the files provided

• Indicate clearly if color should be used for any figures in print

*Graphical Abstracts / Highlights files* (where applicable)

*Supplemental files* (where applicable)

Further considerations

• Manuscript has been 'spell checked' and 'grammar checked'

• All references mentioned in the Reference List are cited in the text, and vice versa

• Permission has been obtained for use of copyrighted material from other sources (including the Internet)

• A competing interests statement is provided, even if the authors have no competing interests to declare

• Journal policies detailed in this guide have been reviewed

• Referee suggestions and contact details provided, based on journal requirements

**Article Structure**

**General**: Manuscripts must be typewritten, double-spaced with wide margins on one side. The corresponding author should be identified (include a Fax number and E-mail address), and full postal addresses must be given for all co-authors. Authors should consult a recent issue of the journal for style if possible, and the Editors reserve the right to adjust style to certain standards of uniformity.

**Paper length**: The Editors insist upon clear, concise statement of facts and conclusions; fragmentation of material into numerous short reports is discouraged.

**Abstracts**: Each paper submitted must be accompanied by an abstract, which must not exceed 170 words and must be suitable for use by abstracting journals. A list of 3-12 (or more) words or short phrases suitable for indexing terms should be typed at the bottom of the abstract page accompanying the manuscript. These terms will be printed with the paper at the end of the abstract. Abstracts should be prepared as follows: MYERS, R.D., C. Melchior and C.Gisolfi. Feeding and body temperature: Changes produced by excess calcium ions...NEUROSCI BIOBEHAV REV 21(1) XXX-XXX, 1998.- Marked differences in extent of diffusion have been...

**Text**: Follow this order when typing manuscripts: Title, Authors, Affiliations, Abstract, Keywords, Main text, Acknowledgements, Appendix, References, Figure Captions and then Tables. Do not import the Figures or Tables into your text. The corresponding author should be identified with an asterisk and footnote. Text footnotes should not be used: the material should be incorporated into the text.

**Drugs**: Proprietary (trademarked) names should be capitalized. The chemical name should precede the trade, popular name, or abbreviation of a drug the first time it occurs.

**Anesthesia**: In describing surgical procedures on animals, the type and dosage of the anesthetic agent should be specified. Curarizing agents are not anesthetics; if these were used; evidence must be provided that anesthesia of suitable grade and duration was employed.

**Units and abbreviations**: All dimensions and measurement must be specified in the metric system. Standard nomenclature, abbreviations and symbols, as specified by Royal Society Conference of Editors. Metrification in scientific journals, Am. Scient. 56:159-164; 1968, should be used throughout.

**Formulas and equations**: Structural chemical formulas, process flow-diagrams, and complicated mathematical expressions should be kept to a minimum. All subscripts, superscripts, Greek letters and unusual characters must be clearly identified.

***Subdivision - numbered sections***

Divide your article into clearly defined and numbered sections. Subsections should be numbered 1.1 (then 1.1.1, 1.1.2, ...), 1.2, etc.

(the abstract is not included in section numbering). Use this numbering also for internal cross-referencing: do not just refer to 'the text'. Any subsection may be given a brief heading. Each heading should appear on its own separate line.

**Essential title page information**

• ***Title.*** Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible.

• ***Author names and affiliations.*** Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. You can add your name between parentheses in your own script behind the English transliteration. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author.

• ***Corresponding author.*** Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. This responsibility includes answering any future queries about Methodology and Materials. **Ensure that the e-mail address is given and that contact details are kept up to date by the corresponding author.**

• ***Present/permanent address.*** If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the work must be retained as the main, affiliation address. Superscript Arabic numerals are used for such footnotes.

**Highlights**

Highlights are mandatory for this journal as they help increase the discoverability of your article via search engines. They consist of a short collection of bullet points that capture the novel results of your research as well as new methods that were used during the study (if any). Please have a look at the examples here: example Highlights. Highlights should be submitted in a separate editable file in the online submission system. Please use 'Highlights' in the file name and include 3 to 5 bullet points (maximum 85 characters, including spaces, per bullet point).

