SCREENING OF COGNITIVE FUNCTIONS:
ANALYSIS AND DEVELOPMENT OF NEUROPSYCHOLOGICAL TEST INSTRUMENTS

by

SAHEEDA BEBE MOHAMED-KALEEL

A thesis submitted to the University of Birmingham for the degree of

DOCTOR OF PHILOSOPHY

School of Psychology
College of Life and Environmental Sciences
University of Birmingham
April 2016

ABSTRACT

INTRODUCTION: Cognitive impairments are common after stroke, particularly those involving the executive functioning, which is a complex cognitive construct encompassing a collection of interrelated functions (or set of processes) that are responsible for controlled goal-directed behaviours to novel or complex situations (Gioa, Isquith, & Guy, 2001). Therefore, deficits in executive processes can affect an individual profoundly. There are numerous executive measures currently available, however they are mostly language-laden, and therefore not ideal for stroke patients who are present with aphasia and neglect. Accordingly, in this thesis we aimed to develop unbiased measures of planning/organisation (the 'systematicity' index) using performance-based, language reduced, nonverbal tasks that are suitable for use in a stroke population. **METHOD:** Initially, we examined the cognitive variation in stroke profile, across various stages, using the Birmingham Cognitive Screen (BCoS: Humphreys, Bickerton, Samson, & Riddoch, 2012). Subsequently, we developed three novel scoring measures, on two key tests: 1) the Broken Hearts test (from the Oxford Cognitive Screen (OCS): Demeyere, Riddoch, Slavkova, Bickerton, & Humphreys, 2015) and 2) the Complex Figure test (from the BCoS/OCS). **RESULTS:** Measures include: 1) The 'Nearest Neighbour' measure – validated against the subjective ratings provided by experienced neuropsychologists (of how systematic a patient is during cancellation) and a measure of executive function (EF); 2) the 'Global-Local Scoring System' – a qualitative scoring system that provides an index of executive measure for the BCoS Complex Figure which was validated against subjective ratings from experienced neuropsychologists and other measures of EF; 3) the 'automated Global-Local Scoring System' – validated against the 'Nearest Neighbour' measure on the overall cancellation performance. **CONCLUSION:**

We conclude that these measures would be beneficial to clinicians in terms of measuring planning/organisation abilities of stroke survivors and freeing them from time consuming and tedious tasks.

“To my late father, A. S. Mohamed-Kaleel, and to my mother, Siththi Saleema,

succumbed in his memories.”

Main supervisor Prof. Glyn W. Humphreys

(Department of Experimental Psychology, Oxford University)

Co-supervisor Dr. Christopher A. Jones

(School of Psychology, University of Birmingham)

Birmingham Cognitive Screen (BCoS)

Project Title	“Birmingham University Cognitive Screen”
Grant Reference	
Grant Recipients	Prof. Glyn W. Humphreys, Prof. M. Jane Riddoch, Dr. Dana Samson

Oxford Cognitive Screen (OCS)

Project Title	“Improving diagnosis and treatment of cognitive problems after stroke”
Grant Reference	RP-DG-0610-10046 (NIHR)
	TSA LECT 2015/02 (Stroke association, UK)
Grant Recipients	Prof. Glyn W. Humphreys

The studies described in this thesis were derived from two United Kingdom (UK) cognitive trials, the Birmingham Cognitive Screen (BCoS) and the Oxford Cognitive Screen (OCS). The BCoS trial and the OCS trial were supported by the Stroke Association and the National Institute of Health Research (NIHR), UK.

Both trials were multi-centre research projects where the data from healthy controls as well as survivors of brain injury are collected as a team, in a pool of data, to be used for individual studies, accordingly. The BCoS data analysed in this thesis were collected by trained examiners from the University of Birmingham and the West Midlands Research Network from several stroke units across the West Midlands, England. The OCS patient data analysed in this thesis were collected by trained examiners from the University of Oxford from the acute stroke unit at the John Radcliffe Hospital, Oxford and chronic stroke patients from the patient panel from CNC lab, Oxford University.

The Doctoral researcher: organised and participated in data collection for the OCS trial healthy controls and stroke patients (acute patients from Moseley Hall Hospital, access granted through an NHS research passport, and chronic patients from the patient panel, University of Birmingham for OCS piloting). In addition, organised and prepared the data used, planned and analysed the data, drafted and revised the content for each chapter. Individual contributions to this thesis are stated in the acknowledgment.

ACKNOWLEDGMENT

This thesis was developed out of a series of studies as part of two large cognitive trials, BCoS and OCS, which involved multi-disciplinary collaborations and different level of teamwork in the research as well as the clinical environment, and I am grateful to be part of these cognitive trials and for the opportunity to grow as a person and deliver a novel contribution to the literature.

First and foremost, I would like to express my warmth and respect to all the stroke survivors and healthy controls that participated in the project and, especially, stroke survivors who willingly shared of their experiences at a difficult period in their lives, without them the studies would be impossible.

Secondly, I would like to express my sincere gratitude towards both the psychologists who acted as expert subjective raters and to the Doctoral researcher who acted as the second examiner for my studies. Being able to see your own test design through different lenses, it was a pleasure.

Thirdly, BCoS and OCS are testing tools that involved a team of individuals who helped the development of the tool through designing, creating materials and in collecting data from healthy controls as well as survivors of brain injury. For the opportunity given to carry out my studies using these trials, you all deserve my sincere gratitude: **BCoS contributors:** Wai-Ling Bickerton, Dana Samson, M. Jane. Riddoch, Glyn W. Humphreys, and **OCS contributors:** Nele Demeyere, M. Jane Riddoch, Elitsa D. Slavkova, Mihaela Duta and Glyn W. Humphreys.

Here, I would like to include a special thanks to everyone else who have been involved in the data collection for both trials. Some of you, I have met during several data recruitment events (for the OCS trial) and others, it was before my time as a Doctoral researcher (BCoS trial). Regardless, I am grateful for everyone who invested their time in collecting the data that has being used extensively for various studies with an aim of understanding cognitive deficits post-stroke.

Finally, my supervisors:
Dr Chris A. Jones, my co-supervisor. For introducing me to the world of psychometrics, by sharing your vast knowledge and passion for various statistical techniques, and practical advice when it came to building the bridge between research-clinical environments. For not abandoning me and guiding me through difficult times, both for me personally and for the thesis, I thank you, with all my heart. **Contribution:** editing/proofreading drafts for content, advice on statistics and study designs, and Ph.D. supervision.

Prof. Glyn W. Humphreys, my main supervisor and the Principle Investigator for BCoS & OCS. For accepting me and giving me a chance to work on these projects, regardless of my lack of knowledge in psychology as my background is Biomedical Sciences. It was not easy in the beginning, but your constant support by sharing your knowledge and broad perspective of neuropsychology in which I found the confidence to voice my opinions. **Contribution:** Principle investigator for BCoS & OCS trials, revising drafts for content**,** study concepts & designs, interpretation of data, study/ PhD co-ordination and supervision.

CONTRIBUTORS

Saheeda Bebe Mohamed-Kaleel University of Birmingham

The design of the studies, data collection, analysis and authorship of all the content contained within this thesis.

Dr. Christopher A. Jones University of Birmingham

(Chapter 2, Chapter 3, Chapter 4, Chapter 5, Chapter 6)

Editing/proof reading drafts for content, advice on statistics and study designs, and PhD supervision.

Prof. Glyn W. Humphreys Oxford University

(Chapter 2, Chapter 3, Chapter 4, Chapter 5, Chapter 6)

Principle investigator for BCoS & OCS trials, revising drafts for content, study concepts & designs, interpretation of data, study/ PhD co-ordination and supervision.

BCoS TEAM

Dr. Wai-Ling Bickerton University of Birmingham

(Chapter 2, Chapter 3, Chapter 5)

Dr. Dana Samson Université de Louvain-la-Neuve

(Chapter 2, Chapter 3, Chapter 5)

Prof. M. Jane. Riddoch Oxford University

(Chapter 2, Chapter 3, Chapter 4, Chapter 5, Chapter 6)

The team of individuals who helped the development of the BCoS screen through designing, creating materials and in collecting data from healthy controls as well as survivors of brain injury.

OCS TEAM

Dr. Nele Demeyere Oxford University

(Chapter 4, Chapter 6)

Elitsa D. Slavkova Oxford University

(Chapter 4, Chapter 6)

Dr. Mihaela Duta Oxford University

(Chapter 4, Chapter 6)

Prof. M. Jane. Riddoch Oxford University

The team of individuals who helped the development of the OCS screen through designing, creating materials and in collecting data from healthy controls as well as survivors of brain injury.

TABLE OF CONTENTS

TABLE OF CONTENTS (CONTINUED)

Page

PART 2

LIST OF FIGURES

Page

CHAPTER 2

CHAPTER 3

CHAPTER 4

CHAPTER 5

CHAPTER 6

LIST OF TABLES

Page

CHAPTER 2

CHAPTER 3

LIST OF TABLES (CONTINUED)

Page

CHAPTER 4

CHAPTER 5

CHAPTER 6

APPENDIX A

APPENDIX B

CHAPTER 1

GENERAL INTRODUCTION

Neuropsychology can be defined as the study of the brain-behaviour relationship. As it is an experimental science, it bridges the disciplines of, most notably, neurology, psychology, and, even, psychiatry in a quest to understand and explain the relationship between the complex properties of the brain, most notably; the relationship between brain structure and cognition, behaviour and affect.

The origin and development of neuropsychology are long and distinguished. In Western culture, it is traced to Hippocrates (460-377 B.C), a Greek Physician, who asserted that the brain, was the organ of intellect. The modern form of the discipline was first observed in the work of work of Paul Broca (1824-1880), Carl Wernicke (1848-1904) and Hughlings Jackson (1835-1911) in the mid 19th century. These physicians examined the onset of different types of speech and language impairments and discovered that they were associated with damage to different areas within the left hemisphere of the brain. These discoveries spur the interest in the 'localisation of function', that is that different regions of the brain are involved in specific and separate aspects of higher cognitive function and, that complex behaviour results from the fractionation of cognitive functioning across geographically distinct regions of the brain.

Cognition

In the literature regarding the functional organisation of the brain, an enduring distinction has been made between the functions of the posterior and anterior neocortex (Lezak, 1982; Luria, 1973). Luria described the posterior neocortex as obtaining, processing and storing information derived from sensory stimulation, whereas the anterior cortex is involved in the programming, monitoring and regulation of mental activity. Accordingly, the posterior cortex became identified with ‘associative processing’ and the anterior neocortex became identified with ‘executive processing’. Although it is now known that a strict anatomical division between associative and executive functioning cannot be maintained, the functional and anatomical distinction between associative perceptual, memorial and learning systems and the executive, control and monitoring systems has exerted considerable influence on neuropsychological models of cognitive functioning. For example, Baddeley’s model of working memory (Baddeley, 1996, 2000) and Norman and Shallice’s (1986) model of attentional control, both make clear distinctions between anatomically unique associative and executive components. In such models, the associative functions are typically depicted as relatively automatic, stimulus-driven processes that act on either modular or inter-modular sensory/perceptual information. In contrast, the executive systems are depicted as controlled processes, commonly used in novel and or complex situations (i.e., when there is not a well-established stimulus-response association) involving multi-modular cognitive, sensory or perceptual information, to achieve and maintain goal-directed behaviour.

The concept of executive functioning

Executive functioning is a complex cognitive construct encompassing a collection of interrelated functions (or set of processes) that are responsible for controlled goal-directed behaviours to novel or complex situations (Gioa, Isquith, & Guy, 2001). More specifically, it is an umbrella term, encompassing a set of higher-level cognitive processes and behavioural competencies needed when carrying out novel or complex tasks, and is inclusive of initiation of activity, inhibition of prepotent response, switching, working memory, the ability to sustain attention, planning ability, organisation, problem solving, self-regulation, utilisation of feedback, and, the adjustment of behaviour to the rapidly changing demands of the environment (Alvarez & Emory, 2006, Damasio, 1995; Diamond, 2013; Elliot, 2003; Grafman & Litvan, 1999; Shallice, 1988; Stuss & Benson, 1986). In other words, executive functions (EF) allow us to behave flexibly, rather than being stimulus-driven and resulting in stereotypical behaviours to particular events. EF equips us with the ability to adapt to a novel, challenging and/or changing, environment.

Dysfunction of executive control systems can produce a wide variety of emotional, cognitive and behavioural symptoms. Executive processes are associated with a number of complex and interrelated anterior neural systems, where the prefrontal cortex (PFC) is dependent on afferent and efferent interconnections with almost all other brain regions – including the occipital, temporal, and parietal lobes, as well as with limbic and subcortical regions (Heyder, Suchan & Daum, 2004; Stuss & Benson, 1984). Thus, dysexecutive syndromes may also be associated with damage or disconnection of the afferent and efferent interconnections to the anterior cortex (Alexander & Stuss, 2000; Lezak, 1995; Stuss et al., 2002).

Fractionation of executive function

Numerous conceptual models of EF have addressed the fractionation of EF and, also, to provide a theoretical framework for the evaluation of cognitive domains. However, to date, no specific model has been generally accepted. Some of these models have focused on the executive control of specific cognitive systems, such as working memory model (Baddeley, 1996, 2000, 2002) and supervisory attentional system (SAS: Norman & Shallice, 1986). In contrast, others have attempted to provide a comprehensive account of the fractionation of EF and their interrelationships. This approach is often based on latent variable analysis of the relationship between different tests of (purported) EF. This approach has generally supported the view of EF as multi-faceted, with sub-functions with distinct focal neural correlates (Stuss, Shallice, Alexander, & Picton, 1995). For example, Miyake et al. (2000) used a latent variable procedure to identify distinct EF components that underlie performance on a range of tasks associated with EF. These components could be described as mental set-shifting, inhibition of prepotent responses, and updating the contents of working memory.

The fractionation of EF has been supported by neuroimaging studies that have provided evidence for the multi-faceted nature of EF. The results support that different regions within the pre-frontal cortex (PFC) underlie different EF components. For example, the ability to maintain information in working memory has been found mostly in lateral PFC (Narayanan et al., 2005); switching between tasks is dependent on medial PFC (Crone, Wendelken, Donohue, & Bunge, 2005; Rushworth, Walton, Kennerley, & Bannerman, 2004); the ability to inhibit responses was found to rely on the orbitofrontal cortex (Aron, Robbins, & Poldrack, 2004; Roberts & Wallis, 2000). Indeed, EF appears as a multi-faceted construct where distinct EF components (from anatomically distinct systems) are likely to contribute in different ways to achieve a goal-directed behaviour.

Accordingly, EF can be described as a series of systems that allow the cognitive and response flexibility, attentional control, and goal oriented cognition and behaviour. A recent attempt to provide a conceptual framework for this collection of functions is provided by Anderson (2002). The model of the executive control system was proposed by Anderson (2002) based on factor analytic studies and the current knowledge of developmental neuropsychology, derived from developmental studies (Brocki & Bohlin, 2004; Kelly, 2000; Lehto, Juujärvi, Kooistra, & Pulkkinen, 2003; Levin et al., 1991; Miyake et al., 2000; O'donnell, Macgregor, Dabrowski, Oestreicher, & Romero, 1994; Welsh, Pennington, & Groisser, 1991).

This model of EF by Anderson (2002) has conceptualised EF, as an overall control system comprised of four distinct domains: attentional control, cognitive flexibility, information processing, and goal setting. These executive domains are considered functionally independent and their discrete functions are assumed to be associated with distinct anterior neural systems. However, according to the executive control system model, these independent domains with discrete functions operate in an integrative manner and have bidirectional relationships. Each domain involves highly integrated cognitive processes, and each receives and processes stimuli from various sources.

The *attentional control* domain includes selective attention that is the capacity to selectively attend to specific stimuli, while inhibiting prepotent responses and maintain attention for a prolonged period; self-regulation and monitoring for successful execution of the goal-directed behaviour according to plans. Impulse control, such as the capacity to control inappropriate responses, also plays an integral role in this domain.

The *cognitive flexibility* domain refers to the ability to sustain divided attention, allowing shift between response sets, learn from mistakes, devise alternative strategies using feedback evaluation, and process multiple sources of information concurrently to perform multiple tasks successfully. Also, in this model, working memory, the ability to process information whereby information is temporarily stored and manipulated, is considered as an element of the cognitive flexibility domain (Anderson, 2002). For such reasons, impairment in this domain is often associated individuals with inflexible behaviours that are generally considered rigid and repetitive (perseverative) behaviour; these individuals continue to make the same mistake or break the same rule, struggling to adapt to new demands.

The *information processing* domain, in this model, refer to quality (fluency), quantity (efficiency) and speed of output (Anderson, 2002). The inclusion of information processing as a separate domain is supported by factor analytic studies that have found that quality/response speed variables from EF tasks load on a separate factor (Kelly, 2000; Welsh et al., 1991) and from clinical observations of impaired day-to-day performance due to otherwise intact cognitive systems not being able to process information with sufficient speed and accuracy to accommodate the demands of everyday tasks. Impairment of the information processing domain may result in reduced output, delayed responses, hesitancy and slowed reaction times.

Finally, the *goal-setting* domain incorporates the ability to develop new initiatives and concepts, as well as the capacity to plan actions in advance and approach tasks in an efficient and strategic manner. A key aspect of this domain is its ability to plan. Related to planning ability is organisation. Organisation in this model refers to the ability to arrange complex information/ a sequence of steps in a logical, systematic, and strategic manner. The organisation has important consequences as to how efficiently and effectively goals are attained and are associated with how well information/plans are remembered and retrieved at a later stage. Impairments in this domain will result in poor problem-solving ability as reflected by incompetent planning, disorganisation, and difficulties developing effective strategies. In most cases, an individual is likely to rely on a previously learned strategy that may result in poor conceptual reasoning.

As it is clear from Anderson's description of the executive control system (Anderson 2002) executive functioning is an umbrella term, which suggests multiple interacting control functions, based upon multiple underlying neurological networks. Specific executive behaviours, such as complex problem solving, will involve the co-ordinated action of multiple executive functional networks.

Systematicity as an executive function

One area of cognitive performance that is sensitively dependent upon executive functioning is 'systematicity'. From within the Anderson (2002) model, systematicity is an organisational skill that allows complex information to be arranged in a coherent or specific manner to reach the end goal. Since, organisation is related to planning, it emphasises an individual's ability to develop goals, workout strategies and monitor performance to achieve future goals. In essence, planning, along with monitoring/regulation, initiation, inhibition and or selecting behaviours are all aspects of executive functions involved in goal-directed behaviour. Therefore, impairments in systematic organisation, such as inability to organise/ disorganisation, will result in inefficient planning leading to difficulties in developing efficient strategies to achieve the set or future goal, through goal-directed behaviour.

Disorders of systematicity: Praxis.

Apraxia is demonstrated as an inability to carry out (previously) learned and purposeful skilled movements despite the motor and sensory systems being intact (Gross & Grossman, 2008). More specifically, apraxia is generally viewed as, any motor ability problems acquired in the absence of motor impairments, such as weakness, akinesia, loss of sensory input, abnormalities of posture, or movement disorders like tremor or chorea (Heilman & Rothi, 1993).

Therefore, apraxia can be classified as a term that describes a variety of apraxic impairments involving different functions of the body as a result of a disorder of higher motor cognition; since they cannot be explained by primary sensorimotor deficits, disordered communication or lack of motivation. Fundamentally, such apraxic disorders appear when an individual is performing a goal-directed behaviour (Dovern, Fink and Weiss, 2012), and therefore, a distinguishing characteristic is the reduced ability of an individual when voluntarily performing a goal-directed behaviour (Rumiati, Papeo, & Corradi-Dell’ Acqua, 2010). In this section, we will identify those apraxia(s) associated with deficits in systematicity in respect to EF.

The classification of different apraxias is still a focus of considerable debate (Goldenberg, 2003; 2008; 2013), therefore, some of the frequently observed upper limb apraxia (UPLA) will be classified and or described according to their (clinical) core motor deficit(s) to demonstrate the importance of the particular function to the body of an individual, especially, their independence in quality of living:

i. Limb-kinetic apraxia describes inaccurate or clumsy distal limb movements. It involves deficits mainly with the loss of fine and co-ordinated movement, especially in the finger movements where the fingers are used in picking up small objects (e.g., a coin or a button on a shirt). This apraxia reflects a basic motor co-ordination deficit, rather than an apraxic disorder.

ii. Conceptual apraxia is considered as impairments in the concept of single action. It is characterised by content errors and the inability to use tools. For example, loss of knowledge for a tool, or tool-object relationship, the mechanical advantage afforded by tools (mechanical knowledge) (Leiguarda & Marsden, 2000; Ochipa, Rothi & Heilman, 1992; Petreska, Adriani, Blanke, & Billard, 2007; Rothi & Heilman, 2014). This deficit identifies more with a loss of knowledge of proper performance rather than a loss of motor function.

iii. Constructional apraxia can be depicted through an individual's inability of construction, such as difficulties in reproducing drawings or patterns and in assembling complex parts into a whole. These deficits are a result of damage to not only the dominant but also to the non-dominant hemisphere. Therefore, this apraxia appears to reflect the loss of bilaterally distributed components for organisation and planning, including visuospatial processing (Damasio, Tranel, & Rizzo, 2000; Laeng, 2006).

iv. Ideomotor apraxia (IMA) is probably one of the widely recognised subtypes of apraxia. It arises from a dissociation of the motor programming with the premotor and motor regions, and as a result, the individual affected is unable to perform skilled limb movements. IMA is typically demonstrated when an individual is given a verbal instruction to perform gestures with a specific limb and, in return, the patient exhibits either the inability to pantomime, imitate the gestures, and, sometimes, use tools properly. Here, the conceptual knowledge is still intact in the individual present with the IMA, but unable to execute the movement. Therefore, individuals with IMA are characterised by spatial and temporal errors affecting timing, sequencing and organisation of gestural movements.

v. Ideational apraxia (IA) is another subtype of apraxia that is mostly studied in scientific literature and is commonly confused with conceptual apraxia. The IA condition occurs when patients have difficulties performing a sequence of actions in a performance of a complex, multiple-step task (e.g., making tea or coffee). The condition is characterised by the distinguishing factor that the tools or objects are identifiable, along with the knowledge of performance but as a failure to sequence the task elements correctly (in the correct order and in a coherent manner) to successfully complete a goal-directed task during the use of multiple tool-object associated tasks. Along with missing the necessary steps, the patient presenting with IA may also exhibit perseveration, that is, repetition of a previously completed step. Therefore, the difficulty in sequencing actions presented in ideational apraxia may not be a direct representation of a higher-order motor programming deficit. Rather, this deficit may ascend due to a general limitation in cognitive resources or specifically, the limitation in a combination of certain cognitive domains, that is, executive, language and memory limitations that operate accordingly to perform a multi-action task (Weintraub, 2000).