***Graphical abstract***

Although a graphical abstract is optional, its use is encouraged as it draws more attention to the online article. The graphical abstract should summarize the contents of the article in a concise, pictorial form designed to capture the attention of a wide readership.

Graphical abstracts should be submitted as a separate file in the online submission system. Image size: Please provide an image with a minimum of 531 × 1328 pixels (h × w) or proportionally more. The image should be readable at a size of 5 × 13 cm using a regular screen resolution of 96 dpi. Preferred file types: TIFF, EPS, PDF or MS Office files. You can view Example Graphical Abstracts on our information site.

Authors can make use of Elsevier's Illustration Services to ensure the best presentation of their images and in accordance with all technical requirements.

***Formatting of funding sources***

List funding sources in this standard way to facilitate compliance to funder's requirements:

Funding: This work was supported by the National Institutes of Health [grant numbers xxxx, yyyy]; the Bill & Melinda Gates

Foundation, Seattle, WA [grant number zzzz]; and the United States Institutes of Peace [grant number aaaa].

It is not necessary to include detailed descriptions on the program or type of grants and awards. When funding is from a block grant or other resources available to a university, college, or other research institution, submit the name of the institute or organization that provided the funding.

If no funding has been provided for the research, please include the following sentence:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

***Footnotes***

Footnotes should be used sparingly. Number them consecutively throughout the article. Many word processors can build footnotes into the text, and this feature may be used. Otherwise, please indicate the position of footnotes in the text and list the footnotes themselves separately at the end of the article. Do not include footnotes in the Reference list.

**Artwork**

***Electronic artwork***

*General points*

• Make sure you use uniform lettering and sizing of your original artwork.

• Embed the used fonts if the application provides that option.

• Aim to use the following fonts in your illustrations: Arial, Courier, Times New Roman, Symbol, or use fonts that look similar.

• Number the illustrations according to their sequence in the text.

• Use a logical naming convention for your artwork files.

• Provide captions to illustrations separately.

• Size the illustrations close to the desired dimensions of the published version.

• Submit each illustration as a separate file.

• Ensure that color images are accessible to all, including those with impaired color vision.

A detailed guide on electronic artwork is available.

**You are urged to visit this site; some excerpts from the detailed information are given here.**

*Formats*

If your electronic artwork is created in a Microsoft Office application

(Word, PowerPoint, Excel) then please supply 'as is' in the native document format.

Regardless of the application used other than Microsoft Office, when your electronic artwork is finalized, please 'Save as' or convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):

EPS (or PDF): Vector drawings, embed all used fonts.

TIFF (or JPEG): Color or grayscale photographs (halftones), keep to a minimum of 300 dpi.

TIFF (or JPEG): Bitmapped (pure black & white pixels) line drawings, keep to a minimum of 1000 dpi.

TIFF (or JPEG): Combinations bitmapped line/half-tone (color or grayscale), keep to a minimum of 500 dpi.

**Please do not:**

• Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); these typically have a low number of pixels and limited set of colors;

• Supply files that are too low in resolution;

• Submit graphics that are disproportionately large for the content.

***Color artwork***

Please make sure that artwork files are in an acceptable format (TIFF (or JPEG), EPS (or PDF) or MS Office files) and with the correct resolution. If, together with your accepted article, you submit usable color figures then Elsevier will ensure, at no additional charge, that these figures will appear in color online (e.g., ScienceDirect and other sites) in addition to color reproduction in print. Further information on the preparation of electronic artwork.

***Figure captions***

Ensure that each illustration has a caption. Supply captions separately, not attached to the figure. A caption should comprise a brief title (**not** on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used.

**Tables**

Please submit tables as editable text and not as images. Tables can be placed either next to the relevant text in the article, or on separate page(s) at the end. Number tables consecutively in accordance with their appearance in the text and place any table notes below the table body. Be sparing in the use of tables and ensure that the data presented in them do not duplicate results described elsewhere in the article. Please avoid using vertical rules and shading in table cells.

**References**

***Citation in text***

Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.

***Reference links***

Increased discoverability of research and high quality peer review are ensured by online links to the sources cited. In order to allow us to create links to abstracting and indexing services, such as Scopus, CrossRef and PubMed, please ensure that data provided in the references are correct. Please note that incorrect surnames, journal/book titles, publication year and pagination may prevent link creation. When copying references, please be careful as they may already contain errors. Use of the DOI is highly encouraged.

A DOI is guaranteed never to change, so you can use it as a permanent link to any electronic article. An example of a citation using DOI for an article not yet in an issue is: VanDecar J.C., Russo R.M., James D.E., Ambeh W.B., Franke M. (2003). Aseismic continuation of the Lesser Antilles slab beneath northeastern Venezuela. Journal of Geophysical Research, https://doi.org/10.1029/2001JB000884. Please note the format of such citations should be in the same style as all other references in the paper.

***Web references***

As a minimum, the full URL should be given and the date when the reference was last accessed. Any further information, if known (DOI, author names, dates, reference to a source publication, etc.), should also be given. Web references can be listed separately (e.g., after the reference list) under a different heading if desired, or can be included in the reference list.

***Data references***

This journal encourages you to cite underlying or relevant datasets in your manuscript by citing them in your text and including a data reference in your Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and global persistent identifier. Add [dataset] immediately before the reference so we can properly identify it as a data reference. The [dataset] identifier will not appear in your published article.

***References in a special issue***

Please ensure that the words 'this issue' are added to any references in the list (and any citations in the text) to other articles in the same Special Issue.

***Reference management software***

Most Elsevier journals have their reference template available in many of the most popular reference management software products. These include all products that support Citation Style Language styles, such as Mendeley. Using citation plug-ins from these products, authors only need to select the appropriate journal template when preparing their article, after which citations and bibliographies will be automatically formatted in the journal's style. If no template is yet available for this journal, please follow the format of the sample references and citations as shown in this Guide. If you use reference management software, please ensure that you remove all field codes before submitting the electronic manuscript. More information on how to remove field codes from different reference management software.

Users of Mendeley Desktop can easily install the reference style for this journal by clicking the following link:

http://open.mendeley.com/use-citation-style/neuroscience-and-biobehavioral-reviews

When preparing your manuscript, you will then be able to select this style using the Mendeley plug-ins for Microsoft Word or LibreOffice.

***Reference formatting***

There are no strict requirements on reference formatting at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/book title, chapter title/article title, year of publication, volume number/book chapter and the article number or pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct. If you do wish to format the references yourself they should be arranged according to the following examples:

***Reference style***

*Text:* All citations in the text should refer to:

1. *Single author:* the author's name (without initials, unless there is ambiguity) and the year of publication;

2. *Two authors:* both authors' names and the year of publication;

3. *Three or more authors:* first author's name followed by 'et al.' and the year of publication.

Citations may be made directly (or parenthetically). Groups of references can be listed either first alphabetically, then chronologically, or vice versa.

Examples: 'as demonstrated (Allan, 2000a, 2000b, 1999; Allan and Jones, 1999).... Or, as demonstrated (Jones, 1999; Allan, 2000)... Kramer et al. (2010) have recently shown ...'

*List:* References should be arranged first alphabetically and then further sorted chronologically if necessary. More than one reference from the same author(s) in the same year must be identified by the letters 'a', 'b', 'c', etc., placed after the year of publication.

*Examples:*

Reference to a journal publication:

Van der Geer, J., Hanraads, J.A.J., Lupton, R.A., 2010. The art of writing a scientific article. J. Sci. Commun. 163, 51–59. https://doi.org/10.1016/j.Sc.2010.00372.

Reference to a journal publication with an article number:

Van der Geer, J., Hanraads, J.A.J., Lupton, R.A., 2018. The art of writing a scientific article. Heliyon. 19, e00205. https://doi.org/10.1016/j.heliyon.2018.e00205.