The distinguishing factor of IA is the error in a goal-directed behaviour. This involves the use of multiple tool-object in a multiple-step/complex task, which is a manifestation of difficulties and or deficit of an executive component consistent with systematicity.

According to Anderson’s (2002) model of the EF system, systematicity is an organisation skill that is related to planning (see above for further details). Therefore, the content of a sequential error is due to impairments in the systematic organisation where the patient demonstrates an inability to systematically organise constituent elements during the performance of a goal-directed task, resulting in unsuccessful task completion.

The importance of assessing systematicity with respect to executive function

Dyspraxic difficulties are often associated with brain damage of vascular aetiology, especially after a left hemisphere stroke (Donkervoort, Dekker, & Deelman, 2006; Donkervoort, Dekker, Stehmann-Saris, & Deelman, 2001; Zwinkels, Geusgens, van de Sande, & van Heugten, 2004). Prevalence rates vary from 10% to 50% for IMA and IA deficits following a lesion in the left parietal and premotor cortices (Cantagallo, Maini, & Rumiati, 2012; Donkervoort et al., 2006; Donkervoort et al., 2001). Therefore, apraxia is one of the most common cognitive deficits following a stroke. It can have negative impacts on an individual’s independence in activities of daily living (ADLs: Donkervoort et al., 2001), following a stroke, due to reduced levels of patients’ self-sufficiency (Goldberg & Hagmann, 1998). These apraxic disorders not only present in clinical/research settings where it is assessed using different types of gestures (e.g., transitive vs. intransitive; meaningless vs. meaningful) under different modalities (e.g., verbal command or visual presentation), but also, in many natural, day-to-day environments (Smania, Girardi, Domenicali, Lora, & Aglioti, 2000) where individuals perform everyday routine actions (ADLs) that are required to live safely and independently at home. Hence, patients with IA tend to be profoundly disabled by their deficits in everyday life.

This is understandable since the successful performance of most ecological relevant, routine tasks (such as brushing teeth, dressing, making tea and toast) in everyday life is dependent on a substantial number of cognitive processes (Humphreys, Forde, & Riddoch 2001). These include; intact stored knowledge of routine actions and performance related to individual tools-objects with the ability to impose such knowledge on behaviour through working memory for action. Nevertheless, even, the most necessary tasks, e.g., making a tea/coffee involve many processes that operate in a relatively automatic fashion, requiring low attentional and executive resources (Norman & Shallice, 1986). As a result of left hemispheric stroke, patients can lose the ability to carry routine actions in a fluent and organised fashion jeopardising their safety and independence.

Measuring deficits in multi-action sequencing in everyday living

Considering this profound impact on functional outcome post-stroke, it may not be a surprise that it has been associated with poor quality of life for the affected individual and an increased burden on the individual's caregiver. Reliable and validated scales are required to measure these functional abilities and assess the individual's level of independence. In this section, we will examine the currently available measures that are used to assess deficits in multi-action sequencing, starting with measures of Activities of Daily Living (ADLs).

ADL measures, such as Barthel Index (BI: Mahoney & Barthel, 1965) and Frenchay Activities Index (FAI: Wade, Legh-Smith, & Hewer, 1985), Functional Independence Measure (FIM: Granger, Hamilton, Keith, Zielezny, & Sherwin, 1986; Hamilton, Granger, Sherwin, Zielezny, & Tashman, 1987) and Nottingham Extended Activities of Daily Living Scale (NEADL: Nouri & Lincoln, 1987) provide a measure of an individual's overall functional status. However, these measures provide an assessment of overall functional performance at the level of the task and do not measure the underlying cognitive causes of disorganisation.

In contrast to these functional assessment scales, there are few neurocognitive assessments that focus upon the underlying cognitive (especially executive) functions, which might account for the disordered performance. For example, two sub-tests from Behavioural Assessment of the Dysexecutive Syndrome (BADS: Wilson, Alderman, Burgess, Emslie, & Evans, 1996; Wilson, Evans, Emslie, Alderman, & Burgess, 1998), the Key Search and the Zoo Map are tests commonly used to assess planning abilities in brain-injured patients. In the Key Search, the patient is instructed to imagine that they have lost their house keys in a field, represented by a piece of paper and them to draw a line to show how they would search the 'field' in order to retrieve their keys. In the Zoo Map, the patient is told to visit a series of designated locations on a map of a zoo, following certain rules. These tests require planning and organisational thinking and are, therefore, measures of systematicity. However, they are language-laden, and therefore not ideal for stroke patients who may present with aphasia and neglect, and the complex instructions/rules of the tests may compete for limited working memory resources required for planning. In addition, BADS scores are interpreted as a total profile score, which includes the time taken to complete the task and the efficiency of the solution. This biasing of the measure of planning efficiency by merging it with information processing speed obfuscates the interpretation of these tasks.

Aims

This thesis aims to develop unbiased measures of planning/organisation (the ‘systematicity’ index) using performance-based, language reduced nonverbal tasks that are suitable for use within a stroke population.

This thesis consists of two parts, Part 1 is involved in examining the cognitive components underlying performance of stroke patients, at various stages of after stroke: sub-acute (<3 months post-stroke), chronic stage (~9 months post-stroke) and the cognition at the recovery phase using the change score between the sub-acute and chronic score test performance. This was done using a Principle Component Analysis (PCA) with varimax rotation on a large stroke-specific cognitive battery, the Birmingham Cognitive Screen (BCoS: Humphreys, Bickerton, Samson, & Riddoch, 2012). Subsequently, the sub-tests (accounted by the dependent variables) that are a better fit to characterise an EF construct and, also, adequate for the aim of this thesis were selected to be used for Part 2.

Part 2 of the thesis involved developing novel measures of planning/organisation (the ‘systematicity’ index) in stroke patients, using visuospatial and constructional tasks. Each systematicity measures were developed by embedding the BCoS philosophy, by making tests **aphasic** and **neglect friendly** (maximising patient inclusion) and **time-efficient** by deriving several measures of cognitive deficits using a singular task. In addition, the measures are designed to be easy to administer and extract data, without extensive training. Generate one score (the ‘systematicity’ index), reflecting the overall planning/organisational ability in the patients’ performance. Such measures would provide easily interpretable results for the clinicians and or the examiners, in short time.

The present thesis comprises five empirical studies across two parts:

PART ONE

This part of the thesis (chapter 2 and chapter 3) involves analysis of the neuropsychological test battery, Birmingham Cognitive Screen (BCoS: Humphreys, Bickerton, Samson, & Riddoch, 2012) to understand the cognitive variation in the profiles of stroke as reflected by BCoS.

In *Chapter 2*, we explored the underlying factors in the cognitive profile of stroke patients with heterogeneous lesions at a sub-acute stage (<3months, 763 patients) and a chronic stage (~9 months, 349 patients) post-stroke, using PCA. PCA is a common method for identifying latent variables (factors). The PCA factors were then rotated, using a varimax method, in order to aid the interpretation of the PCA factors. The varimax method allows for the identification of orthogonal (uncorrelated) factors, which reduces individual variables loading onto more than one factor. In this study, our objective was to identify and state the latent factors underlying the cognitive profile of stroke survivors at a sub-acute stage and chronic stage, respectively (see in this Volume: Chapter 2, page 36).

In *Chapter 3*, we used the same BCoS dataset as Chapter 2, however, only data of patients who contributed at the acute stage (<3 months) and the chronic stage (~9 months) post-stroke. In this study, we calculated the difference in test performance between sub-acute stage and chronic to assess the factors contributing to the changes in cognitive performance between the two-test periods using PCA (331 patients) (see in this Volume: Chapter 3, page 78).

PART TWO

This part of the thesis (chapter 4, 5 and 6) involves the development of executive measures for stroke. Here, we will present novel procedures for measuring planning/organisation (the ‘systematicity’ index) in performance-based, nonverbal tasks.

In *Chapter 4* we present an automated systematicity scoring system in a visual cancellation task, the Broken Hearts test from Oxford Cognitive Screen (OCS: Demeyere, Riddoch, Slavkova, & Humphreys, 2015) using sub-acute stroke patients (*n*=30) and normative data on healthy controls (*n*=52). In this study, we used two expert raters, to clinically judge how well each patient performed the cancellation task (see in this Volume: Chapter 4, page 108).

In *Chapter 5*, we describe a qualitative scoring method that provides an index of executive function measure for the BCoS Complex Figure Copy (Humphreys et al., 2012). For this study, we randomly selected 100 patient samples that had completed the Complex Figure Copy task, from dataset analysed in *Chapter 2* and *Chapter 3*. In this study, 30% of this sample was clinically judged on how well each patient performed/drew the complex figure using two expert raters on how well each patient performed/drew the complex figure (see in this Volume: Chapter 5, page 139).

In *Chapter 6,* we present a pilot study to demonstrate a principle for an automated systematicity scoring system in a visuospatial task, Figure Copy test from Oxford Cognitive Screen – Dementia (OCSd). This principle was demonstrated in a sample of chronic stroke patients (*n*=16) (see in this Volume: Chapter 6, page 173).

Chapter 7 includes the main findings presented in this thesis and provides suggestions for clinical practice and future research (page 195).

PART 1: Analysis of the Birmingham Cognitive Screen to understand the cognitive variation in the profiles of stroke.

Confirmatory Factor Analysis (CFA) and Exploratory Factor Analysis (EFA) are two major classes of factor analysis that are commonly used statistical approaches in the development and evaluation of neuropsychological test instruments. Both models aim to identify the underlying structure of a set of variables. However, CFC is confined by theoretical or empirical hypothesis, whereas EFA is limited by few restrictions placed on the relationship between the measured variables and the number of factors identified (Fabrigar, Wegener, MacCallum, & Strahan (1999). In this part of the thesis, as we are interested in analysing the BCoS battery to understand the cognitive variation in the stroke profiles, the EFA was deemed as the appropriate model.

To examine the cognitive components underlying performance on the BCoS sub-tests, a principal component analysis (PCA) with varimax rotation was used (Floyd & Widaman, 1995)

CHAPTER 2

THE FACTORS UNDERLYING COGNITIVE PROFILES AT SUB-ACUTE AND CHRONIC PHASES AFTER STROKE: FROM ANATOMICAL TO FUNCTIONAL COUPLING OVER TIME

ABSTRACT

INTRODUCTION: Birmingham Cognitive Screen (BCoS) was created for stroke-specific problems across 5 cognitive domains: i) attention and executive function, ii) language, iii) memory, iv) number processing and v) praxis and was designed to measure domain-specific and domain-general deficits. Here, we present the underlying factors that explain the variation in the profile of stroke survivors after carrying out the BCoS via Principle Component Analysis (PCA). **METHOD:** We assessed the cognitive profiles of a large group of stroke survivors at 1) a sub-acute stage (<3 months, 763 patients) and 2) a chronic stage post-stroke (~9 months, 349 patients) using the BCoS battery (Humphreys, Bickerton, Samson, & Riddoch, 2012). **RESULTS:** A varimax rotated PCA revealed that performance loaded onto seven factors in both samples, respectively, but there was a shift from anatomically-linked factors (e.g., based on a left hemisphere lesion) in the sub-acute stage to functionally differentiated factors at a chronic phase (language, praxis, memory, spatial attention, sustained attention/working memory, response suppression, capacity for attentional selection). **CONCLUSION:** The analysis suggests that the cognitive profile after stroke changes from the sub-acute to a chronic phase, and that domain-specific cognitive deficits become more evident over time.

INTRODUCTION

The prevalence of cognitive impairments is high following a stroke (Jaillard, Naegele, Trabucco-Miguel, LeBas, & Hommel, 2009), with as many as around 80% of stroke survivors experiencing some form of deficit (Leśniak, Bak, Czepiel, Seniów, & Członkowska, 2008; Patel, Coshall, Rudd, & Wolfe, 2003). Problems with language, memory, attention and skilled actions are particularly common (Bickerton et al., 2012; Bickerton, Samson, Williamson, & Humphreys, 2011; Humphreys, Bickerton, Samson, & Riddoch, 2012). These deficits significantly interfere with rehabilitation and can affect the degree of recovery (Ballard et al., 2003; Barker-Collo & Feigin, 2006; Bickerton et al., 2012, 2011; de Haan, Nys, & van Zandvoort, 2006; Donovan et al., 2008; Edwards et al., 2006; Fure, Bruun Wyller, Engedal, & Thommessen, 2006; Narasimhalu et al., 2009; Nys et al., 2006; Pohjasvaara et al., 2000; Stephens et al., 2005; van Zandvoort, Kessels, Nys, de Haan, & Kappelle, 2005; Zinn et al., 2004). In addition, these deficits have a major influence on the quality of life of stroke survivors (Moon, Kim, Kim, Won, & Kim, 2004; Nichols-Larsen, Clark, Zeringue, Greenspan, & Blanton, 2005; Paul et al., 2005). Therefore, it is important that cognitive deficits are identified soon after a stroke, so there can be early intervention and targeted rehabilitation to the specific problems experienced by a given patient.

BCoS (the Birmingham Cognitive Screen; Humphreys et al., 2012) is a clinical tool that attempts to provide an all-around profile of cognition in stroke survivors. It assesses cognition across five primary domains that can be affected after stroke: i) attention and executive function, ii) language, iii) memory, iv) number processing and v) praxis. This cross-domain analysis is important, because the presence of co-occurring deficits (e.g., in executive function as well as in spatial attention) is more predictive of long-term outcomes than the presence of a single deficit in one domain (e.g., a measurement of neglect; Bickerton et al., 2015). BCoS is designed to be applied in around one hour in clinical settings and unlike other instruments used to assess cognition after stroke, such as the Montreal Cognitive Assessment (MOCA: Nasreddine et al., 2005), the Addenbrooke's Cognitive Examination - Revised (ACE-R: Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, 2000; Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006) and the Mini-Mental State Examination (MMSE: Folstein, Folstein, & McHugh, 1975), it is designed to be relatively uncontaminated by poor language (aphasia) and poor spatial attention (unilateral neglect). For example, tests not aiming to assess language use short, high frequency words, forced-choice (multiple-choice) testing and multi-modal stimulus presentations to minimise the effects of language on performance. Similarly, tests not designed to assess spatial attention use vertical layouts to minimise the impact of neglect. In addition, BCoS evaluates spatial attention and praxis, both of which are prevalent after stroke (Bickerton et al., 2015, 2012, 2011). Sub-tests in BCoS also aim to measure several cognitive processes, to give time-efficient testing. For example, the assessment of neglect (the Apple Cancellation task; Bickerton et al., 2015, 2011) measures two forms of spatial deficit (allo-and egocentric); similarly, the test of Auditory Attention provides measures of response inhibition, working memory and sustained attention. These different measures are recorded on a 'wheel of cognition' for use in case management, where clinicians can view the cognitive profile at a glance (Bickerton et al., 2015; Humphreys et al., 2012).

Recently, Massa et al. (2015) analysed data from a large trial of the BCoS in stroke survivors using graph modelling. Graph modelling attempts to examine the relationships between performances on different tests by assessing the co-variance in performance across patients. The relations between tests in the BCoS were examined when each domain was considered in isolation (e.g., attention, language, memory, number processing and praxis) and when all the domains were considered together. One important result was that the profile of the tests changed substantially when the data were analysed across all domains relative to when the analyses took place separately within each domain. For example, the cross-domain analysis indicated that the Auditory Attention test was strongly related to language and memory rather than spatial attention, whilst the Complex Figure Copy task was linked not only to other aspects of praxis but also to spatial attention. The analysis pointed to the utility of including domain-general tests in developing a cognitive profile for stroke patients.

The graph modelling analysis emphasises the importance of cognitive profiling to understand cognitive deficits after strokes, but it does not identify underlying factors that can contribute to performance across different tests. A contrasting approach to this is to use analyses that attempt to isolate underlying factors that may cut across different tests. An example of this approach has recently been reported by Corbetta and colleagues (2015). After screening a large number of patients 1- 2 weeks post-stroke, Corbetta and colleagues entered 67 individuals into a Principal Components Analysis (PCA) using data from a set of cognitive tests of attention, language, memory and motor function. The results highlighted three factors reflecting (i) language and memory (including both verbal and spatial memory), (ii) indices of right hemisphere damage (left motor impairment, bias against the left field, general performance and spatial memory) and (iii) indices of left hemisphere damage (right motor impairment, bias against the right field and poor attention shifting). Corbetta and colleagues propose that behavioural variations after stroke can be accounted for by a small number of anatomically-ground factors that do not necessarily reflect classic neuropsychological syndromes (e.g., distinguishing between language comprehension and production).

The BCoS battery goes beyond the measures used by Corbetta and colleagues. It sub-divides some of the domains examined in that study (e.g., spatial attention is divided into egocentric and allocentric aspects of spatial representation) and it includes additional domains not present in their analysis (e.g., measures of apraxia, measures of number processing). As mentioned earlier in the introduction (page 39), BCoS is designed to measure two forms of spatial neglect; egocentric neglect (where some patients may fail to attend to stimuli on the contralesional side of the patients' body/viewpoint: Doricchi & Galati, 2000; Riddoch & Humphreys, 1983) and allocentric neglect (where some patients may fail to report the contralesional side of stimuli, independent of where the stimuli are presented to the patients' body/viewpoint: Kleinman et al., 2007; Olson, 2003; Walker & Young, 1996). Though, there are some behavioural/theoretical studies that have emphasised the dissociation between egocentric and allocentric neglect (e.g., Bickerton et al., 2011; Hillis et al., 2005; Kleinman et al., 2007; Marsh & Hillis, 2008; Medina et al., 2009; Ota, Fujii, Suzuki, Fukatsu, & Yamodori, 2001) along with some lesion analysis studies which have suggested that both neglects may have separate anatomical correlates (see Karnath & Rorden, 2012 for review), the association between the two forms of neglect remains debatable. Some patients' may experience ego-and allocentric neglect together, while it may occur independently in others (Marsh & Hillis, 2008). Also, both neglects can even be expressed on different sides in patients with bilateral lesions (Humphreys & Riddoch, 1994; Riddoch, Humphreys, Luckhurst, Burroughs & Bateman, 1995). However, despite the debate, the spatial attention task from BCoS (the Apple Cancellation test) has been proven to measure both forms of neglect, ego-and allocentric neglect, in chronic as well as in acute stroke patient samples (two groups of samples analysed in the present study) and highlights that the test is clinically applicable (Bickerton et al., 2011).

In addition, we were able to assess performance not only at a sub-acute stage (here <3 months post-stroke) but also at a chronic stage (~9 months post-stroke) and we included substantially larger numbers of patients (763 at a sub-acute stage and 349 at the chronic phase). Here, we provide a stronger test of the notion that the cognitive profile represents the anatomical clustering of stroke patients. For example, both apraxia and impairments in number processing have been associated with left hemisphere damage. If the hemisphere of lesion is a critical factor then these domains should cluster with impairments in language and verbal memory, reflecting a general left hemisphere component. Alternatively, they may reflect independent components, if the profiles of stroke survivors stem from a functionally -based modular organisation of cognition. Also by testing at both a sub-acute and chronic stage, we ask whether the underlying factors determining cognitive performance are constant across this time period, when the brain may have undergone functional recovery following the initial insult. To address these issues, we employed a PCA approach to extract the underlying domain-specific and domain-general factors that best explain the variation in the profiles of patients after carrying out the BCoS (Bickerton et al., 2015, 2012).

The chapter is divided into two sections. In Part 1 we report the results on a large sample of patients tested at a sub-acute stage, within 3 months after their latest stroke. In Part 2 the data were derived from patients at a chronic stage ~9 months post-stroke.