Reference to a book:

Strunk Jr., W., White, E.B., 2000. The Elements of Style, fourth ed. Longman, New York.

Reference to a chapter in an edited book:

Mettam, G.R., Adams, L.B., 2009. How to prepare an electronic version of your article, in: Jones, B.S., Smith , R.Z. (Eds.), Introduction to the Electronic Age. E-Publishing Inc., New York, pp. 281–304.

Reference to a website:

Cancer Research UK, 1975. Cancer statistics reports for the UK. http://www.cancerresearchuk.org/aboutcancer/statistics/cancerstatsreport/ (accessed 13 March 2003).

Reference to a dataset:

[dataset] Oguro, M., Imahiro, S., Saito, S., Nakashizuka, T., 2015. Mortality data for Japanese oak wilt disease and surrounding forest compositions. Mendeley Data, v1. https://doi.org/10.17632/xwj98nb39r.1.

Reference to software:

Coon, E., Berndt, M., Jan, A., Svyatsky, D., Atchley, A., Kikinzon, E., Harp, D., Manzini, G., Shelef, E., Lipnikov, K., Garimella, R., Xu, C., Moulton, D., Karra, S., Painter, S., Jafarov, E., & Molins, S., 2020. Advanced Terrestrial Simulator (ATS) v0.88 (Version 0.88). Zenodo. https://doi.org/10.5281/zenodo.3727209.

***Journal abbreviations source***

Journal names should be abbreviated according to the List of Title Word Abbreviations.

**Video**

Elsevier accepts video material and animation sequences to support and enhance your scientific research. Authors who have video or animation files that they wish to submit with their article are strongly encouraged to include links to these within the body of the article. This can be done in the same way as a figure or table by referring to the video or animation content and noting in the body text where it should be placed. All submitted files should be properly labeled so that they directly relate to the video file's content. In order to ensure that your video or animation material is directly usable, please provide the file in one of our recommended file formats with a preferred maximum size of 150 MB per file, 1 GB in total. Video and animation files supplied will be published online in the electronic version of your article in Elsevier Web products, including ScienceDirect. Please supply 'stills' with your files: you can choose any frame from the video or animation or make a separate image. These will be used instead of standard icons and will personalize the link to your video data. For more detailed instructions please visit our video instruction pages. Note: since video and animation cannot be embedded in the print version of the journal, please provide text for both the electronic and the print version for the portions of the article that refer to this content.

**Data visualization**

Include interactive data visualizations in your publication and let your readers interact and engage more closely with your research. Follow the instructions here to find out about available data visualization options and how to include them with your article.

**Supplementary material**

Supplementary material such as applications, images and sound clips, can be published with your article to enhance it. Submitted supplementary items are published exactly as they are received (Excel or PowerPoint files will appear as such online). Please submit your material together with the article and supply a concise, descriptive caption for each supplementary file. If you wish to make changes to supplementary material during any stage of the process, please make sure to provide an updated file. Do not annotate any corrections on a previous version. Please switch off the 'Track Changes' option in Microsoft Office files as these will appear in the published version.

**Research data**

This journal encourages and enables you to share data that supports your research publication where appropriate, and enables you to interlink the data with your published articles. Research data refers to the results of observations or experimentation that validate research findings. To facilitate reproducibility and data reuse, this journal also encourages you to share your software, code, models, algorithms, protocols, methods and other useful materials related to the project.

Below are a number of ways in which you can associate data with your article or make a statement about the availability of your data when submitting your manuscript. If you are sharing data in one of these ways, you are encouraged to cite the data in your manuscript and reference list. Please refer to the "References" section for more information about data citation. For more information on depositing, sharing and using research data and other relevant research materials, visit the research data page.

***Data linking***

If you have made your research data available in a data repository, you can link your article directly to the dataset. Elsevier collaborates with a number of repositories to link articles on ScienceDirect with relevant repositories, giving readers access to underlying data that gives them a better understanding of the research described.