Part 1: Examining the cognitive profile at sub-acute stage after stroke (<3 months)

METHOD

Patients and materials

Dataset 1 contained the cognitive profile of 763 stroke patients who completed the BCoS. All the patients included were stroke survivors recruited from several stroke units across the West Midlands, England (United Kingdom) as part of a multicentre trial (http://www.bucs.bham.ac.uk). The patients were medically and physically stable during the sub-acute stage post-stroke (<3 months). Patients were excluded on the basis of: i) poor English and/or comprehension impaired to the extent that the basic instructions could not be followed, or ii) unable to concentrate for 35 minutes (judged by a multi-disciplinary clinical stroke team). Diagnosis of a stroke was based on the assessment by the clinical team and confirmed by Computerised Tomography (CT) scan wherever possible.

All patients gave informed consent in agreement with an ethics protocol approved by the U.K. National Research Ethics Committee. The neuropsychological testing was conducted at the stroke ward by trained examiners who were clinical neuropsychologists, occupational therapists or stroke researchers (doctoral researchers or research assistants). These examiners had all attended a full day's training and successfully completed the given assessments that were supported by the BCoS team.

In the dataset, there were 40 variables with four personal information variables, three clinical information variables and 33 behavioural variables (the cognitive test scores from BCoS sub-tests). The personal information variables included: age, gender, handedness and the total numbers of years spent in education. The clinical information included the patient's previous medical history, that is, patient's stroke history (previous stroke, TIA), head injury and dementia along with any other neurological condition (brain tumour, encephalitis etc.), the type of stroke (TIA, haemorrhagic or ischaemic), the side of the lesion (left, right or bilateral). For demographic and clinical details of the sub-acute stroke patients, see Table 1 (Demographic details) and Table 2 (Clinical details). ***Behavioural variables.*** The behavioural variables specified the performance of the patients in different cognitive sub-tests in the BCoS. The BCoS test instrument is made up of 22 cognitive sub-tests and a qualitative score for verbal comprehension. The sub-tests cover 5 primary cognitive domains: i) attention and executive function, ii) language, iii) memory, iv) number skills, v) praxis and action. These domains can be broken down further to separate, at a within-domain level: i) spatial attention (neglect and extinction), ii) controlled attention (e.g., sustained attention and working memory, along with executive function), iii) written and spoken language, iv) immediate and delayed memory and v) constructional and limb apraxia (Humphreys et al., 2012). For the majority of the sub-tests high scores indicate better performance. On some tests, however, relative differences between the conditions are recorded (e.g., as in the Apple Cancellation asymmetry score – a measure of relative performance on the left and right sides of space), where higher scores stand for a stronger deficit. A brief description of BCoS is given in Appendix A and an overview of the BCoS sub-tests (assessments) and their associated scores (behavioural variables) included in the analysis are also provided in Appendix A (Table A1). The full details of the sub-tests making up the BCoS, along with inter-rater reliability and validity are reported in Humphreys et al. (2012).

Table 1. *Demographic details for Sub-acute (n=763) and Chronic (n=349) Stroke Patients*

	Age		Gender	Handedness	Education (Years)	
	Range	$\bar{x}$ (SD)	M/F	L/R/A	Range	$\bar{x}$ (SD)
Sub-acute	18 - 95	70.12 (13.78)	346/ 417	76/ 673/ 14	3 - 25	11.34 (2.68)
Chronic	19 - 92	70.21 (13.04)	153/ 196	36/ 306/ 7	6 - 24	11.78 (2.81)

***Note*: L =** Left, **R =** Right, **A =** Ambidextrous

Table 2. *Clinical details for Sub-acute and Chronic Stroke Patients*

Clinical details	Sub-acute (*n*=763)	Chronic (*n*=349)
Previous medical history		
No known history	496	239
Previous stroke/ TIA	222	91
Head injury	8	4
Dementia	8	0
Brain tumour	1	0
Encephalitis	0	0
Other	28	15
Type of stroke		
TIA	22	8
Haemorrhage:		
Intracerebral	93	48
Subarachnoid	13	5
Ischemic stroke	598	270
Other (specified)	3 (Vasculitis with CNC involvement, Meningioma, Right middle cranial fossa arachnoid cyst)	1 (Meningioma)
Unknown	34	17
Lesion side		
Left lesion	230	97
Right lesion	278	143
Bilateral lesion	102	39
Unknown	153	70

Note: **TIA** = Transient Ischemic Attack, **CNS** = Central Nervous System

Table 3. *BCoS Variables: Mean and SD for Sub-acute and Chronic group, with Cut-off scores for Impairments*

		Cut-off points across age groups			*Sub-acute*			*Chronic*		
Variables	*Max. Score*	≤64	65-74	≥75	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*
Language										
Picture naming	14	11	11	10	10.41	3.59	748	11.79	2.83	347
Sentence construction	8	8	8	6	6.72	2.07	716	7.49	1.28	344
Sentence reading	42	42	42	41	36.42	10.71	711	39.25	7.16	339
Nonword reading	6	5	4	4	4.23	2.1	706	4.77	1.85	339
Word/nonword writing	5	3	3	3	2.96	1.79	660	3.6	1.55	334
Number skills										
Number reading	9	8	8	8	7.43	2.68	658	8.33	1.7	333
Number writing	5	5	5	3	3.7	1.76	661	4.29	1.34	333
Calculation	4	2	2	2	2.41	1.43	664	2.83	1.32	337
Praxis										
Complex figure copy	47	42	41	37	33.91	11.86	668	38.58	8.81	332
Complex figure copy (asymmetry) [a]	15				-0.49	3.66	668	-0.07	2.81	332
Multiple object use	12	11	10	10	9.95	3.57	690	11.08	2.48	342
Gesture production	12	10	9	9	10.25	2.83	709	10.99	1.86	342
Gesture recognition	6	5	5	4	4.9	1.24	707	5.29	0.99	342
Gesture imitation	12	9	9	9	9.16	2.96	709	10.25	2.16	339

Table 3. (*Continued*)

		Cut-off points across age groups			*Sub-acute*			*Chronic*		
Variables	*Max. Score*	≤64	65-74	≥75	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*
Memory										
Immediate free recall	15	6	6	3	6.12	3.2	707	7.11	3.36	342
Immediate recognition	15	13	13	11	11.53	3.44	750	12.54	2.61	346
Delayed free recall	15	8	6	4	6.84	4.15	670	8.07	4.33	340
Delayed recognition	15	13	13	12	12.3	3.36	711	13.12	2.75	344
Task recognition	10	9	9	8	8.3	2.19	686	9.1	1.36	338
Attention										
Spatial										
Apple cancellation (FP Right) [a]	50				1.65	5.53	623	0.99	3.63	330
Apple cancellation (FP Left) [a]	50				2.82	7.14	623	1.66	5.26	330
Apple cancellation (Egocentric neglect)	20	<-2 or >2	< -2 or >3	<-2 or >3	1.32	5.01	623	0.7	4.12	330
Apple cancellation (Allocentric neglect)	50	<-1 or >1	<-1 or >1	<-1 or >1	1.05	4.46	623	0.51	3.88	330
Left visual extinction	8	8	7	7	0.41	1.71	717	0.29	1.37	340
Right visual extinction	8	8	8	8	0.04	1.06	717	0.06	0.9	340
Left tactile extinction	8	7	7	7	0.4	1.91	717	0.35	1.47	343
Right tactile extinction	8	8	8	7	0.06	1.37	717	0.01	1.02	343

Table 3. *(Continued)*

		Cut-off points across age groups			*Sub-acute*			*Chronic*		
Variables	Max. Score	≤64	65-74	≥75	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*
Control										
Auditory attention	54	51	50	46	41.74	14.68	677	46.79	11.57	341
Auditory attention (FP)[a]	27				3.44	5.07	677	2.15	4.16	341
Auditory attention (Omission)[a]	27				3.94	4.88	677	2.77	4.19	341
Auditory attention (Idx)[b]		>1	>1	>2	0.98	2.2	571	0.62	1.89	320
Auditory attention (WM)	3	3	3	2	2.46	0.84	676	2.74	0.61	339
Rule finding	18	<6	<5	<4	6.48	5.64	680	8.53	5.61	333

Note: **Max.** = Maximum, **FP** = False positive (response to distractors), **Idx.** = Sustained attention Index, **WM**= Working memory, ***n*** = total number of stroke patients analysed for that variable. The cut-off points (impairment = less than given scores, unless otherwise specified) for BCoS variables were obtained from the established BCoS manual (Humphreys et al., 2012). BCoS consists of 22 subtests, covering 5 cognitive domains: i) language, ii) number skills, iii) memory, iv) praxis, v) attention & executive function. For the purposes of PCA, we only used 33 BCoS scores (variables; derived across 32 sub measures). This was mainly to reduce the number of variables.

[a] There are no established norms for these variables (the asymmetry score for Complex Figure Copy was calculated for the BCoS dataset used in this thesis; it is not part of the original BCoS Manual). [b] Sustained attention index is calculated by the difference between the total number of correct responses in block 1 *minus* the total number of correct responses in block 3. If stopped after block 1 or 2, indexed as N/A.

DATA ANALYSIS

Principal Component Analysis. Patients' raw scores on each BCoS assessment were converted into Z-scores, using the sub-acute patient group mean and standard deviation across each assessment. We calculated the Z-scores using the standard formula:

$$\mathrm{Z} = \frac{(x - \mu)}{\sigma}$$

where x was the raw score of the patient's performance which was standardised (Z-score), μ was the mean of the patients' performance in that assessment and σ was the standard deviation of the patients' performance for the assessment. These Z-scores were entered into the PCA with varimax rotation (conducted using SPSS 22.0). ***Sample adequacy for PCA.*** There is no clear guide to the number of cases needed to conduct PCA, but Comrey and Lee (1992) recommend a sample size of at least 300 cases. Our sample size was adequate for this.

Factors with an eigenvalue ≥ 1.0 were extracted and then rotated. After orthogonal varimax rotation on the extracted factors, the factor loadings of each test allowed interpretation of which cognitive domains/impairments were represented by the different factors. The variables were considered to be part of the factor if their factor loading was great than 0.40. For subsequent analysis, we saved factor scores, which represent each individual's placement on the factors identified from the PCA, under the Anderson-Rubin method (Anderson & Rubin, 1956). This method was chosen to ensure that the factor scores are uncorrelated.

Finally, since, the sub-acute testing was conducted at the stroke ward and, sometimes, the patients did not complete every single sub-test (e.g., due to other hospital demands or fatigue on the part of the patient), therefore, missing values were excluded in pairwise (available-case analysis) where only cases relating to each pair of variables with missing data involved in an analysis are deleted.

Interpretation of factors for the sub-acute stage patient performance on BCoS

Principle Component Analysis was conducted on 763 sub-acute stroke survivors. The mean time of the test administration time post-lesion was 24.98 days (SD = 21.06), range = 1 to 93 days. Summary statistics (mean and SD) of the sub-acute patients' performance across each BCoS sub-test score (behavioural variable) included in this analysis are provided in Table 3.

The rotated PCA produced seven principle factors that accounted for 64.26% of the variance in performance across patients (F1 = 21.46%, F2 = 13.21%, F3 = 7.82%, F4 = 6.69%, F5 = 5.58%, F6 = 4.82% and F7 = 4.68%). The factor loadings for performance in the sub-acute patient group are provided in Table 4.

Table 4. *Factor Loading for Sub-acute stage Patient Performance on BCoS*

	Factors						
BCoS Variables	1	2	3	4	5	6	7
Number reading	.832						
Sentence reading	.822						
Nonword reading	.765						
Number Writing	.736						
Picture naming	.72						
Word/nonword writing	.693						
Sentence construction	.689						
Gesture production	.654	.442					
Gesture imitation	.602						
Calculation	.569						
Gesture recognition	.541						
Complex figure copy	.538		- .453				
Auditory attention	.52	.404		.451			
Immediate recognition		.789					
Delayed recognition		.756					
Immediate free recall		.732					
Delayed free recall		.73					
Task recognition	.471	.636					
Multiple object use	.456	.471					
Complex figure copy (Asymmetry)			- .768				
Apple cancellation (Allocentric neglect)			.743				
Apple cancellation (Egocentric neglect)			.731				
Auditory attention (Omission)				- .788			
Auditory attention (Sustained attention Idx.)				- .733			
Auditory attention (WM)				.6			
Apple cancellation (FP Right)					.934		
Apple cancellation (FP Left)			.428		.876		
Auditory attention (FP)						- .76	
Rule finding						.449	
Right tactile extinction							.702
Right visual extinction							.607
Left tactile extinction							.574
Left visual extinction							.504

Note: Total percent of variance = 64.26%. Orthogonal varimax rotation performed on factors with eigenvalues ≥ 1 and only BCoS variables with coefficient absolute values > .40 are shown. **WM** = Working memory, **FP** = False positive

Identifying the primary-cognitive factors in sub-acute stroke patients

Fifteen variables loaded on Factor 1. As Table 4 makes clear, the factor grouped together language, number processing and skilled action (praxis). In addition, overall performance on the Auditory Attention task is also loaded on this factor. As we have noted above, a previous graph modelling analysis has shown that performance on the Auditory Attention test is linked to that on other tests of language and the task requires that three target words are verbally maintained and detected. We conclude that this factor reflects the hemisphere of lesion – in this case to the left hemisphere (Factor: 'Left hemisphere lesion').

Eight variables loaded on Factor 2. These consisted of measures of patients' short and long-term memory, including a strong weighting being given to an assessment of visual episodic memory (Task Recognition: forced-choice discrimination on which items had previously been encountered). This factor we labelled as 'Memory'.

The remaining five factors were weaker, accounting for 29.59% of the variance. Factor 3 consisted of variables measuring spatial attention/neglect including measures of egocentric and allocentric neglect (Bickerton et al., 2011), plus also an asymmetry score from the Complex Figure Copy task. This factor we labelled as 'Spatial attention'. We note too that this factor could also reflect the presence of a right hemisphere lesion.

Factor 4 consisted of measures derived from the Auditory Attention task reflecting sustained attention, target omissions and working memory. We labelled this factor as 'Controlled attention'. The data suggest that the ability to maintain performance across a selection task (the sustained attention measure) is closely related to the ability to hold the selection targets in mind (the working memory measure) and to detect the targets (omission errors).

Factor 5 consisted of a very heavy loading on false positive errors made to distractors in the Apple Cancellation task. These errors provide a measure of allocentric neglect (Bickerton et al., 2011). Interestingly, however, this factor loaded for both left and right asymmetries and thus may stem from a more general underlying factor in focusing attention on the local parts of objects. Hence, we labelled this factor as ‘Attention to detail’.

Factor 6 consisted of items that loaded on the measure of response suppression from the Auditory Attention task and also on the Rule Finding task (finding and then switching the rule by which a black dot moves across a matrix). Both measures reflect aspects of executive function (response inhibition and switching set), and particularly the ability to suppress information (in the Auditory Attention task, distractors related to targets; in the Rule Finding task old rules must be suppressed). We interpreted the factor as ‘Response suppression/Executive function’. The results suggest that response suppression can be distinguished from these other aspects of controlled attention.

The final factor, Factor 7, consisted of variables related to the measures of extinction in BCoS (both left and right-side extinction with both visual and tactile stimuli). This loading across the side of lesion and the test modality may reflect a common underlying factor that leads to extinction, such as a loss of processing resource when attentional selection is required. We labelled this factor as ‘Attentional capacity during selection’.

There were several variables that seemed to contribute to more than one factor. Gesture Production, for instance, was heavy loaded on Factor 1 (left hemisphere function: weighting .654) and Factor 2 (memory: weighting .442). This may reflect that this task taps both general left hemisphere functions (Factor 1) and memory (Factor 2). Task Recognition loaded on Factor 1 (left hemisphere function: weighting .471) but more heavily on Factor 2 (memory: weighting .636); here verbal retrieval processes (Factor 1) were likely required as well as access to memory. Multiple-step Object Use similarly provided relatively equal loadings into Factor 1 (left hemisphere functions: weighting .456) and Factor 2 (memory: weighting .471). Note that the Multi-step Object Use task requires actions to be performed in a set sequence and may call on left hemisphere sequencing operations along with memory for the actions to be performed, to limit perseverations.

Complex Figure Copy loaded positively on Factor 1 (left hemisphere function: weighting .538) and on Factor 3 (spatial attention: weighting - .453). Here, there may be contributions from a general left hemisphere component (planning and sequencing the sequential actions; Factor 1) plus also spatial attention (Factor 3).

Performance on the Apple Cancellation task also loaded on several factors. Spatial asymmetries, both across the page and in terms of false positives to distractors loaded into Factor 3 and reflected the asymmetric allocation of spatial attention. In terms of both, test performance, and also brain lesion, the page and item-asymmetries can dissociate (Bickerton et al., 2011; Chechlacz et al., 2010) suggesting distinct forms of neglect (allo-and egocentric). However, the two forms of neglect also co-occur in many patients and this pattern is associated with brain lesions around the right temporo-parietal junction

(Chechlacz et al., 2010). The joint loading of the two forms of neglect on Factor 3 may reflect the common variance coming from such patients and the general impact of the right hemisphere lesion. In contrast to this, the loading on Factor 5 was based on the item-asymmetry measure (allocentric neglect; Bickerton et al., 2011) and was present for both left and right asymmetries. We link this to the ability to focus attention onto the local details of objects. Previously, it has been argued that attention to local detail is mediated by the left hemisphere (Delis, Robertson & Efron, 1986), but the data on this are often inconsistent and may better reflect the sensitivity of left hemisphere patients to the saliency of stimuli (Mevorach, Humphreys, & Shalev, 2006). The current results were left and right asymmetries load on the same factor, suggests that the ability to focus on local details is not strongly lateralised. See Table 5 for the spatial asymmetry of the sub-acute stroke patients.

Table 5. *Spatial asymmetries of the Sub-acute Stroke Patients, by Lesion Side*

	Egocentric neglect	Allocentric neglect
Left hemisphere lesion (*n*=230)	186	194
Right hemisphere lesion (*n*=278)	234	235
Bilateral hemisphere lesion (*n*=102)	67	68
Unknown lesion (*n*=153)	136	141

Note: n = number of sub-acute stroke patients

Part 2: Examining the cognitive profile at chronic stage after stroke (~9 months)

METHOD

Unless otherwise specified, the methodology for the analysis of patient performance at the chronic stage was the same as for the acute stage.

Patients and materials

Dataset 2 contained the cognitive profile of 349 stroke survivors who agreed to participate and completed the BCoS in a follow-up session (at least 9 months post-initial testing). There was no feedback from the initial testing session. For details on BCoS battery and the assessment protocol, refer to Part 1[1].

The data were typically collected in a home-visit to individuals, with a minority of tests either done in a nursing home (if the stroke survivor had moved to such a location) or in the School of Psychology, University of Birmingham. For demographic and clinical details of the chronic stroke patients, see Table 1 (Demographic variables) and Table 2 (Clinical variables).

---

[1] The PCA for the sub-acute data was repeated using just those patients who also contributed follow-up results (*n*=331, 18 cases were removed as the nature of one of the key test changed from the initial stage of data collection on the BCoS to the follow-up stage). This made no difference to the factor structure we reported in Part 1. We report the results for the larger patient group since this provided the most powerful analysis.

Table 6. *Factor Loading for Chronic Stage Patient Performance on BCoS*

	Factors						
BCoS Variables	1	2	3	4	5	6	7
Immediate recognition	.824						
Immediate free recall	.819						
Delayed free recall	.793						
Delayed recognition	.718						
Rule finding	.522						
Task recognition	.448		.44				
Sentence reading		.855					
Number reading		.766					
Nonword reading		.756					
Sentence construction		.64					
Word/nonword writing		.623					
Number writing		.531	.51				
Picture naming	.467	.497	.414				
Gesture recognition			.731				
Gesture imitation			.633				
Gesture production		.401	.605				
Multiple object use			.582				
Complex figure copy			.461				
Calculation			.426				
Auditory attention (WM)				.758			
Auditory attention (Sustained attention Idx.)				- .754			
Auditory attention				.648			
Auditory attention (Omission)				- .628			
Apple cancellation (Allocentric neglect)					.734		
Left tactile extinction					.666		
Apple cancellation (FP Left)					.636	- .604	
Apple cancellation (Egocentric neglect)					.63		
Complex figure copy (Asymmetry)					- .571		
Apple cancellation (FP Right)						- .822	
Auditory attention (FP)						- .46	
Right tactile extinction							.715
Right visual extinction							.651

Note: Total percent of variance = 61.51%. Orthogonal varimax rotation performed on factors with eigenvalues ≥ 1 and only BCoS variables with coefficient absolute values > .40 are shown. **WM** = Working Memory, **FP** = False Positive

Interpretation of factors for chronic stage patient performance on BCoS

Principle Component Analysis was conducted on 349 chronic stroke patients. Summary statistics (mean and SD) for the chronic patients' performance across each BCoS assessment included in this analysis, and the number of cases analysed is provided in Table 3.

The rotated PCA produced seven principle factors that accounted for a total of 61.51% of the variance in patients' performance (F1= 12.83 %, F2 = 12.68 %, F3 = 9.97 %, F4 = 8.05 %, F5 = 7.65 %, F6 = 5.64 % and F7 = 4.69 %). The factor loadings for performance in the chronic patient group are provided in Table 6.

Identifying the primary-cognitive factors in chronic stroke patients

Five out of seven variables that loaded on Factor 1 were related to memory (short and long-term memory, in combination with episodic memory for the tasks undertaken). There was also loading on this factor from the rule accuracy measure (well above the cut-off at .522). This might reflect the role of working memory in having to hold the rule that had been followed, when making the prediction of the next move to be generated in the task. This factor was labelled as 'Memory'.