There are different ways to link your datasets to your article. When available, you can directly link your dataset to your article by providing the relevant information in the submission system. For more information, visit the database linking page.

For supported data repositories a repository banner will automatically appear next to your published article on ScienceDirect.

In addition, you can link to relevant data or entities through identifiers within the text of your manuscript, using the following format: Database: xxxx (e.g., TAIR: AT1G01020; CCDC: 734053; PDB: 1XFN).

***Mendeley Data***

This journal supports Mendeley Data, enabling you to deposit any research data (including raw and processed data, video, code, software, algorithms, protocols, and methods) associated with your manuscript in a free-to-use, open access repository. During the submission process, after uploading your manuscript, you will have the opportunity to upload your relevant datasets directly to *Mendeley Data*. The datasets will be listed and directly accessible to readers next to your published article online.

For more information, visit the Mendeley Data for journals page.

***Data statement***

To foster transparency, we encourage you to state the availability of your data in your submission. This may be a requirement of your funding body or institution. If your data is unavailable to access or unsuitable to post, you will have the opportunity to indicate why during the submission process, for example by stating that the research data is confidential. The statement will appear with your published article on ScienceDirect. For more information, visit the Data Statement page.

# Appendix C

## Instructions for Submission for Journal of the International Neuropsychological Society

**Manuscript Length**

In order to increase the number of manuscripts that can be published in the *Journal of the International Neuropsychological Society*, please adhere to the following length requirements. Please provide a word count on the title page for the abstract and manuscript (not including abstract, tables, figures, or references). Manuscripts will be returned if they exceed length requirements.

**Regular Research Article:** Maximum of 5,000 words (not including abstract, tables, figures, or references) and a 250 word abstract. Regular Research Articles are original, creative, high quality papers covering all areas of neuropsychology; focus may be experimental, applied or clinical.

**Manuscript Preparation and Style**

The entire manuscript should be typed double-spaced throughout using a word processing program. Unless otherwise specified, the guideline for preparation of manuscripts is the *Publication Manual of the American Psychological Association*

*(6th edition)* except for references with 3 or more authors (see References section). This manual may be ordered from: APA Order Dept., 750 1st St. NE, Washington, DC 20002-4242, USA.

Pages should be numbered sequentially beginning with the Title Page. The Title Page should contain the full title of the manuscript, the full names and institutional affiliations of all authors; mailing address, telephone and fax numbers, and e-mail address for the corresponding author; and the word count for the abstract and manuscript text (excluding title page, abstract, references, tables, and figures). At the top right provide a short title of up to 45 characters preceded by the lead author's last name. Example: Smith-Memory in Parkinson's Disease. This running head should be repeated at the top right of every following page.

Page 2 should include an Abstract and a list of at least six keywords or mesh terms. Note: structured abstracts must be included with papers submitted after January 1, 2014. A structured abstract must include four header labels: Objective, Method, Results, and Conclusions. A total of six mesh terms (http://www.nlm.nih.gov.uea.idm.oclc.org/mesh/) or keywords should be provided and should not duplicate words in the title.

The full text of the manuscript should begin on page 3. For scientific articles, including *Regular Research Articles, Brief Communications, Rapid Communications,* and *Symposia*, the format should include a structured Abstract, Introduction, Method, Results, and Discussion. This should be followed by Acknowledgments, References, Tables, Figure Legends, Figures, and optional Appendices and Supplemental Material.

The use of abbreviations, except those that are widely used, is strongly discouraged. They should be used only if they contribute to better comprehension of the manuscript. Acronyms should be spelled out at first mention. Metric system (SI) units should be used.

Appendices and Supplemental Materials may be submitted. Appendices include material intended for print and should be included with the manuscript file. Supplementary material will appear only online and should be submitted as a separate file. Supplementary material is replicated as-is.