Eight variables loaded onto Factor 2. These tests involved aspects of language – involving the comprehension, and both the written and spoken production of words and numbers. These variables all loaded onto a common factor also apparent for the tests done at <3 months, but in addition, the critical factor then also included aspects of gesture processing. Here, language and gesture processing loaded onto distinct factors, with various gesture and action recognition and production tasks loading onto a third factor. This third factor also included a loading for the complex figure drawing, consistent here with action sequencing in construction as well as in action production (e.g., the multi-step object task) involving common underlying factors. We interpreted Factor 2 as 'Language processing' and labelled Factor 3 as 'Praxis'. Note that, in Part 1, these different tasks loaded onto a common 'Left hemisphere' factor.

The fourth factor was built from aspects of the Auditory Attention task – with loadings for the overall score on this task, the working memory measure (index), the sustained attention measure and the number of omission errors. A similar clustering to this was reported in the PCA conducted at the sub-acute (<3 months) stage. The results point to the close linkage between working memory for targets, target detection and the ability to sustain attention across a task. This factor was labelled 'Controlled attention', same as Factor 4 of the sub-acute (<3 months) cluster.

The fifth factor appeared to reflect disorders of spatial attention and included both ego-and allocentric neglect measures, Left tactile extinction and also spatial deficits in the Complex Figure Copy task. This factor was labelled as 'Spatial attention' but may again stem from the co-location of the components in the right hemisphere.

Factor 6 was built from loadings based on false positive responses to distractors with a right-side gap, in the Apples task, and also to false positive responses in the Auditory Attention task. This factor may reflect poor response suppression, especially associated with left-side lesions (and thus affecting right allocentric neglect and poor inhibition of responses to auditory distractor words in the Auditory Attention test). This factor was labelled as

‘Response suppression’. In the sub-acute (<3 months; Part 1), Factor 6 consisted of somewhat a similar cluster that involved only the overall accuracy of the Rule Finding assessment and false positive responses in the Auditory Attention task. In the chronic sample, the cluster is built exclusively from loadings on false positive responses to distractors in the Auditory Attention task. The change in factor loading compared to the sub-acute stage may reflect that impairments in the chronic stage are more compartmentalised and stable than in the sub-acute stage – here a ‘purer’ measure of response suppression (on the Auditory Attention task) was apparent (extracting out effects of Rule Finding).

Finally, Factor 7 loaded on variables measuring right-side visual and tactile extinction – both likely reflecting reduced attentional capacity after left hemisphere lesions. It is interesting that, in the PCA of performance at <3 months, there was a loading of extinction tests across different modalities, left, and right sides. However, at 9 months there was a clearer differentiation across the side of extinction. It is possible that, in the sub-acute stage, extinction reflects a more general loss of resource irrespective of the hemisphere of damage. However, at 9 months, and some degree of recovery, there are fewer demands on overall resource and more on hemisphere-specific resources. This factor we labelled as ‘Visual-attention capacity after left hemisphere lesion’.

There were a few test variables that loaded onto more than one factor. Task Recognition loaded equally on Factor 1 (memory: weighting .448) and Factor 3 (praxis: weighting. 440). It is possible that there are contributions to the praxis factor from processes involving retrieval and item sequencing, both of which may impact on Task Recognition. Picture Naming variable loaded above the cut-off on Factor 1 (memory: weighting .467), Factor 2 (language processing: weighting .497) and Factor 3 (praxis: .414). Picture Naming clearly involves access to long-term memory for object names, and perhaps also a prolonged retrieval process, to generate a low frequency name; hence some loading onto the memory factor. Naming has also long been linked to action production and both can reflect damage to left parietal cortex (for review see Roby-Brami, Hermsdörfer, Roy, & Jacobs, 2012). This may explain the loading of Picture Naming onto the praxis factor, plus also the loading of Gesture Production on the language (weighting .401) as well as the praxis factor (weighting .605).

Finally, we note that the false positive score for left-side gaps in the Apple Cancellation task loaded on both Factor 5 (spatial attention: weighting .636) and Factor 6 (response suppression: weighting - .604). The ability to refrain from responding to the distractors in the Apple Cancellation task may reflect both poor allocentric attention and poor response suppression.

Intergroup comparison

Having established seven principle factors, respectively, for the sub-acute stage and the chronic stage post-stroke, we then investigated the difference of the patients' performance between patients with left and right hemisphere lesion on these factors, using the factor scores generated for each patient. The factor scores represent each individual's placement on the factors identified from the PCA. Here, an independent sample *t*-test was performed comparing the factor scores of each patient with a unilateral left hemisphere lesion and patients with a unilateral right hemisphere lesion on each established factor. Note, as a patients' factor score is an average sum of his/her performance based on the constituent variables, not all patients had a factor score calculated (due to missing values).

All *p* values were accepted at 0.5, the correlations were in small numbers as expected.

The differences between the left and right hemisphere lesions on the established factors are provided in Table 7.

The similarities and dissimilarities between the BCoS test variables between the sub-acute and chronic stage are displayed in Table 8. The cognitive variations in the profiles of stroke patients in the sub-acute stage and chronic stage after stroke, reflected by BCoS test variables are displayed in Figure 1.

GENERAL DISCUSSION

The present study examined the underlying factors in the cognitive profile of stroke survivors, in sub-acute and chronic stage, using a PCA to objectively explore the latent factors affecting cognitive deficits after stroke, measured through the BCoS (Humphreys et al., 2012). Our main goal was to identify and state the factors underlying the cognitive profile of stroke survivors at both a sub-acute and a chronic stage (<3 and ~9 months). In brief, the results of the PCA analysis in both samples suggest that the performance of stroke survivors reflected up to seven principle factors, but the linking of tests to the factors differed across the test periods.

The sub-acute stage

In the sub-acute sample, the evidence indicated a substantial grouping of factors based on the anatomical locations of lesions. Factor 1, which accounted for most variance, loaded on tests of language, number processing and praxis – all of which are associated with left hemisphere processing though they are typically distinguished in terms of neuropsychological theory (Beaumont, 2012). Factor 3, which loaded on tests of spatial attention and Complex Figure Copy, can also be linked to the presence of a right hemisphere lesion (Chechlacz, Mantini, Gillebert, & Humphreys, 2015; Corbetta, & Shulman, 2011). These results, for undifferentiated cognitive functions linked by a common site of lesion, are supported by the data reported by Corbetta and colleagues (2015). They also argued for over-arching factors that reflected the neuroanatomical damage more than the standard functional decomposition of tasks.

On the other hand, the other factors emerging from the PCA were better associated with specific cognitive components covering: memory (Factor 2), sustained attention/working memory (Factor 4), attention to detail (Factor 5), response suppression/executive function (Factor 6) and attentional capacity during selection (Factor 7). One of the interesting aspects of this is that there was some, but not complete fractionation of cognitive functions. Within the domain of executive functions there was separate loading onto at least two factors – Factor 4 covered the working memory and sustained attention measures from the Auditory Attention task, while Factor 6 included aspects of response suppression (e.g., false positive responses on the Auditory Attention task), even though the measures were derived from the same task. Miyake et al. (2000), in their factor analysis of executive function tests distinguished between the maintenance/updating of a task set and the inhibition of prepotent responses. The current results are consistent with this, assuming that working memory and sustained attention are required to maintain and/or update the task set. Different aspects of attention also appeared to fractionate. Factor 5 was related to false positive responses to local distractors in the Apples test of Neglect, but this included both left-and right-sided errors and so seems more to reflect attention to local detail in the stimuli than how attention is tuned to allocentric spatial representations. Factor 6 was associated with measures of extinction in patients (poor performance on trials where 2 rather than 1 stimulus was present), but again this covered poor performance on each side of space. We suggest that this follow if there were general reduced attentional resources in the patients. These attentional deficits were distinct from impairments in spatial attention, demonstrated through spatial asymmetries in egocentric and allocentric space, again consistent with the fractionation of different attentional functions. Although these latter factors each accounted for relatively small amounts, together they explained around 43% of the variance across the patients.

The chronic phase

In the chronic data set, the underlying factors matched some, but not all of the components isolated at the sub-acute stage. There were commonalities in factors related to memory (Factor 1, chronic), working memory/sustained attention (Factor 4) and response inhibition (Factor 6, false positives on the Auditory Attention task). However, and in contrast to the sub-acute results, there was clearer evidence for fractionation of cognitive processes. For example, language and praxis performance now separated into two factors (Factors 2 and 3), although both are associated with left hemisphere localisation. In addition, the reduced resources factor from the sub-acute stage (Factor 7, acute) then separated into a clearer right-lateralised deficit in spatial attention (Factor 5, chronic) and reduced attention following left hemisphere lesion (Factor 7, chronic). Also, the factor linked to attention to local detail was eliminated.

This clearer fractionation into specific aspects of cognition may come about for several reasons. One is that, following the initial brain insult there can be widespread disruption to activation patterns within the affected hemisphere with the result that multiple processes supported by that hemisphere are impaired, not just those represented within the lesioned area. A second is that there is some degree of functional re-organisation over time. This re-organisation may be linked to experience in specific cognitive modules, which enables those processes to become functionally linked and more distinct from other processes localised in the affected hemisphere. Though this is possible, we think the first proposal is the more likely and parsimonious, reflecting some degree of localised cognitive function in both the sub-acute and chronic stages.

Though there was evidence for greater fractionation at the chronic stage, there remains a quite broad grouping of cognitive processes. For example, there was no evidence for separate loading of different aspects of language and also number processing, all of which remained linked to one factor. This was despite the fact that sub-tests of the BCoS are designed to try and distinguish particular cognitive processes (receptive and expressive language, reading vs. writing and so forth; see Appendix A) (see also Corbetta et al., 2015). It may be that the different processes are represented in sufficiently close anatomical areas and that fractionation is difficult to establish at a group level, where many patients may have large lesions and co-occurring deficits. Alternatively, it may be that different parts of a language network (for instance) interact, so that, across a large group of patients, damage to one sub-region generates some degree of impairment in other regions. The same arguments may be applied to the results on spatial attention at the chronic stage. Although the measures of egocentric and allocentric neglect examined in the BCoS can be dissociated and can be shown to link to contrasting lesion sites (Chechlacz et al., 2010), across a large patient group there may be sufficient commonality (due to large lesions and/or lesions affecting brain regions where both egocentric and allocentric representations are held), and that the two forms of neglect cluster together.

Taking the analyses at the two stages together, the results highlight that the tendency to have a profile of anatomically-grouped cognitive deficits decreases, when stroke patients move into a chronic from a sub-acute stage and a greater dissociation of cognitive processes is evident. Our conclusions about the functional localisation of cognition, then, should be tempered by a consideration of what period following the stroke the patients were tested.

Study limitations

Although there is an evolving picture of the cognitive profile for patients at each stage after stroke, there are some potential methodological implications that need to be considered. One important methodological concern is the presence of multiple neurological conditions within the stroke group. The criteria for selection of patients, especially, in the sub-acute data set; whose final diagnosis was stroke with accompanying deficits (e.g., TBI, dementia etc.). It is important to note that the context of the present study was to characterise the cognitive profile of stroke in the general population. While the current sampling of data was sufficient for the purpose of the present study, it should be noted that the presence of other neuropathological aetiologies may confound and obscure the description of the stroke cognitive profile. Therefore, one conservative way to assess the variation of the cognitive profile in the acute stage would be through the modification of patient selection criteria for example including patients who only exhibit stroke (or further categorised by first time vs. repeated stroke) in the study to present a stroke-specific picture.

Another methodological point was the inclusion of stroke patients irrespective of the (total) number of sub-tests completed in the BCoS Battery. This practice may result in a reduction of the measure variability between sub-tests. However, again, the context of the present study was to represent the general stroke population, thus, the study unlikely missed out severe cases at both stages (sub-acute and chronic). Nevertheless, further research could follow more detailed criteria for selection for patients such including patients who completed a certain number of BCoS sub-test or of patients, only, with complete BCoS scores. This might have an impact on the underlying factors in relation to patient performance across the sub-tests.

Finally, given the emphasis on identifying the cognitive profile that might be associated with stroke, this chapter has focused on the between-subject commonalities, rather than the differences, across patient performance on the BCoS sub-tests. However, it would be of interest to examine underlying latent variables and individual difference factors that affect patient performance. Such underlying latent variables and individual difference factors may be identified using methods derived from item response theory (such as the Rasch model). Such methods quantify the latent trait based on a particular patient’s ability and the sensitivity and/or discriminative power of each test item or scale score. This approach allows for the interpretation of test performance to include and accommodate for key individual different factors and to modify the sensitivity and specificity of each test item or scale score according to the circumstances of the individual respondent.

CONCLUSION

In summary, the present study identified seven primary factors that underpin to the cognitive profile of stroke patients at the sub-acute (<3 months) and chronic (~9 months) stages, post-stroke, reflected by the stroke patient's performance on the BCoS (Humphreys et al., 2012). In the sub-acute stage, the factors were largely reflected by clusters of test variables that were anatomically-linked, while in the chronic stage, the factors reflected clusters of test variables that were functionally-linked, indicating that cognitive performance after the initial stroke changes over time where domain-specific cognitive deficits are more evident. As a result of this finding, further interest would be to examine the underlying factors contributing to the changes of cognitive performance across these two time periods. In the next chapter, we will be exploring the underlying factors in the changes in the cognitive performance.

Table 7. *Established Factors from Sub-acute and Chronic stage, and their Relation to Left Hemisphere and Right Hemisphere Lesion Patients*

	Sub-acute (<3 months)				Chronic (~9 months)			
	Left (*n*=99)	Right (*n*=168)			Left (*n*=78)	Right (*n*=116)		
Factors	$\bar{x}$ (SD)		*t (df)*	*p*	$\bar{x}$ (SD)		*t (df)*	*p*
1	**.24 (.71)**	**.38 (.59)**	**- 1.68 (265)**	**.095***	**- .04 (.97)**	**.32 (.81)**	**- 2.8 (192)**	**.006***
2	.25 (.74)	.35 (.81)	- .99 (265)	.324	**- .24 (1.3)**	**.18 (.57)**	**- 2.64 (97.54)**	**.01***
3	**- .44 (.51)**	**.37 (1.17)**	**-7.8 (248.23)**	**< .001***	.06 (.95)	.14 (.74)	- .66 (137.58)	.509*
4	.07 (1.00)	1.18 (.88)	- .91 (265)	.363	.17 (.9)	.17 (.76)	.05 (192)	.963
5	- .04 (1.01)	.01 (1.00)	- .43 (265)	.671	**- .27 (.48)**	**.29 (1.35)**	**- 4.08 (154.77)**	**< .001***
6	- .02 (.9)	.08 (.99)	- .78 (265)	.438	.13 (.78)	- .06 (.91)	1.51 (192)	.133
7	- .09 (.77)	- .01 (78)	- .79 (265)	.432	.09 (1.08)	- .07 (.59)	1.32 (192)	.187

Note: *t*-tests significant at $p < 0.05$ (2-tailed) are in bold. Values where equal variance not assumed are marked with *

Established factors from sub-acute stage: F1 = Left hemisphere lesion, **F2** = Memory, **F3** = Spatial attention, **F4** = Controlled attention, **F5** = Attention to detail, **F6** = Response suppression/Executive function, **F7** = Attentional capacity during selection. **Established factors from chronic stage**: **F1** = Memory, **F2** = Language processing, **F3** = Praxis, **F4** = Controlled attention, **F5** = Spatial attention, **F6** = Response suppression, **F7** = Visual-attention capacity after left hemisphere lesion

Table 8. *An Overview of Stroke Survivors Performance on BCoS across time (sub-acute & Chronic)*

BCoS		*PCA Factors*	**Factor 1**		**Factor 2**		**Factor 3**		**Factor 4**		**Factor 5**		**Factor 6**		**Factor 7**	
Domains	***Sub-domains***	***Variables***	1	2	1	2	1	2	1	2	1	2	1	2	1	2
LANGUAGE	**Spoken**	Picture naming (PIC)	**0.72**	**0.467**		**0.497**		**0.414**								
		Sentence construction (SNC)	**0.689**			**0.64**										
	Written	Sentence reading (SNR)	**0.822**			**0.855**										
		Nonword reading (NWR)	**0.765**			**0.756**										
		Word/nonword writing (WNW)	**0.693**			**0.623**										
NUMBER		Number reading (NMR)	**0.832**			**0.766**										
SKILLS		Number writing (NMW)	**0.736**			**0.531**		**0.51**								
		Calculation (CAL)	**0.569**					**0.426**								
PRAXIS		Complex figure Copy (CFC)	**0.538**				**-0.453**	**0.461**								
		Complex figure Copy (CFC: Asymmetry)					**-0.768**					**-0.571**				
		Multiple object use (MOU)	**0.456**		**0.471**			**0.582**								
		Gesture production (GEP)	**0.654**		**0.442**	**0.401**		**0.605**								
		Gesture recognition (GER)	**0.541**					**0.731**								
		Gesture imitation (GEI)	**0.602**					**0.633**								
MEMORY	**Short term**	Immediate free recall (IMFR)		**0.819**	**0.732**											
		Immediate recognition (IMR)		**0.824**	**0.789**											
	Long term	Delayed free recall (DEFR)		**0.793**	**0.73**											
		Delayed recognition (DER)		**0.718**	**0.756**											
	Episodic	Task recognition (TAR)	**0.471**	**0.448**	**0.636**			**0.44**								

BCoS		*PCA Factors*	**Factor 1**		**Factor 2**		**Factor 3**		**Factor 4**		**Factor 5**		**Factor 6**		**Factor 7**	
Domains	***Sub-domains***	***Variables***	1	2	1	2	1	2	1	2	1	2	1	2	1	2
ATTENTION	**Spatial**	Apple cancellation (APC: FP Right)									**0.934**			**-0.822**		
&		Apple cancellation (APC: FP Left)					**0.428**				**0.876**	**0.636**		**-0.604**		
EXECUTIVE		Apple cancellation (APC: Egocentric neglect)					**0.731**					**0.63**				
FUNCTION		Apple cancellation (APA: Allocentric neglect)					**0.743**					**0.734**				
		Left visual extinction (LVE)													**0.504**	
		Right visual extinction (RVE)													**0.607**	**0.651**
		Left tactile extinction (LTE)										**0.666**			**0.574**	
		Right tactile extinction (RTE)													**0.702**	**0.715**
	Controlled	Auditory attention (AUD)	**0.52**		**0.404**				**0.451**	**0.648**						
		Auditory attention (AUD: FP)											**-0.76**	**-0.46**		
		Auditory attention (AUD: Omission)							**-0.788**	**-0.628**						
		Auditory attention (AUD: Idx.)							**-0.733**	**-0.754**						
		Auditory attention (AUD: Working memory)							**0.6**	**0.758**						
		Rule finding (RUL)		**0.522**									**0.449**			

Factor loading Legend

⬜	🟨	🟨	🟧	🟧	🟥	🟥
< .4(-.4)	.4 (-.4)	.5(-.5)	.6(-.6)	.7(-.7)	.8(-8)	.9 (-.9)