The Acknowledgements Section should include two parts: a Conflicts of Interest disclosure (see above) and a statement to disclose all Funding sources of financial support for the paper. If no Conflicts of Interest exist, you will be required to state as such

("COI: None." or a similar statement). In documenting financial support, please provide details of the sources of financial support for all authors, including grant numbers. For example, "This work was supported by the National Institutes of Health (grant number XXXXXXX)". Multiple grant numbers should be separated by a comma and space and where research was funded by more than one agency, the different agencies should be separated by a semicolon with "and" before the final funding agency. Grants held by different authors should be identified using the authors' initials. For example, "This work was supported by the Wellcome Trust (A.B., grant numbers XXXX, YYYY), (C.D., grant number ZZZZ); the Natural Environment Research Council (E.F., grant number FFFF); and the National Institutes of Health (A.B., grant number GGGG), (E.F., grant number HHHH)."

Tables and Figures should be numbered in Arabic numerals. Figures should be numbered consecutively as they appear in the text. Figures should be twice their intended final size and authors should do their best to construct figures with notation and data points of sufficient size (recommended ≥ 300 dpi) to permit legible photo reduction to one column of a two-column format. Please upload figure(s) in either a .doc, .jpeg, .tiff, or .pdf format. There is no additional cost for publishing color figures. The approximate position of each table and figure should be provided in the manuscript with call-outs: [INSERT TABLE 1 HERE]. Tables and figures should be on separate pages. Tables should have short titles and all figure legends should be on separate pages. All tables and figures must have in-text citations in order of appearance.

Figures submitted in color will appear online in color, but all figures will be printed in black and white unless authors specify during submission that figures should be printed in color, for which there may be a fee. There is no additional cost for publishing color figures in the print version of the journal for corresponding authors who are INS members. For non-members, the cost for publishing color figures in print version of the journal will be $320 per figure with a cap of $1600 per article.

References should be consistent with the *Publication Manual of the American Psychological Association (6th Edition)*. In-text references should be cited as follows: "...Given the critical role of the prefrontal cortex (PFC) in working memory (Cohen et al., 1997; Goldman-Rakic, 1987; Perlstein et al., 2003a, 2003b)..." with multiple references in alphabetical order. Another example: "...Cohen et al. (1994, 1997), Braver et al. (1997), and Jonides and Smith (1997) demonstrated..."

References cited in the text with two authors should list both names. References cited in the text with three, four, or five authors, list all authors at first mention; with subsequent citations include only the first author's last name followed by et al. References cited in the text with six or more authors should list the first author et al. throughout. In the reference section, for works with up to seven authors, list all authors. For eight authors or more, list the first six, then ellipses followed by the last author's name. Examples of the APA reference style are as follows:

**Online/Electronic Journal Article with DOI:** Dikmen, S., Machamer, J., Fann, J. & Temkin, N. (2010). Rates of symptom reporting following traumatic brain injury. *Journal of the International Neuropsychological Society*, 16, 401-411. doi:10.1017/S1355617710000196

**Scientific Article:** Giovannetti, T., Britnell, P., Brennan, l., Siderowf, A., Grossman, M., Libon, D.J., Seidel, G.A. (2012).

Everyday action impairment in Parkinson's disease dementia. *Journal of the International Neuropsychological Society*, 18, 787-798.

**Book**: Lezak, M.D., Howieson, D.B., Bigler, E.D., Tranel, D. (2012). *Neuropsychological Assessment*. New York: Oxford University Press.

**Book Chapter:** Mahone, E.M. & Slomine, B.S. (2008). Neurodevelopmental disorders. In J.E.Morgan, & J.H. Ricker (Eds.), *Textbook of Clinical Neuropsychology* (pp. 105-127). New York:Taylor & Francis.

**Report at a Scientific Meeting:** Weintraub, S. (2012, June). Profiles of dementia: Neuropsychological, neuroanatomical and neuropathologic phenotypes. International Neuropsychological Society, Oslo, Norway.

**Manual, Diagnostic Scheme, etc.**: American Psychiatric Association (1994). *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.). Washington, DC: American Psychiatric Association Press.