***Note: 1** = Sub-acute stage (<3months, n=743), **2** = Chronic stage (~9 months, n=349)*

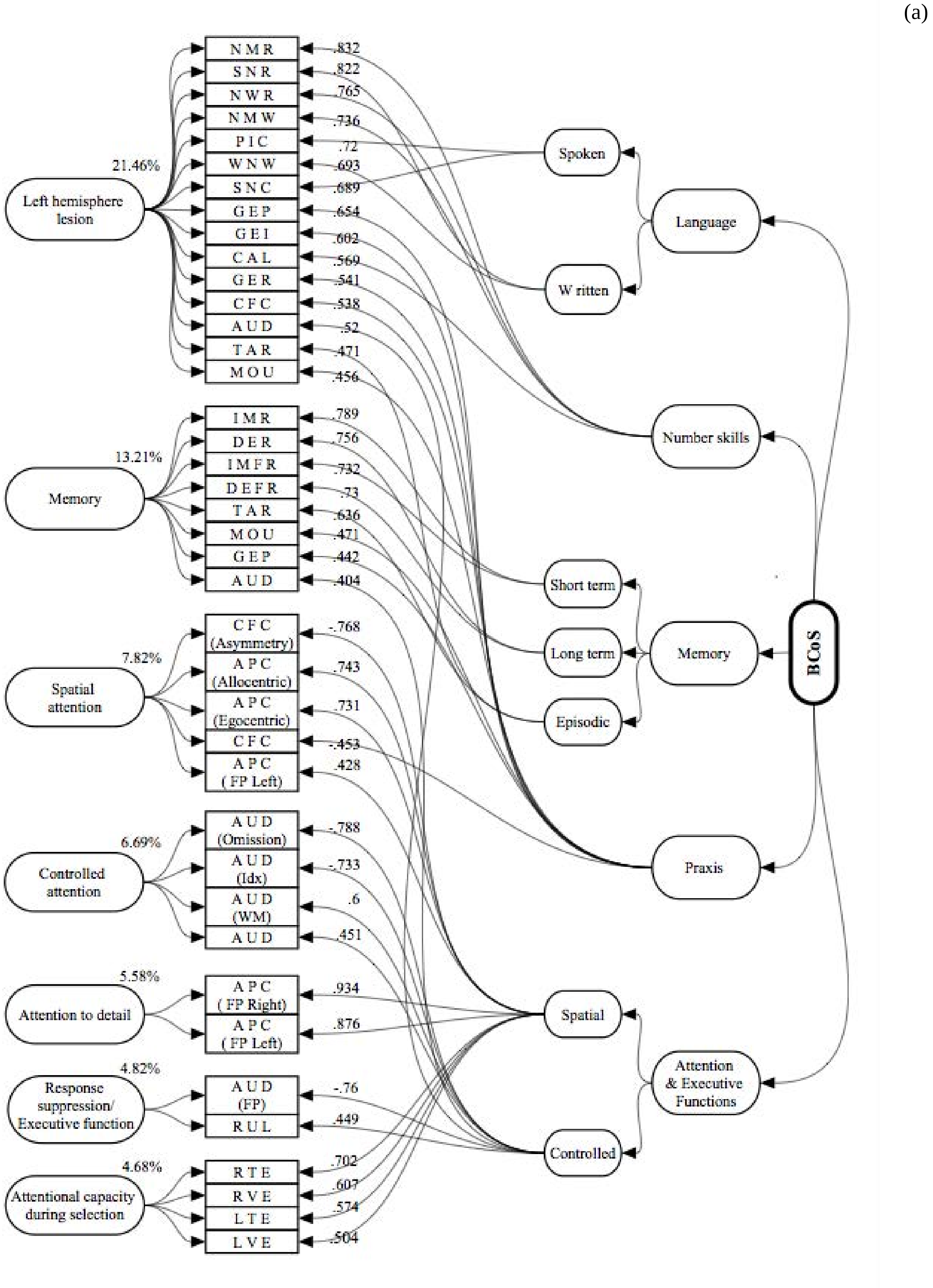
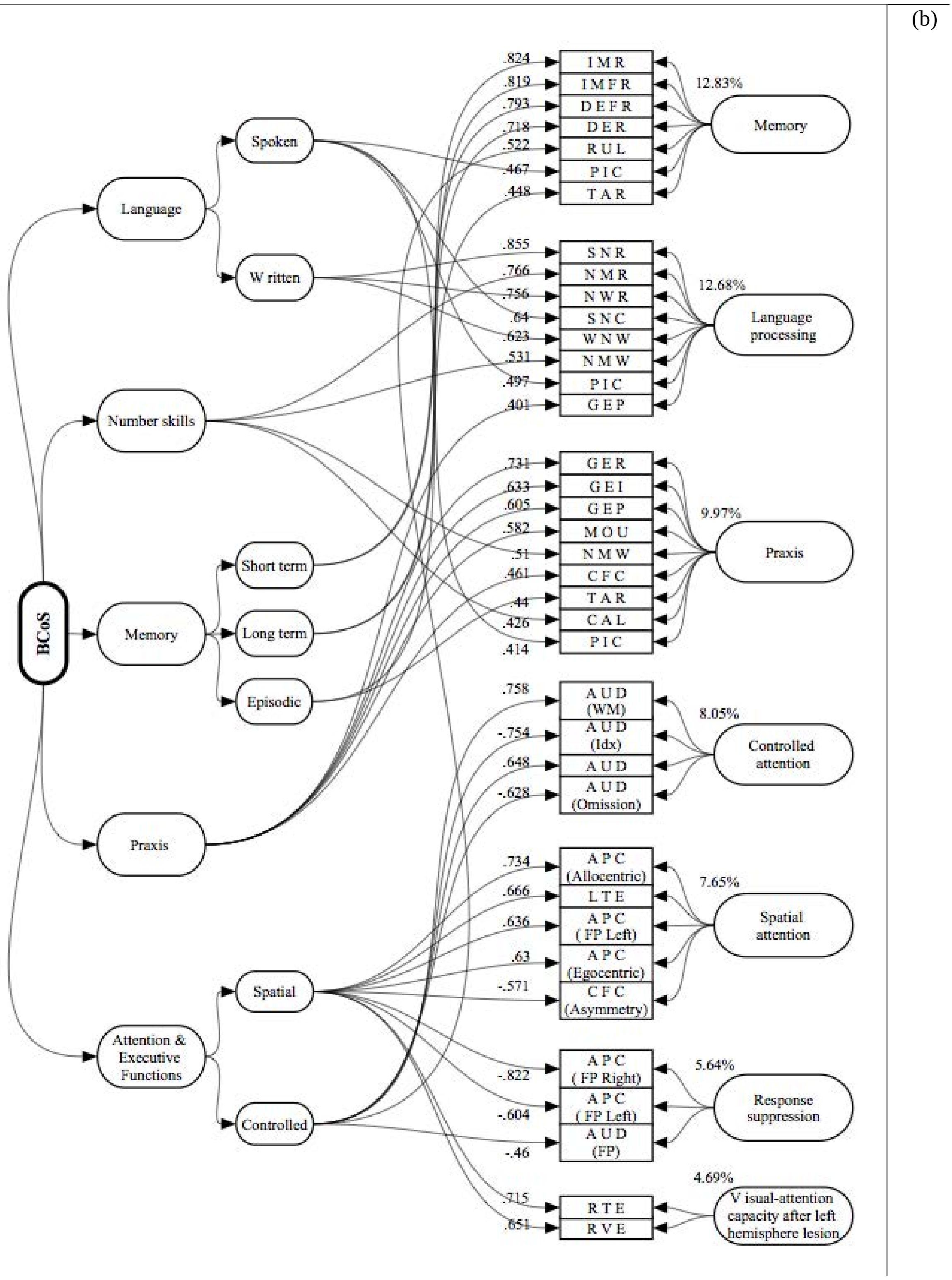


Figure 1. The underlying factors (and the associated (BCoS) variables) in the cognitive abbreviations, refer to Table 8 (page 73-74).



profile of stroke survivors, in the sub-acute (a) & chronic (b) stage after stroke. For

CHAPTER 3

UNDERLYING FACTORS CONTRIBUTING TO THE CHANGES IN COGNITIVE PERFORMANCE BETWEEN 3 MONTHS AND 9 MONTHS AFTER STROKE

ABSTRACT

INTRODUCTION: Although there has been some progress in identifying the factors that predict the prognosis of cognitive disorders post-stroke, the assessments of the cognitive predictors of recovery have focused on the predictive validity of individual tests addressing isolated impairments, in particular cognitive domains. Here, we present the underlying factors contributing to the changes in cognitive performance across two periods post-stroke. **METHOD:** The underlying factors contributing to the changes in cognitive performance between the 1) sub-acute (<3 months) and chronic (~9 months) stage, post-stroke, were examined using the Birmingham Cognitive Screen (BCoS: Humphreys, Bickerton, Samson, & Riddoch, 2012) via Principle Component Analysis (PCA). BCoS is a cognitive screen that cover 5 areas of cognition primarily affected by stroke: i) attention and executive function, ii) language, iii) memory, iv) number processing and v) praxis and was designed to measure domain-specific and domain-general deficits. **RESULTS:** A varimax rotated PCA was conducted on a set of 331 stroke survivors, revealing nine factors. The largest factor (motor output processes of post-stroke) reflected physical abilities by cutting across several test domains, while other factors better represented specific aspects of cognition (memory, working memory, competition for selection, attention to local detail, sustained attention, spatial attention). In addition, some of these factors were further fractionated to distinguish classic neuropsychological syndromes (speech output, verbal retrieval). **CONCLUSION:** The factor structure of the change score suggests that recovery is more compartmentalised.

INTRODUCTION

It is well established that cognitive impairments can be prevalent in the sub-acute stage after stroke (Jaillard, Naegele, Trabucco-Miguel, LeBas, & Hommel, 2009). While many of these deficits can show a natural process of resolution over time (Black., et al 1995; Campbell & Oxbury, 1976; Cassidy, Lewis, & Gray, 1998; Colombo, De Renzi, & Gentilini, 1982; Karnath, Rennig, Johannsen, & Rorden, 2011; Samuelsson, Jensen, Ekholm, Naver, & Blomstrand, 1997; Stone, Patel, Greenwood, & Halligan, 1992), many deficits persist and lead to long-term demands on stroke services and carers. The factors that predict whether the cognitive impairments resolve or persist are still far from understood. Several studies indicate that the persistence of the deficits can be indicated by the initial cognitive profile of the patients (Bickerton et al., 2015; Nys et al., 2005), or by the site of the lesion (Chechlacz, et al., 2012; Karnath et al., 2011), independent of effects of the size of the lesion. However, the analysis of the cognitive predictors of recovery have focused on the predictive validity of individual tests addressing isolated impairments (e.g., neglect by Verdon, Schwartz, Lovblad, Hauert, & Vuilleumier, 2009, executive dysfunction by Miyake et al., 2000), in particular cognitive domains, and not on whether there are underlying (latent) factors that are critical.

Nys et al. (2005) examined the predictive value of domain-specific cognitive disorders in relation to long-term cognitive and functional outcomes. They employed stepwise multiple logistic regressions to identify the independent predictor variables (i.e., demographic, clinical, neuropsychological and neuroimaging factors) in relation to long-term cognitive impairments (examined using a follow-up neuropsychological examination) and functional impairments (measured with modified Barthel Index and the Frenchay Activities Index). Areas under the receiver-operator characteristic curves were used to compare the predictive value of three models: i) medical model (included demographic data, pre-stroke vascular risk factors, neuroimaging and medical factors obtained at hospital admission), ii) cognitive model (included data covering seven different cognitive domains) and, iii) a combined model (included medical and cognitive predictors). Nys and colleagues found that impairments in early abstract reasoning and executive functioning were important predictors of long-term cognitive impairment. In contrast, inattention and perceptual disorders were important in predicting long-term functional impairment. The authors concluded that cognitive impairments at an acute stage could provide important prognostic information on both long-term cognitive and functional outcomes. However, the generalisation of these results to the stroke population at large can be questioned, as they only sampled patients with relatively mild deficits.

Bickerton et al. (2015) examined a wider group of patients who were tested at a sub-acute stage (<3 months post-stroke) and at longer-term follow-up (~9 months) using the BCoS battery (Humphreys, Bickerton, Samson, & Riddoch, 2012). Along with the predictive validity of domain-specific deficits (e.g., in spatial attention and apraxia; see Bickerton et al., 2012, 2011), Bickerton et al. (2015) highlighted the importance of co-occurring deficits for predicting outcome. For example, the presence of a domain-specific symptom such as unilateral neglect was reliably linked to outcome, this relationship increased significantly in the presence of a 'domain general' deficit (e.g., in executive function). The results indicate the importance of considering clustering's of abilities that together disrupt cognitive function.

Massa et al. (2015) extended the analysis of the BCoS by carrying out a graph model analysis, which assesses the relations between the different tests comprising the test battery. They showed that the relations between tasks within a given cognitive domain (e.g., language) changed considerably when the relations across all the tests in the battery were considered so that (e.g.) executive and other domain-domain general cognitive functions were taken into account. One limitation of graph model analyses, however, is that they are confined to analysis of the relations between the component tests in a test battery, but do not elucidate the factors that might underpin the relations between the tests. In contrast to this, in the previous chapter (see in this Volume: Chapter 2), we assessed the BCoS data using a Principal Components Analysis (PCA), which attempts to highlight latent factors that may contribute to several different tests. This study identified seven principle factors as underpinning cognitive performance at both stages, sub-acute stage post-stroke (<3 months) and at a chronic stage (~9 months). Some of the factors appeared to reflect the neuroanatomical site of lesion (a general ‘left hemisphere’ component) and some reflected cognitive components cutting across individual tests (see Table 1 for a list of factors identified at sub-acute and chronic stages in Chapter 2). These authors suggested that the common factors reflected both domain-specific deficits (e.g., an impairment in long-term memory) and domain general factors (e.g., sustained attention).

In the present study we attempted to assess, not the relations between the factors determining performance at the sub-acute and chronic stages post-stroke, but rather, what the underlying factors contributing to the changes in cognitive performance across the two test periods are. Are there particular underlying factors that relate to the cognitive changes that take place across this period? The cognitive profiles of the patients were assessed using the BCoS

(Humphreys et al., 2012) which covers 5 areas of cognition: i) attention and executive function (including controlled and spatial attention), ii) language (written, spoken, production, comprehension), iii) memory (immediate, delayed, recall and recognition), iv) number processing (comprehension, calculation, and production) and v) praxis (single, multiple actions, and constructional abilities). Unlike other screens currently used to analyse cognitive deficits after stroke – for example the Addenbrooke's Cognitive Examination III (ACE-III: Hsieh, Schubert, Hoon, Mioshi, & Hodges, 2013), the Montreal Cognitive Assessment (MOCA: Nasreddine et al., 2005) and the Mini-Mental State Examination (MMSE: Folstein, Folstein, & McHugh, 1975) the BCoS is designed to measure deficits that are prevalent after stroke (e.g., apraxia, neglect, poor number processing, none of which are specifically assessed in these screens). In addition, the BCoS is designed to minimise the impact of impairments in language and spatial neglect on tests not aiming to examine these factors. For example, tests not evaluating language use short, high frequency words and forced-choice tests which can be passed by aphasic patients; tests not assessing spatial processing use vertical arrays and multi-modal presentation conditions to minimise the impact of unilateral neglect. Here, we used this instrument to assess the underlying factors that determine the cognitive profile of factors that change across time.

We aimed to evaluate whether there is a pattern in the changes of the test scores from a sub-acute stage (<3 months) to the chronic stage (~9 months). The issue was addressed by undertaking a PCA on the longitudinal changes in the cognitive performances between the initial testing and follow-up testing. PCA provides an effective method of identifying the latent components that underlie a correlation matrix. In terms of the BCoS, PCA would identify how sub-tests cluster together and allow for speculation regarding how the clusters of sub-tests might relate to the fractionation of cognition within processing modules. The PCA of change score (i.e., the difference between acute and chronic sub-tests scores) would identify clusters of tests that evidence similar patterns of change over time and allow for speculation regarding the recovery or deterioration of the cognitive processing modules. No other methods were considered. The changes in the cognitive performance were calculated by comparing the differences in the scores (difference scores) from session 1 (initial testing, <3 months) and to session 2 (follow-up, ~9 months), post-stroke.

Table 1. *Established Factors from the Sub-acute stage and Chronic stage (Chapter2) and, the Recovery.*

Factors	Sub-acute (*n*=763)	Chronic (*n*=349)	Recovery (*n*=331)
1	Left hemisphere lesion	Memory	Motor output processes of post-stroke
2	Memory	Language processing	Memory
3	Spatial attention	Praxis	Speech output
4	Controlled attention	Controlled Attention	Working memory
5	Attention to detail	Spatial Attention	Competition for selection
6	Response suppression/ Executive function	Response suppression	Attention to local detail
7	Attentional capacity during selection	Visual-attention capacity after left hemisphere lesion	Sustained attention
8			Verbal retrieval
9			Spatial attention

Note: **Sub-acute** = <3 months, **Chronic =** ~9 months, **Recovery =** difference between sub-acute and chronic stage post-stroke

METHOD

Patients and materials

The dataset contained a set of calculated difference scores for 331 stroke survivors who participated in the BCoS trial (http://www.bucs.bham.ac.uk). The BCoS trial consisted of two sessions: *Session 1* (initial testing**)** - stroke victims completed the BCoS screen <3 months post-stroke and *Session 2* (follow-up) **-** stroke survivors completed the BCoS screen ~9 months dated from their initial BCoS testing. For the initial testing, stroke victims were recruited if they were medically stable, within 3 months of their latest stroke, and able to provide informed consent. Diagnosis of a stroke was confirmed on the basis of clinical assessments and Computerised Tomography (CT) scans (when possible) conducted by the clinical team in the stroke units. The inclusion criteria for the patients were: i) sufficient English comprehension to understand the primary tests in the BCoS screen, and ii) could concentrate for an average of 30min (as judged by the clinical team and the examiner). The BCoS screen took approximately 1 hour for completion depending on the patient's performance. However, patients were given breaks when or if appropriate to minimise the effects of fatigue or motivation on performance. The neuropsychological testing was conducted by trained examiners (see later for details, page 86) at the stroke units, in most cases by the patient's bedside. Informed consent was obtained according to the approved ethics protocols of the U.K National Research Ethics Committee from all participants before inclusion in the study.

In the follow-up testing session, participants received the same neuropsychological screen as in the initial testing session, and there was no feedback from the initial testing session.

The data were typically collected during a home-visit to individuals who agreed to participate in the follow-up session, with a minority of tests either done in a nursing home (if the stroke survivor had moved to such a location) or at the School of Psychology, University of Birmingham.

The examiners responsible for conducting the BCoS were trained on the tests and were either occupational therapists and/or stroke researchers such as doctoral researchers and research assistants from University of Birmingham. These examiners had all attended and participated in a full day's BCoS training course and successfully completed the given assessments that were supported by the BCoS team.

In the dataset, there were 47 variables including: i) Patient's socio-demographic data; age, gender, handedness, level/years of education and ethnicity, and ii) Patients' clinical information such as their previous medical history, type of stroke and lesion location. This information was obtained from the hospital clinical notes. For the demographic and clinical details of patients included in this dataset, see Table 2. The vital information in the dataset was the iii) Behavioural variables.

Behavioural variables comprised of the cognitive outcome that is the difference scores calculated from the initial and follow-up BCoS test scores. **Cognitive outcome**. The BCoS battery consists of 22 cognitive tests covering 5 cognitive domains: i) attention and executive function, ii) language, iii) memory, iv) number skills, v) praxis and action. Within these domains other sub-domains can also be distinguished: i) attention domain: spatial/controlled attention, ii) language domain: written and spoken stimulus and response; iii) memory domain: immediate and delayed recall and recognition, and iv) apraxia domain: constructional and limb apraxia. Generally, high scores reflect better performance, though in some cases (e.g., when difference scores are taken across two test conditions), a higher score can indicate worse performance. The tests scores are evaluated and reported for case management at a domain-specific level using a visual snapshot of the cognitive profile for a given patient (see Humphreys et al., 2012), supporting the rapid interpretation and understanding of the patients' cognitive skills. Humphreys et al. (2012) report the data on inter-rater reliability and validity, along with a further description of the tests (see also http://www.cognitionmatters.org.uk). A brief description of the BCoS tasks, according to the impairments assessed, is given in Appendix A. An overview of the BCoS design (sub-tests and the associated scores included in the analysis), relative to the cognitive impairment, is also provided in Appendix A (Table A1).

Table 2. *Demographic and Clinical Details of the Stroke Patients in the Initial Session and Follow-up Session*

	Initial testing (<3 months)	Follow-up testing (~9 months)
Patient demographic detail		
Time post stroke (days; SD)	25.45 (20.24)	279.56 (28.07)
Mean age (SD)	69.12 (13.04)	69.93 (13.17)
Gender (F/M)	139/192	
Handedness (L/R/Ambidextrous)	36/ 286/ 9	34/ 290/ 7
BCoS Hand (L/R/Ambidextrous)	62/ 268/ 1	56/ 274/ 1
Ethnicity	White Caucasian = 316/ Asian-Pakistani = 4/ Black-African/Caribbean = 10/ Other black background = 1	
Level of education	Primary School = 5/ Secondary school =223/ College = 60/ Non-University diploma = 11/ University degree (undergraduate & postgraduate) = 32	
Years of education: Mean (SD)	11.71 (2.85)	
Patient clinical detail		
Previous medical history	No known history = 225/ Previous stroke or TIA = 86/ Head injury = 3/ Dementia = 2/ Brain tumour = 0/ Encephalitis = 0/ Other = 15	
Type of stroke	TIA = 8/ Subarachnoid haemorrhage = 4/ Intracerebral haemorrhage = 45/ Ischemic stroke = 256, Other = 3 (subdural bleed, subdural hematoma and meningioma)/ Unknown = 15	

Note: **L** = Left hand, **R** = Right hand, **BCoS hand** = The patient was asked to write his/her name with his/her left and right hand and the examiner judges which is the best hand to use for further testing.

Table 3. *BCoS assessments: mean and standard deviation (SD), along with the cognitive statues of the stroke patients*

	Cut-off points across age groups			Sub-acute			Chronic			Recovery			Cognitive status	
Variables	≤64	65-74	≥75	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*	Imp.	Det.
Language														
Picture naming	11	11	10	10.94	3.51	330	11.92	2.74	329	0.94	2.45	331	160	60
Sentence construction	8	8	6	7.06	1.74	316	7.52	1.24	326	0.68	1.73	327	101	27
Sentence reading	42	42	41	37.35	9.72	321	39.43	7	321	2.04	8.41	327	133	49
Nonword reading	5	4	4	4.48	1.96	319	4.82	1.8	322	0.38	1.45	326	104	47
Word/nonword writing	3	3	3	3.3	1.67	315	3.61	1.54	318	0.34	1.27	328	115	59
Number skills														
Number reading	8	8	8	7.84	2.28	310	8.41	1.6	316	0.7	2.43	324	94	28
Number writing	5	5	3	3.94	1.61	318	4.34	1.3	317	0.37	1.45	328	86	36
Calculation	2	2	2	2.66	1.39	314	2.88	1.29	320	0.27	1.21	328	113	67
Praxis														
Complex figure copy	42	41	37	35.46	10.41	314	38.77	8.49	315	3.3	11.48	327	212	92
Complex figure copy (asymmetry)[a]				-0.65	3.69	313	-0.07	2.82	315	0.55	3.25	327	151	117
Multiple object use	11	10	10	10.36	3.12	321	11.18	2.35	325	0.93	3.87	331	111	44
Gesture production	10	9	9	10.65	2.5	327	11.08	1.74	325	0.36	2.64	331	111	62
Gesture recognition	5	5	4	5.14	1.1	325	5.34	0.98	325	0.19	1.57	331	113	68
Gesture imitation	9	9	9	9.4	2.77	326	10.33	2.12	322	0.79	3.14	331	161	83

Table 3. *(Continued)*

	Cut-off points across age groups			Sub-acute			Chronic			Recovery			Cognitive status	
Variables	≤64	65-74	≥75	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*	Imp.	Det.
Memory														
Immediate free recall	6	6	3	6.41	3.35	317	7.13	3.32	325	0.88	3.08	327	187	119
Immediate recognition	13	13	11	12.09	2.93	329	12.61	2.52	329	0.51	2.62	331	148	110
Delayed free recall	8	6	4	7.48	3.96	312	8.14	4.28	323	0.91	3.49	327	182	109
Delayed recognition	13	13	12	12.72	3.07	326	13.2	2.66	327	0.51	3.25	331	128	80
Task recognition	9	9	8	8.64	1.9	315	9.14	1.32	321	0.64	2.63	330	126	62
Attention														
Spatial														
Apple cancellation (FP Right) [a]				1.34	4.66	306	0.92	3.63	313	-0.37	5.25	326	50	53
Apple cancellation (FP Left) [a]				2.72	6.84	306	1.62	5.33	313	-0.99	6.74	326	44	83
Apple cancellation (Egocentric neglect)	<-2 or >2	<-2 or >3	<-2 or >3	1.56	5.34	306	0.78	4.08	313	-0.72	5	326	131	132
Apple cancellation (Allocentric neglect)	<-1 or >1	<-1 or >1	<-1 or >1	1.2	4.32	306	0.53	3.97	313	-0.61	4.38	326	59	87
Left Visual extinction	8	7	7	0.4	1.63	327	0.29	1.33	323	-0.11	1.72	330	36	45
Right Visual extinction	8	8	8	0.07	0.97	327	0.06	0.92	323	-0.01	1.46	330	26	33
Left Tactile extinction	7	7	7	0.38	1.95	324	0.32	1.37	326	-0.06	1.78	330	36	43
Right Tactile extinction	8	8	7	0.06	1.4	324	0.01	1.04	326	-0.05	1.63	330	28	38

Table 3. *(Continued)*

	Cut-off points across age groups			Sub-acute			Chronic			Recovery			Cognitive status	
Variables	≤64	65-74	≥75	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*	Imp.	Det.
Attention														
Controlled														
Auditory attention	51	50	46	43.8	13.52	317	47.13	11.36	324	4.2	14.54	330	174	84
Auditory attention (FP) [a]				3.13	4.97	317	2.02	3.98	324	-1.03	5.26	330	83	130
Auditory attention (omission) [a]				3.44	4.63	317	2.66	4.17	324	-0.69	4.95	330	94	132
Auditory attention (Idx.) [b]	>1	>1	>2	0.87	2.09	279	0.58	1.85	305	-0.2	2.63	320	104	116
Auditory attention (WM)	3	3	2	2.55	0.77	317	2.75	0.6	322	0.23	0.92	330	82	27
Rule finding	<6	<5	<4	7.21	5.59	317	8.73	5.6	316	1.45	4.99	326	171	112

Note: **Max.** = Maximum, **FP** = False positive (response to distractors), I**dx.** = Sustained attention Index, **WM**= Working memory, ***n*** = total number of stroke patients analysed for that variable. **Imp.** = Improvement (number of stroke patients who has improved in the BCoS assessments between the two test periods), **Det.** = Deteriorated (number of stroke patients who has deteriorated in the BCoS assessments between the two test periods).

The cut-off points (impairment = less than given scores, unless otherwise specified) for BCoS variables were obtained from the established BCoS manual (Humphreys et al., 2012). BCoS consists of 22 subtests, covering 5 cognitive domains: i) language, ii) number skills, iii) memory, iv) praxis,

v) attention & executive function. For the purposes of PCA, we only used 33 BCoS scores (variables; derived across 32 sub measures). This was mainly to reduce the number of variables.

[a] There are no established norms for these variables (the asymmetry score for Complex Figure Copy was calculated for the BCoS dataset used in this thesis; it is not part of the original BCoS Manual). [b] Sustained attention index is calculated by the difference between the total number of correct responses in block 1 *minus* the total number of correct responses in block 3. If stopped after block 1 or 2, indexed as N/A

STATISTICAL ANALYSIS

First, we computed the difference score for the BCoS assessments taken at the sub-acute and chronic stages. The difference score indicated the amount of change between two test occasions. Second, these raw differences in the BCoS variables were converted into Z-scores based on the mean and standard deviation of individual tasks for the patient group. Z-score is the number of standard deviations a raw score is from the group mean. For example, in this case, if a Z-score yields a value of Zero, the raw score is equal to the group mean and if the Z-score transformation yields a positive value, the raw score is above the group mean (indicating good performance by the stroke patients) whereas a negative Z-score means that the raw score is below the group mean (indicating poor performance/ impairment by the patients). Subsequently, these Z-scores were entered into a ***Principal Components Analysis.*** After factor extraction, an orthogonal varimax rotation was performed on factors with eigenvalues ≥ 1.0. This procedure reduced the number of variables with high loadings on each extracted factor and allowed for a more straightforward interpretation of which cognitive domains/impairments were represented by the different factors. Other rotations were not explored. Missing data were controlled through listwise deletion to provide a relatively stable dataset for the PCA analysis. All statistical analyses were performed using SPSS 22.0.

Table 4. *Factor loadings for Recovery phase analysed using the Difference scores*

	Factors								
BCoS Variables	1	2	3	4	5	6	7	8	9
Gesture production	.78								
Gesture recognition	.709								
Complex figure copy	.706								
Gesture imitation	.663								
Multiple object use	.608								
Number reading	.574		.465						
Calculation	.554								
Number writing	.517								
Immediate free recall		.746							
Delayed free recall		.698							
Delayed recognition		.69							
Immediate recognition		.684							
Sentence reading			.754						
Nonword reading			.75						
Auditory attention				.818					
Auditory attention (WM)				.791					
Left tactile Extinction					.755				
Right tactile Extinction					.701				
Right visual Extinction					.596				
Left visual Extinction					.545				
Apple cancellation (FP Right)						.9			
Apple cancellation (FP Left)						.854			
Auditory attention (Omission)							.845		
Auditory attention (Sustained attention Idx.)							.781		
Picture naming								.706	
Task recognition	.424							.49	
Sentence construction			.439					.49	
Complex figure copy (Asymmetry)									-.694
Apple cancellation (Egocentric neglect)									.685

Note: Recovery phase is analysed using the differences scores where the patient’s sub-acute scores were subtracted from the patient’s chronic scores. Variable loading |.40| is considered to be part of the component and, loading < .40 are suppressed in this table.

INTERPRETATION OF FACTORS

The contrast between follow-up and initial patient scores

Prior to running the PCA analysis on the Z-Scores of the difference score between the BCoS assessments, a paired-sample *t*-test was conducted, on the raw scores, to compare the difference between the means from the initial and follow-up BCoS assessments. There was a significant difference in the scores for the follow-up test scores ($\bar{x}$ = 8.43, SD = 11.57) and initial test ($\bar{x}$ = 8, SD = 10.68) and, t (32) = 2.44, p = .02. These results indicate that there was a general improvement in performance across the two test times. Summary statistics (mean and SD) of the patients' performance across each BCoS sub-test scores included in these variables are individual cognitive tests in the initial assessment, the ~ 9 months follow-up, and the raw difference scores, alongside number patients who improved and deteriorated on the BCoS assessments are reported in Table 3.

Identifying impairments - primary cognitive factors

Three hundred and thirty one difference scores calculated from stroke survivors who completed the BCoS trial were entered into the PCA. Since the missing values were corrected using listwise deletion, the PCA was conducted only on 306 samples. According to Comrey and Lee (1992), a sample number of 300 is an adequate sample size for this type of factor analysis. Our sample size was adequate for the purpose of this analysis.

Nine factors were retained in the PCA following varimax rotation. Provided that our sample size was > 200, the scree plot test was utilised in conjunction with the eigenvalues to select the number of factors to retain (see, Stevens 2002, for more details). All nine factors had eigenvalues ≥ 1 and they accounted for a total of 56.32% of the total variance. The factor loadings of each of the different BCoS behavioural variables are given in Table 4.

Factor 1 accounted for 12.27% of the variance. The factor consisted of nine test variables (based on the factor loading being greater than 0.40, see, Table 4, for factor loadings), the majority of which were concerned with praxis and also with written production (Complex Figure Copy but also Number Writing) and aspects of working memory and sequencing (Task Recognition, Calculation). It is interesting that changes in these tests captured the largest change across the patients between sub-acute (<3 months) and chronic (~9 months follow-up) performance. Suggesting that natural recovery in praxis is likely also linked to working memory and sequencing, and may be an area that sees substantial natural recovery after stroke. In addition, the majority of the test variables in this component (5 out of 9) reflected physical activity and *improvements* in physical abilities might provide an important contribution to this factor. For these reasons, we refer to this factor as 'Motor output processes of post-stroke'.

Factor 2 ('Memory') accounted for 7.21% of the variance and consisted of four variables each with a loading on tests related to episodic memory (i.e., immediate and delayed memory, free recall and recognition).

Factor 3 ('Speech output'), accounted for 6.20% of the variance. This factor consisted of four BCoS variables related to spoken language for words and numbers and sentence processing (Number Reading, Nonword and Sentence Reading, along with Sentence Construction). It is interesting that the analysis indicates that written and spoken aspects of language show different recovery profiles, with a reliable effect of improving speech output occurring even when variance reflecting improvements in written language is extracted.

Factor 4 (‘Working memory’) accounted for 5.89% of the variance and consisted of two variables from the Auditory Attention task; weighting the measure of overall responses to targets and working memory. Here we note that improvements in working memory over the recovery period should generate general improvements in detecting targets on the task. Interestingly, the analysis indicates that recovery in working memory can improve independently of recovery of episodic memory.

Factor 5, accounted for 5.68% of the variance; this related to the measures of extinction in BCoS and included measures of both left and right-side extinction with both visual and tactile stimuli (four BCoS variables). In *Chapter 2,* the left and the right extinction measures were explicitly separated at both the sub-acute stage (<3 months) and the chronic stage (>9 months). Here, the loading across the side of lesion and the test modality may reflect some common underlying component that leads to improvement, but also a factor that is exclusive to extinction. We suggest that this reflects a factor involved in resolving competition for attentional selection (Factor 5: ‘Competition for selection’). It is noteworthy that this apparent attentional factor shows a pattern of improvement distinct from improvements in written and spoken language production, long-term and working memory.

Factor 6 (‘Attention to local detail’) accounted for 5.64% of the variance and consisted of 2 variables; there was weighting on the number of false positive responses that were made to distractors in the Apple Cancellation task. In *Chapter 2*, PCA extracted a similar factor in the sub-acute sample, which consisted of the same two variables reflecting as one of the most common impairment at the sub-acute stage. Therefore, here, it may alternatively reflect recovery in the ability to pay attention to local detail, required in order not to respond to distractors in the Apples test.

Factor 7 (‘Sustained attention’) accounted for 4.70% of the variance. This factor loaded on sub-components of the Auditory Attention task - the weighting reflecting the measure of sustained attention (weighting: .781) and omission responses to targets (weighting: .845). Note that target omissions should reduce as sustained attention improves. The decomposition of the different aspects of the Auditory Attention task suggests that the working memory and sustained attention factors show a different recovery profile. These factors also loaded on different factors when the data sets were analysed separately at both the sub-acute and chronic stages (*Chapter 2*), supporting the argument that these components can dissociate.

Factor 8 (‘Verbal retrieval’) accounted for 4.59% of the variance and loaded on three test variables all of which involved language processing (Picture Naming, Sentence Construction and Task Recognition). This is an interesting factor as it dissociates from other test variables showing improvement in the language domain (Factor 3). The heavy loading in Picture Naming (weighting: .706) taps into retrieval from stored memory, crystalized intelligence and the other test variables; this can also be argued to be the case for Task Recognition, Sentence Construction, hence, verbal retrieval.

Factor 9 (‘Spatial attention’) accounted for 4.14% of the variance. This factor consisted of variables reflecting spatial attention and neglect through two asymmetry scores (the egocentric asymmetry score calculated for the Apple Cancellation task, and the spatial asymmetry score calculated for the figure copy task). This is interesting as the factor loaded the egocentric asymmetry score and not the allocentric asymmetry score from the Apple Cancellation task. In the sub-acute (<3 months) and chronic (~9 months), both analyses reported a ‘Spatial attention’ factor that consisted of a similar cluster but also involved the allocentric asymmetry score from the Apple Cancellation task. The decomposition of the different forms of neglect of the Apple Cancellation task suggests that the egocentric neglect can improve independently of the allocentric neglect. Also, it supports the argument that both forms of neglect can dissociate (Bickerton et al., 2011; Chechlacz et al., 2010).

There were few variables that have factor loadings greater than 0.40 on more than one factor. Task Recognition fell within Factor 1 (weighting: .424) and Factor 8 (weighting: .49). This is understandable as we propose that Factor 1 is based on the patient making a motor response and the memory for test items may be stronger when combined with a motor response (e.g., one of the items probed in Task Recognition was an apple from the Apple Cancellation task). In addition, we proposed that Factor 8 weights on verbal retrieval, which may also modulate Task Recognition. Alternatively, the loading on Factor 1 may stem from the tasks all being linked to the left parietal cortex and all showing improvement if there is recovery around that brain region. Number Reading loaded on Factor 1 (weighting: .574) and 3 (weighting: .465). The loading on Factor 1 may again be attributed to the tests having a common neuroanatomical underpinning, while the tests linked to Factor 3 stem from this factor reflecting reading.

DISCUSSION

The present study evaluated the underlying factors contributing to the changes in the cognitive performance across two test periods, sub-acute (<3 months) and chronic stage (~9 months) post-stroke. The changes in cognitive performance were addressed by conducting a PCA on the difference scores between the sub-acute and chronic test performance, measured by the BCoS (Humphreys et al., 2012). The results of the PCA analysis suggests that the changes in the cognitive performance of stroke survivors reflected up to nine factors were some of the independence between these factors are consistent with the fractionation of the different cognitive processes.

As depicted in Figure 1, Factor 1 (‘Motor output processes of post-stroke’) captures the largest changes in cognitive performance across the sub-acute and chronic stage post-stroke, accounting for 12.27% of the 56.32% total variance. This factor comprises of nine test variables, and most of these variables were associated with improvement in motor deficits, as it cut across variables testing physical activities across different domains. On one hand, this could be that motor deficits are simpler to detect at the earliest time after the latest stroke, and become the focus of the therapeutic intervention that enhances that particular (neurological) functioning (in this case, motor control abilities exhibited through variables measuring physical activities). On the other hand, given most of the variables loaded in the factor are for testing praxis (5 out of 9), the improvement in physical activities might be the result of Compensatory treatment approaches such as Strategy training. Strategy training is to helps apraxic patients to perform more independently in daily life by teaching them efficient strategies to improve their activities of daily living (ADL) despite the persistent apraxia. The ability to perform these tasks may compensate for the impairment; there by improving the ability of the patients to perform daily tasks, which in turn may help, regain the overall physical abilities of the patients.

The rest of the (eight) factors emerging from the PCA were associated with specific cognitive components and although each of these factors only accounted for small amount of variance, together they explained around 44% of the 56.32% total variance across the patients' performance between the sub-acute and chronic stages. These factors include: memory (Factor 2), speech output (Factor 3), working memory (Factor 4), competition for selection (Factor 5), attention to local detail (Factor 6), sustained attention (Factor 7), verbal retrieval (Factor 8) and spatial attention (Factor 9). Some of these factors identified with some of the established factors from the sub-acute and chronic stage analysis (*Chapter 2*: 'Memory' and 'Spatial attention'). Perhaps, the commonalities between the factors, especially, the factors established at the sub-acute stage is a reflection of recovery/improvement in particular abilities, initially, affected by stroke. However, the interesting aspect of these data was the evidence for greater fractionation of the cognitive processes. The executive function domain separated into two different factors ('Working memory' and 'Sustained attention') although, the variables for both factors were derived from the same BCoS task, the Auditory Attention task. In addition, the language domain, also, loaded into two separate factors, one that involved variables for spoken words ('Speech output') and another that involved variables for processing language ('Verbal retrieval'), distinguishing neuropsychological syndromes. The fractionation of the language domain is in line with the designs of the BCoS sub-tests, that is, to distinguish between particular cognitive processes (receptive and expressive language).

The data here points that independence between these factors, revealed by PCA are consistent with the fractionation of different cognitive components. However, the factor structure of the BCoS needs to be further explored using Confirmatory Factory Analysis (CFA) of the theoretical model described in Figure 1. This would be an important and interesting direction for future research.

Future direction may also consider evaluating changes in cognitive performance exclusively related to stroke. The present study sample consisted of patients with pre-existing neurological conditions (e.g., previous stroke, brain injury etc.) but with the final diagnoses of stroke. The criteria for selection of patients allowed the findings of the present study to be generalised to the population with stroke as a whole. Future study may modify the selection criteria to impose analysis on patients who exhibit only stroke (to be precise, only those patients whose type of stroke has been identified). Although, the result of that would not be generalised to the stroke population as whole, it would provide a stroke-specific picture.

CONCLUSION

In this section (Part 1) of the thesis, we analysed the BCoS battery to understand the cognitive variation in the profiles of stroke. In Chapter 2, we examined the cognitive profiles of a large group of stroke survivors at two test periods, sub-acute (<3 months, 763 patients) and chronic stage (~9 months, 349 patients), using the BCoS battery. PCA analysis with varimax rotation revealed seven principal factors, respectively, highlighting that in the sub-acute profile the factors were neuro-anatomically linked, whereas, in the chronic stage, the factors better represented functional impairments. In the current chapter, we examined the cognitive profile of the recovery phase (331 patients) by conducting a PCA on the changes in cognitive performance between the sub-acute and the chronic stage. The analysis revealed nine principal factors, ranging from physical abilities (the largest factor) to factors that reflected neuropsychological syndromes, suggesting that recovery is more compartmentalised.

Although all three stages of stroke consist of different patterns of the cognitive profile, one of the similarities across the 3 cognitive profiles is the factor ‘Spatial attention’. This factor is made of variables associated with spatial attention (Apple Cancellation task; attention and executive domain) and constructional tasks (Complex Figure Copy; praxis domain) from the BCoS battery. The inter-relationship between these test variables characterise an EF construct. In addition, both tests are not language-laden. The Apple Cancellation and Complex Figure Copy tasks are deemed appropriate for the development of executive measures that are suitable within a stroke population. Therefore, these have been used in part 2 of this thesis.

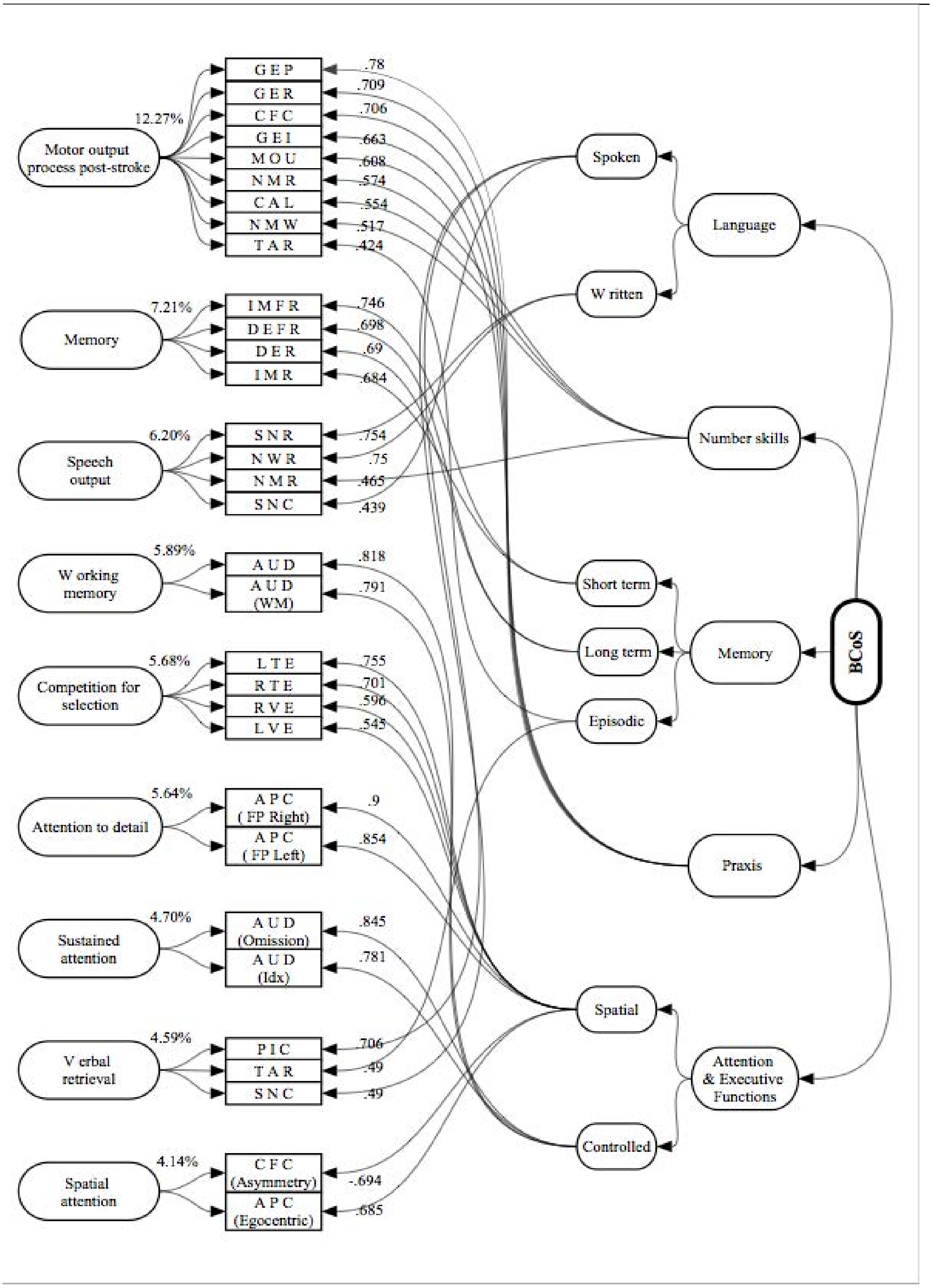


Figure 1. Underlying factors contributing to the changes in cognitive performance across

BCoS		
Domains	**Sub-domains**	Variables (Abbreviations)
LANGUAGE	**Spoken**	Picture naming (PIC)
		Sentence construction (SNC)
	Written	Sentence reading (SNR)
		Nonword reading (NWR)
		Word/nonword writing (WNW)
NUMBER SKILLS		Number reading (NMR)
		Number writing (NMW)
		Calculation (CAL)
PRAXIS		Complex figure copy (CFC)
		Complex figure copy (CFC: Asymmetry)
		Multiple object use (MOU)
		Gesture production (GEP)
		Gesture recognition (GER)
		Gesture imitation (GEI)
MEMORY	**Short term**	Immediate free recall (IMFR)
		Immediate recognition (IMR)
	Long term	Delayed free recall (DEFR)
		Delayed recognition (DER)
	Episodic	Task recognition (TAR)
ATTENTION & EXECUTIVE FUNCTION	**Spatial**	Apple cancellation (APC: FP Right)
		Apple cancellation (APC: FP Left)
		Apple cancellation (APC: Egocentric neglect)
		Apple cancellation (APC: Allocentric neglect)
		Left visual extinction (LVE)
		Right visual extinction (RVE)
		Left tactile extinction (LTE)
		Right tactile extinction (RTE)
	Controlled	Auditory attention (AUD)
		Auditory attention (AUD: FP)
		Auditory attention (AUD: Omission)
		Auditory attention (AUD: Idx)
		Auditory attention (AUD: Working memory)
		Rule finding (RUL)

the sub-acute (<3 months) and chronic (~9 months) stage, post-stroke.

PART 2: The development of executive measures for stroke

The planning/organisation aspect of executive function (EF) is complicated by a number of factors associated with goal-directed behaviour (such as the inability of patients to generate goals, monitor progress, correct their errors, and their lack of insight concerning errors), providing a great challenge to the rehabilitation of their day-to-day routine action. Furthermore, EF has been reported one of the factors predicting long-term cognitive impairments post-stroke (Nys et al., 2005). Therefore, the detection of potential impairments in particular processes of EF would benefit from a detailed study of an individual's performance in a specific task, where the affected process possibly isolated and targeted during rehabilitation. In addition, using singular tasks to extract multiple measures of cognitive deficits will be time efficient in clinical settings, minimising clinicians from undertaking time-consuming and tedious tasks.

CHAPTER 4

A SIMPLE MEASURE OF SYSTEMATICITY IN VISUAL CANCELLATION

ABSTRACT

INTRODUCTION: Visual cancellation tasks are typically used to measure disorders of spatial attention, such as unilateral neglect. The task usually requires the participant to search and strike out the target stimuli and, as a result, the number of cancelled targets and their position can be utilised to detect spatial biases. However, the search organisation of the target stimuli provides the potential to be used for more than a measure of spatial biases, such as providing a measure of executive control over the target search. **METHOD:** In this study, we present an automated scoring procedure as a measure of search organisation (the 'systematicity' index), as a patient cancels targets across a page. We evaluated stroke survivors at an acute stage (<3 weeks, *n*=30) after stroke using the tablet version of the Oxford Cognitive Screen (OCS: Demeyere, Riddoch, Slavkova, Bickerton, & Humphreys, 2015) and subjective ratings from two experienced neuropsychologists were utilised to validate the 'systematicity' index. **RESULTS:** We show that a 'Nearest Neighbour' scoring procedure captures subjective ratings of how systematic a patient is during cancellation. In addition, the automated systematicity score correlates with a measure of executive function (performance on the trails test from the OCS: Demeyere et al., 2015). **CONCLUSION**: The additional information provided by the automated systematicity measure indicates that the score is a useful clinical addition to standard indices of spatial attention (Bickerton, Samson, Williamson, & Humphreys, 2011).

INTRODUCTION

Unilateral spatial neglect occurs in around 60% of right hemisphere stroke survivors (Bickerton, Samson, Williamson, & Humphreys, 2011) and is maintained over the longer term in around 30 - 40% of individuals (Nijboer, Kollen, & Kwakkel, 2013a). In addition, stroke patients suffering from neglect are hospitalised longer than other stroke survivors and face profound problems later in life (Nijboer, Van de Port, Schepers, Post, & Visser-Meily, 2013b; Nys et al., 2005). The main characteristic of neglect is a lack of awareness for sensory events located on the contralesional side of space (e.g., towards the left space following a right-side lesion), so, for example, neglect patients may only eat from one side of the plate, shave or make-up only one side of their face.

Unilateral neglect is very often measured using cancellation tasks, in which patients are asked to mark a set of target items which are presented on the page, intermixed with distractors, examples being the Star Cancellation Task in the Behavioural Inattention Test (BIT: Wilson, Cockburn, & Halligan, 1987), the Apple Cancellation task in the Birmingham Cognitive Screen (BCoS: Bickerton et al., 2011; Humphreys, Bickerton, Samson, & Riddoch, 2012), and the Hearts Cancellation task in the Oxford Cognitive Screen (OCS: Demeyere, Riddoch, Slavkova, Bickerton, & Humphreys, 2015). In such tasks neglect is revealed by a spatial bias in performance in which more targets are detected on the ipsilesional compared to the contralesional side of space (Bickerton et al., 2011). There are also often additional difficulties. For example, neglect has been associated with poor visual memory for targets, so that a patient may return to cross-out targets several times showing poorly organised, perseverative performance (Malhotra et al., 2005). Such results provide evidence that the neglect syndrome comprises more than just lateralised deficits (Husain & Rorden, 2003), and deficits of spatial working memory and/or sustained attention can contribute to the clinical picture.

Although cancellation tasks have been vital for measuring spatial biases in attention, these tasks have the potential to be used for more than measures of spatial bias. Notably, cancellation performance may be structured or unstructured in patients, and the organisation of the search for targets may be an important index of how well a patient can plan a sequence of actions. Impairments in planning have typically been associated with executive control of attention and with frontal lobe lesions in patients. Patients with frontal lobe damage are often described as lacking initiative and the organisational skills required to complete multi-stage tasks (Hanks, Rapport, Millis, & Deshpande, 1999). In the context of neglect, patients with frontal lobe lesions have been shown to be affected by ‘visual clutter’, so that neglect becomes more exacerbated in more complex displays (Husain et al., 2001), consistent with the patients being susceptible to increased planning demands as the complexity of the display increases.

Nature of systematicity in respect to executive function

Executive functioning, mediated by anterior brain regions, is primarily involved in programming and or generating specific goals, and then the monitoring and the regulation of mental activities in respect to the progression of these goals. Hence, executive functioning is considered as a control system overarching a range of skills, often referred as the higher-level cognitive skills that are used to control and co-ordinate other cognitive abilities for goal-directed behaviours during a novel or a difficult situation. The higher-level cognitive skills of the executive system are a set of interrelated functions which include: i) the ability to main attention over a period of time, ii) the competence to reason and solve problems, iii) the ability to plan and organise complex information, iv) the ability to initiate actions, monitors accordingly as-well as the resistance to interference in resource demanding situation, v) the ability to utilise feedback, vi) multi-tasking (i.e., the successful usage of working memory and divided attention), vii) cognitive flexibility (shifting strategies flexibly) (Alvarez & Emory, 2006; Diamond, 2013; Elliot, 2003). These executive skills/processes are interdependent and given that frontal lobes are richly interconnected (Stuss & Benson, 1984) means damage to any of these aspects of the executive system can produce a range of cognitive and or behavioural deficits.

Anderson (2002) proposed a developmentally oriented model of EF. Anderson (2002) model of EF was based on knowledge obtained from studying executive functioning in childhood and adolescent population and prior factor analytic studies (Brocki & Bohlin, 2004; Kelly, 2000; Lehto, Juujärvi, Kooistra, & Pulkkinen, 2003; Levin et al., 1991; Miyake et al., 2000; O'donnell, Macgregor, Dabrowski, Oestreicher, & Romero, 1994; Welsh, Pennington, & Groisser, 1991). Anderson’s model of EF comprised four distinct but related EF domains: i) *attention control* domain that includes selective attention, regulation and monitoring of actions so that plans are executed successfully, and impulse control, ii) *information processing* domain account for efficiency, fluency, and speed of output, iii) *cognitive flexibility* domain includes the ability to generate and develop alternative strategies, shift attention between response sets, multi-tasking and use information from feedback and finally, iv) *goal setting* domain includes the ability initiate actions and develop new concepts as well as the ability to plan in advance and organisation of information for tasks to be approached strategically and efficiently. The Executive Control System by Anderson (2002) suggests that, although the domains are independent and comprise of discrete functions, they must interact cohesively to execute certain tasks, suggesting goal-oriented behaviour. In this model, Anderson places considerable emphasis on the role of 'planning'. Planning is highly dependent upon other executive systems (organisation of complex information in (temporal/causal) order, the anticipation of future outcomes monitoring and execute coordinated actions). In the following, we termed this aspect of executive function as 'systematicity'. Systematicity is the ability to organise information to facilitate the planning and execution of future, goal-oriented behaviours.

In the past, studies have been conducted where the search pattern in cancellation is recorded by asking the participant to change the colour of their pencil upon marking every 10-15 targets (Weintraub & Mesulam, 1988), video recording participants performance on the cancellation task for analysis (Mark, Woods, Ball, Roth, & Mennemeier, 2004; Woods & Mark, 2007) and the examiner observing and recording the predominant search pattern as the participant performs the task (Warren, Moore, & Vogtie, 2008). Clearly, all these methods of data collection are time-consuming and labour-intensive. However, the advent of modern computing technology enables cancellation patterns to be recorded automatically, as a patient cancels potential targets. This offers the potential to measure the planning and organisation of search in a time-efficient manner.

Recently, Dalmaijer and colleagues (2015) developed software for the automated administration and analysis of cancellation tasks. This software allows researchers and clinicians to administer computerised cancellation tasks using stimuli of their choice, and to directly analyse data at their own convenience. The authors also presented two new measures of search organisation: the standardised inter-cancellation distance and the standardised angle (also see Dalmaijer et al, 2015). However, the authors did not provide data on how well the measures conformed to clinical judgements about search organisation, nor did they demonstrate that the organisation measure could serve as a proxy for other indices of executive function. These were the aims of our study.

The present study

In this paper, we present a measure of search organisation (the 'systematicity' index) in cancellation, which correlates with human judgements of how organised a patient is; which generates results that are linked to independent indices of executive function in patients. By adding a new measure of the organisation of search, we can add to the utility of cognitive screening – for example, supporting any diagnosis being made by independent measures of executive function or even reducing the test time if the organisation serves as a reliable proxy for executive function.

To measure cancellation, we chose the Broken Hearts cancellation task from the OCS (Demeyere et al., 2015) – an overall screen of cognition, designed to be applied in acute as well as chronic stroke patients. The Broken Hearts test has been shown to correlate with other standard measures of neglect (Demeyere et al., 2015) and is automated in tablet-based versions of the screen. Here we assessed cancellation performance in relation to a 'Nearest Neighbour' algorithm, designed to index whether patients progressed cancellation through neighbouring items (this would generate a low score indicating highly systematic search) or jotted about the field, not progressing across neighbouring stimuli (which would generate a high score, indicating poor systematicity in search).

In addition, we also evaluated whether our measure of search organisation linked to an index of executive cognitive control taken from a ‘trails’ test of executive function in the OCS (and see Demeyere et al., 2015, for a validation of this measure relative to other indices of executive function). The results highlight that measuring search organisation can be a useful addition to the clinical testing of search, providing an index of executive function in addition to the traditional measure of biases in spatial attention gained through target cancellations and false alarms to distractors (e.g., Bickerton et al., 2011).

We analysed the data from a group of stroke participants who were assessed using the tablet version of the OCS (Demeyere et al., 2015) at an acute stage after stroke. In addition, data for the cancellation task from 52 neurologically healthy controls were acquired to establish a normative measure of ‘systematicity’. We also evaluated the utility of the Nearest Neighbour scoring approach, particularly as to whether the scoring approach results in a logical and theoretically explicable pattern of associations with other cognitive measures. For this comparison, three additional tests were selected from the OCS (Picture Naming task from language assessments, number skill and memory).

METHOD

Participants

Thirty acute stroke patients were recruited from the stroke ward at the John Radcliffe University Hospital, Oxford, as part of a larger trial of cognitive screening after stroke: The Oxford Cognitive Screen (OCS) Trial. Patients were included on the basis: a) the participant should be <3 weeks of confirmed stroke, b) should be able to concentrate for 15 minutes (OCS is designed to be administered in 15 minutes), approximately, judged by the multidisciplinary clinical team and the examiner, and c) able to provide informed consent[1]. The patient cohort consisted of 9 females and 21 males. The patients' age ranged from 44-91 years, with an average age of 76.30 years (SD = 13.05). The average length of education was 11.45 years (SD = 2.28). The mean time of testing the patient was 5.52 (SD = 5.45) days post admission.

A control group of ≥50 years of age was assembled only for the cancellation task as normative data for the automated systematicity measure. The control group consisted of 52 healthy control participants living in the community (Oxford, UK). Participants were unpaid volunteers with no history of neurological disease drawn from a participant panel held in the Cognitive Neuroscience Centre (CNC) at the University of Oxford. There were 30 females and 22 males. The controls' age ranged 51-90 years, with an average of 70.71 years (SD = 8.92). The average length of education was 15.14 years (SD = 4).

---

[1] Since, the assessments were conducted at a very early stage post stroke, some patients had severe language and/or motor difficulties for signing the form and, in such cases, a witness was present during consenting.

Two ‘expert raters’ were also recruited to provide an ‘expert rating’ of how systematic each patient in their completion of the Broken Hearts cancellation task. The experts were independent of the project and each had over 12 years of experience in neuropsychological assessment. They were recruited through word of mouth, with interest for the specific study, and were blind to the patients’ clinical details, as well as patients’ performance on any other measures. These expert ratings are described in detail in the methods section (see page 124).

Standard protocol approval and participant consents

The study was approved by the National Research Ethics service (Ref: 11/WM/0299; Protocol number: RP-DG-0610-10046). For patients and the healthy control participants, informed consent was obtained.

Procedure for data collection

The patient data in this study was collected as part of a large research trial, OCS trial, by trained examiners (researchers, doctoral researchers, and research assistants) involved in the OCS trial at the acute stroke unit at the John Radcliffe hospital, Oxford. The first author, who is also a trained examiner for the OCS trial, did not participate in the acute patients’ data collection. The first author’s responsibilities in the data collection for the present study involved: i) collection of control data from the participant panel at Cognitive Neuroscience Centre (CNC), Oxford University, ii) organisation and the preparation of the patients (*n*=30) and controls (*n*=52) samples used, and iii) scoring the search organisation of each OCS cancellation (patients and controls) following the Nearest Neighbour algorithm (for details see page 118 and page 124-5 for the algorithm).

Materials and procedures

OCS neuropsychological examination. The OCS was developed to assess cognitive deficits after stroke around five domains: Attention and executive function, Language, memory, Number processing and Praxis. The battery consists of 10 tasks, and a task from each domain is utilised to assess the specificity of the Nearest Neighbour measure. The OCS battery was conducted as part of larger study, where the battery was presented in an electronic format on a tablet PC. With the exception of the cancellation task, all other task materials were presented in a portrait format, with the content distributed vertically to minimise effects of neglect. The OCS tasks were implemented in Matlab using PsychToolbox (Brainard, 1997; Pelli, 1997) and were run on a Windows Surface Pro tablet and the participants used a stylus to complete the tasks. Measures of executive function, language, number skills and memory were used as comparisons to assess if the systematicity measure, derived using our Nearest Neighbouring procedure related to other aspects of a patient's cognition. For the purpose of this study, we chose those tests that best represents the proposed domain (see the materials section for further details). Summary statistics of the selected OCS tests, with the average score for neurologically healthy controls is given in Table 1.

All OCS tasks were implemented in Matlab (see above), including the Broken Hearts cancellation task. However, the 'Nearest Neighbour' algorithm was not inherent as part of the original OCS screen (software), for it to be scored in real time. For the purpose of this study, patients' performance on the cancellation test were extracted separately as visual 'plots'. These plots showed the order of cancellation using numbers and red arrows in the direction of proceeding on the test page. The extracted data were used by the first author to score the search organisation of each OCS cancellation (patients and controls), following the Nearest Neighbour scoring criteria (page 124-5). The ‘Nearest Neighbour’ algorithm was developed by the first author, however, the OCS software (including the extraction of raw data) was developed as part of the OCS trial.

1. OCS cancellation task. We used a clinical test typically used to measure unilateral neglect after stroke, the Hearts cancellation task. The test involved a set of ‘complete’ (target) and ‘incomplete’ (distractor) hearts scattered in a random array on an A4 page presented in a landscape orientation. The hearts were one of two sizes, where the larger hearts were approximately 50% bigger than the smaller hearts. The total area of the test-page was divided into ten sections, 2 central (top and bottom), four left (far and near, top and bottom) and four-right (far and near, top and bottom). Each section contained 15 hearts (5 complete and 10 incomplete; 5 right-side opening and 5 left-side opening), making a total of 50 targets and 100 distractors (50 left and 50 right) per sheet (also see Bickerton et al., 2011). The test was presented on a tablet PC. The tablet PC had a 10.6” widescreen display, resulting in the hearts being smaller than the paper-and-pencil version (the smaller hearts were around .4cm and the larger ones were around .7cm). The screen was positioned at the patient’s midline on a bedside desk and the patient was instructed to start cancelling with the stylus pen. The instruction was to strike out all of the complete hearts and not to cancel the incomplete (broken; left or right opening) hearts. Here, the test was conducted on a tablet; this meant that the total number of complete and/ incomplete hearts cancelled was recorded automatically, along with the cancellation order (Figure 1). Participants were given a maximum of three minutes to complete the task. The time limit was not disclosed to the participant before the test, the display was automatically closed at the end of three minutes.

The overall accuracy score corresponded to the total number of targets selected (maximum = 50). The asymmetry score for egocentric neglect (failing to cancel complete items on one side of the page) corresponded to the difference between the numbers of selected targets on the right side and the number of targets selected on the left side of the page (excluding the 2 central columns: maximum = 20). A second score was derived for allocentric neglect (Bickerton et al., 2011; the failure to detect a gap (the broken heart) on the contralesional side of an object). Here an asymmetry score corresponded to the difference between the total number of distractors cancelled with the left opening and the number cancelled with the right opening (total left opening *minus* total right opening). Positive values on the egocentric score indicated that more targets were selected on the right than the left side of the page (left neglect) and negative values indicated the opposite (right neglect). Similarly, positive values for distractor cancellations indicated left-side allocentric neglect; negative values indicated right-side allocentric neglect.

1. Executive assessment. To assess the relationship between the systematicity score and executive cognitive function, the performance of the sub-acute patients on the OCS Trails task was used. The OCS Trails task requires participants to draw connecting lines between simple geometric shapes. There are three parts to this test, two baselines and one experimental task (mixed/switch). The two baseline tests compromise: i) connecting together circles in decreasing order of size in the presence of triangle distractors, and ii) connecting together triangles in decreasing order of size, in the presence of circle distractors. The baselines were compared with a switch task in which participants drew a trail alternating between circles and triangles, each going down in order of size (largest triangle to the largest circles to the second largest triangle to the second largest circle etc.) (Figure 2). The geometric shapes were presented randomly on the central section of the page. Therefore, the trail could be connected correctly without going through any of the other shapes. The Tablet PC timed performance. The effect of switch task is assessed by subtracting performance in the task switching condition from that in the baselines. Here, the subtraction eliminates the effect of spatial biases on performance (shapes can be missed on one side of the page in the baseline or the task switching condition) and provide an executive score.

In all three conditions, there were seven circles and seven triangles on the screen. One point was given for each correct connection (if an error is made at some point, but subsequent performance is correct, the correct connections are acknowledged). Patients scored 1 for each correct connection for the baseline task (maximum = 6, each), and for the switch task (maximum = 13). The executive score is the result of the sum of accuracy in the baseline tasks versus the switch task. In the present study, we correlated the executive score against the automated systematicity score.

3. ***Language assessment.*** Picture Naming – to assess the level of expressive language, a visual object-naming task was used with stimuli with low frequency names. The patient was separately presented with four pictures (grey shaded hand drawings) to name, each on consecutive screens. The patient scored 1 for each correct answer (maximum = 4). Self-correction was permitted and the final answer was taken as the patients' response.
4. ***Number skills.*** The task consisted of two parts:
    i) *Number writing* – the patient was asked to write three numbers on the device (space provided; maximum = 3).

ii) Calculations – the patient was presented with four complex calculations, two additions and two subtractions. The material was presented visually to optimise performance in patients with speech problems. First, the target question was given, centred, on the tablet PC screen for free responses. If the patient could not provide free responses (e.g. due to expressive dysphasia), he/she was asked to select, by pointing, the correct response out of four multiple choices. Patients were not penalised for needing multiple-choice options. A score of one was provided for each calculation (maximum = 4). For this study, we summed both number tasks to derive an overall score for number skill (maximum = 7) to be correlated against the automated systematicity scores.

5. ***Memory.*** Delayed Recall & Recognition – this task consisted of two parts:

i) Verbal memory – at the beginning of the OCS, the patient was given a sentence to read and he/she was reminded to remember the sentence and then the patient was asked to repeat the words at the end-stage of the battery. There were four target words in the sentence. Patients were required to recall the target words in free recall. After this, a verbal recognition test was given, with a multiple-choice assessment provided for each missed or incorrect target word. For each target word, the patient was shown a page with four options distributed vertically: the target word, a semantically similar distractor and two unrelated words. The examiner pointed to each word on the screen in turn and read it aloud. If the patient could recall any of the words from the sentence correctly, their recognition of those words was not assessed. A score of 1 was given for each target word recalled correctly. The total score reflected the number of total correct responses after the multiple-choice options (maximum = 4).

i) Episodic memory – visual episodic memory was also tested on items encountered during the first part of the OCS. On four trials the patient was shown a page with four options distributed vertically, in a portrait format, and he/she was asked which of the stimuli/actions they had seen earlier. The distractors were chosen to be closely related to the correct response (e.g., for a vegetable target other fruits and vegetables were shown). A score of 1 was given for each correct answer (maximum = 4). Scores from the two memory tasks were summed to derive a memory score (maximum = 8), which we correlated with the systematicity score.

Table 1. *Patient Mean and SD for the chosen OCS sub-tests with normative mean*

		Patients		Normative
Sub-tests	Measure	$\bar{x}$	SD	$\bar{x}$
Trails	Executive score	1.17	3.72	1.36
Picture naming	Overall	3.07	.98	3.82
Number skills:		6.13	1.2	-
Number writing	Overall	2.53	.94	2.93
Calculation	Overall	3.6	.56	3.90
Memory:		6.9	1.63	-
Verbal memory	Overall	3.47	1.01	3.72
Episodic memory	Overall	3.43	.97	3.83

Note: The normative data for neurologically healthy controls is adapted from Demeyere et al., 2015. The values for number skills (sum of number writing and calculation) and memory (sum of verbal memory and episodic memory) are unavailable, since, these values were calculated specifically for the present study.

Introducing the Nearest Neighbour measure to the cancellation task.

The subjective scores given by the raters were performed blind as to whether the task had been completed by a patient or a control. The subjective raters were presented with the printed A4 copies of the participants completed Broken Hearts cancellation test. The raters observed the end product (order of cancellation was denoted using numbers and red arrows in the direction of proceeding) and then rated the performance using a scale of 1 to 10, 1 being systematic cancellation and 10 being non-systematic cancellation. Both expert raters followed the same protocol.

Nearest Neighbour measure. An automated systematicity score was derived. This used a simple Nearest Neighbour approach. For each cancellation, we computed the nearest neighbour target to the current target (+1), the next nearest (+2), and then next-to-next nearest (+3) etc. based on the distance between the current and other targets. A score was then given according to the target the participant went to next. Once the next cancellation had taken place, the nearest neighbours were recalculated to provide a score for the next assessment.

When a distractor was cancelled, then that distractor was assigned a number based on the number of nearer targets that were present. Then, once the distractor error was made, the numbers of nearest neighbour targets were calculated, to provide a score for the next response. Perseverations (cancelling the stimuli more than once) took two forms: i) several strokes being made to the same stimulus without moving to the other stimuli, and ii) returning to cancel an already stroked out stimulus. The former perseveration was recorded as zero; the latter was recorded in the same manner as cancelling a new target or distractor (assigned a number based on the number of nearer targets that were present). The final systematicity score was generated by adding the total nearest neighbour cancellation scores divided by the total number of cancellations, complete (target) and incomplete (distractor) hearts. Division by the total cancellation was done to correct for the effects of neglect, where, patients may cancel relatively few targets and so generate a low total systematicity score. Normalising by the total number of items cancelled corrected for this and provided a standardised score independent of the total number of cancellations.

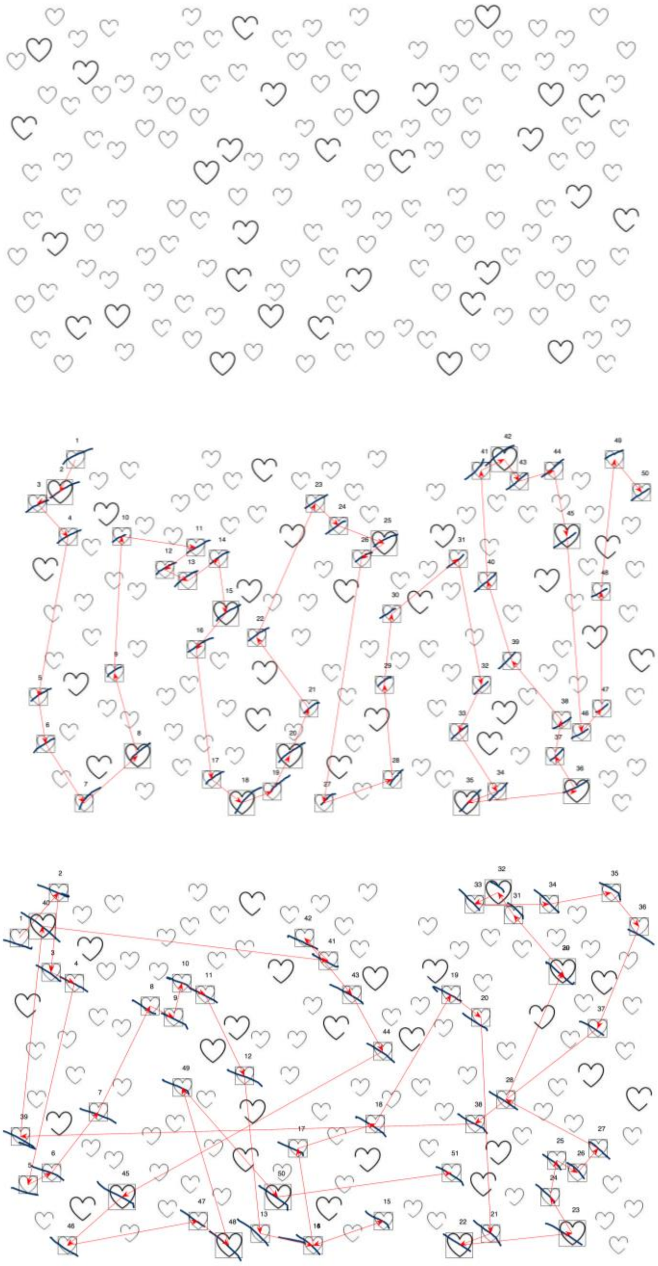


Figure 1. Illustration of the initial Broken Hearts test screen: cancellation task from the OCS (a). Participants are to cancel the complete hearts (targets) and not the incomplete hearts (distractors; left and right opening). According to Nearest Neighbour approach, organisation is systematic when targets are cancelled within the proximal distance (b), and targets cancelled further produce an incoherent/ non-systematic performance (c).

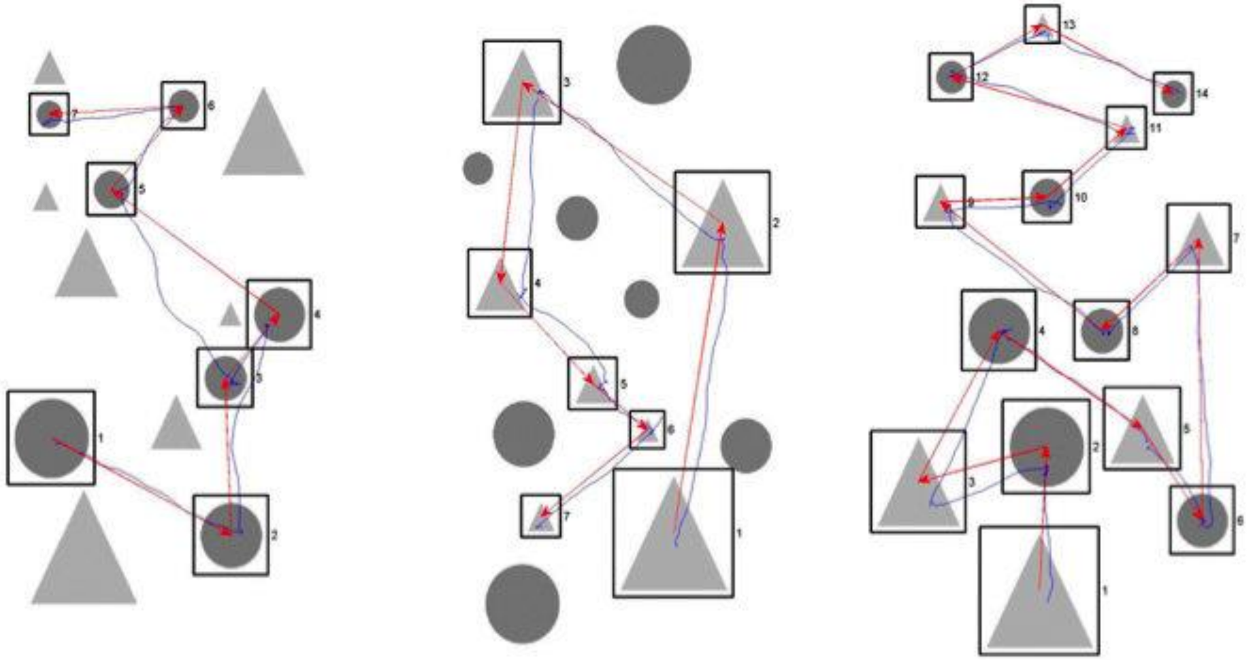


*Figure 2***.** Illustration of the Executive test: trails from the OCS. In the baseline conditions, the task is to connect the circles (a) and the triangles (b) from the largest to smallest. In the switch condition (c) the task is to switch from the largest triangle to the largest circle, to the next largest triangle and so forth. The difference between performance in the switch and the baseline conditions provide an index of the effects of executive load on performance.

DATA ANALYSIS

Descriptive analyses were conducted on all of the cognitive outcomes, and the inference assumptions of the parametric tests were checked. When the data did not meet parametric assumptions then appropriate transformations to the data were made. If the data were not successfully transformed then the appropriate nonparametric test was used.

We evaluated differences among performance of search organisation (the automated systematicity score) between groups (neurologically healthy controls vs. acute stroke patients) and within group (acute stroke patients with neglect vs. without neglect) using an independent *t*-test. In addition, using the healthy controls data, a cut-off score was calculated for the automated systematicity scores, based on 95% confidence interval, suggesting that high systematicity scores reflect poor performance.

The relationship between the automated systematicity score and the expert raters were examined using Pearson's correlation. The inter-rate reliability between expert rater 1 and expert rater 2 was examined using Cohen's kappa test.

Participants with extreme scores (outliers) were removed. Here, the outlier was calculated using the Tukey's (1977) Method (Boxplot). The graphical display makes it easier to understand the information about continuous univariate data (e.g., median, lower quartile, upper quartile, lower extreme and upper extreme of the given data). Weintraub & Mesulam (1988) asserted that erratic search strategy is more present when stimuli are presented in an unstructured array in comparison to a structured array that prompts a more systematic search. Since, our cancellation task is imbedded on an unstructured array, Tukey, is less likely to be influenced to extreme values of the data, in comparison to methods that use sample mean and standard deviation. For all correlations, the value of significance was set at 0.05. The software used was SPSS version 24.

Table 2. *Summary Statistic of the Overall Accuracy for the Participants: group average (SD) for the Broken Hearts tests from OCS*

	Patient (*n*=30)		Controls (*n*=52)	
	$\bar{x}$	SD	$\bar{x}$	SD
	Static scores			
Overall accuracy	28.77	16.72	48.06	1.84
False positive left	1.8	3.23	.06	.24
False positive right	2	3.02	.17	.43
Page-based asymmetry	1.83	6.37	.06	1.42
Object-based asymmetry	- .2	2.51	- .12	.51
	Dynamic scores			
Automated systematicity score	4.65	3.26	2.99	.96

Note: The automated systematicity score is derived using the nearest neighbour measure; low scores indicate good systematicity and high scores indicates poor systematicity in search organisation (see page 124-125, for an explanation on how the automated systematicity score was calculated). ***Score scale:*** score of 10 represents poor systematicity whereas a score of 1 represents optimal systematicity and score >5 represent impairment in performance.

Table 3. *Subjective Systematicity Ratings from two Expert raters*

			Subjective ratings	
Patient	Targets cancelled	Distractors cancelled	Expert 1	Expert 2
1 *	11	13	8	3
2	49	0	1	6
3	46	0	3	7
4	29	0	6	8
5	14	4	9	7
6	43	0	2	4
7	47	2	4	6
8*	4	3	3	2
9*	18	5	5	6
10	32	0	7	8
11	46	0	2	3
12	32	5	6	7
13*	8	13	3	2
14	49	1	1	1
15*	2	4	5	5
16	47	0	3	5
17	31	2	2	3
18*	1	1	5	3
19	44	0	7	8
20	31	3	6	9
21	45	0	2	6
22*	14	25	6	3
23	34	1	3	4
24*	12	12	2	2
25	38	10	5	7
26	50	1	1	2
27*	11	1	6	4
28*	19	8	1	2
29	10	0	3	9
30	46	0	4	6

Note: * patients who showed neglect in the cancellation task. Target cancelled = total number of complete hearts cancelled. Distractor cancelled = total number of broken hearts (broken in the right and left sides) cancelled. Subjective ratings were scored on a scale of 1 to 10, 1 being systematic and 10 being non-systematicity.

RESULTS

Demonstration of the utility of the nearest neighbour approach

First, we conducted an independent sample *t*-test to compare the automated systematicity scores between healthy controls and the acute patients post-stroke. There was a significant difference in the score on the Broken Heart cancellation task between the healthy controls ($\bar{x}$ = 2.99, = .96, *n*=52) and the acute patients' ($\bar{x}$ = 4.65, = 3.26, *n*=30) scores, *t* (31.96) = - 2.72, *p* = .01 (two-tailed), equal variance not assumed. Table 2 presents the summary statistics for the overall accuracy score on the Broken Hearts cancellation task for the healthy participants and the acute stroke patients, along with the false positives for each participant group.

Second, we generated the cut-off for the automated systematicity scores based on data obtained from 52 healthy control participants. The cut-off for impairments reflected scores >95th percentile cut-off >5. Out of 30 acute patients, seven patients showed clinical impairment in the organisation of their cancellation performance.

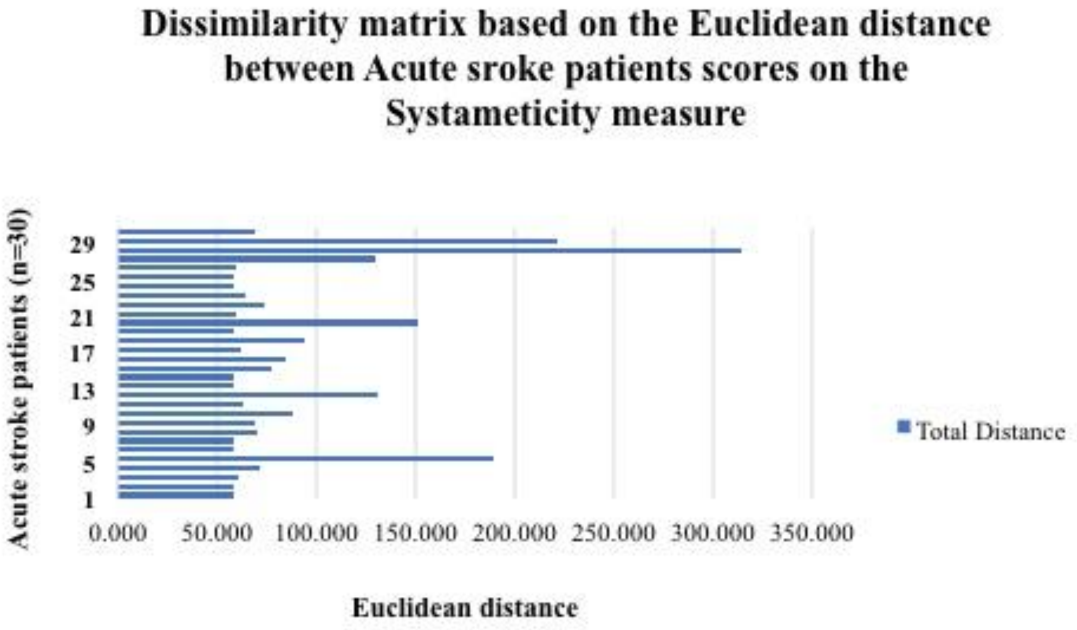
Finally, the automated systematicity scores were also compared across the patients with and without neglect. There was no evidence for a difference in systematicity for the patients with neglect ($\bar{x}$ = 4.74, SD= 4.09, *n*=10) compared to the non-neglect patients ($\bar{x}$ = 4.61, SD = 2.87, *n*=20), *t* (28) = .10, *p* = .92 (two-tailed).

Correlation between systematicity scores and subjective ratings

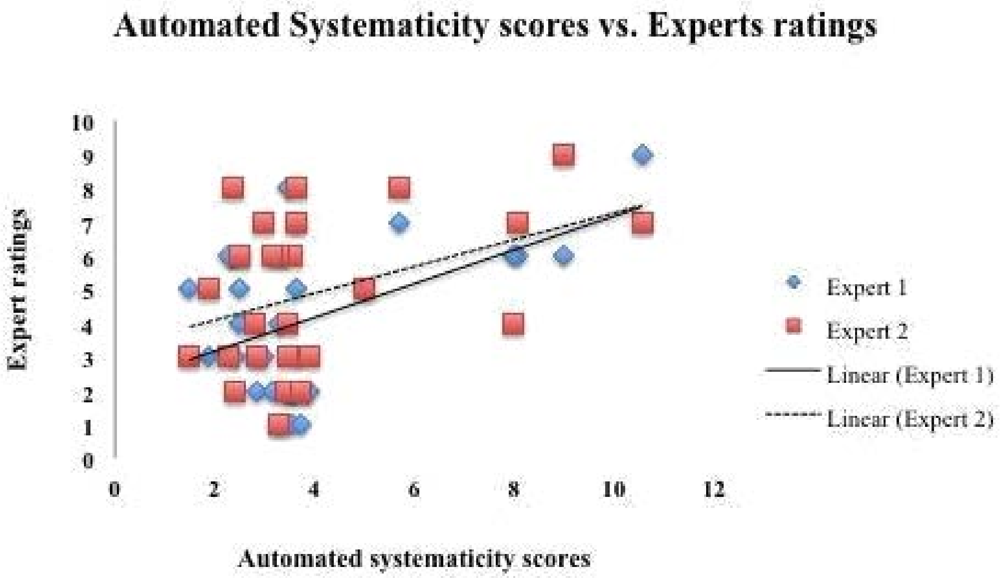
To investigate whether our Nearest Neighbour measure can be used as a systematicity index, in agreement with subjective ratings, a Pearson correlation was derived to between the individual ratings of the two experts against the automated systematicity score, generated by the Nearest Neighbour approach. For these correlations, participants with extreme scores (outliers) were removed. Two highly visible outliers were omitted, with an aid of a dissimilarity matrix graph, produced based on the Euclidean distance between participants' scores on the systematicity measure (Graph 1). Here, there were statistically significant correlation between the automated systematicity scores ($\bar{x}$ = 4.02, SD = 2.24) and the subjective ratings from the experts: expert 1 ($\bar{x}$ = 4.18, SD = 2.23), *r* (26) = .501, *p* = .003, expert 2 ($\bar{x}$ = 4.89, SD = 2.27), *r* (26) = .391, *p* = .02 (Graph 2). Low scores on the automated systematicity score (indicating a highly systematic performance) were associated with a high rated systematicity score (indicating that the patient was systematic and tended to cancel nearest neighbour targets). In order to measure the inter-rater agreement between the two expert raters, a kappa test was conducted using the ratings of the expert raters, resulting in a poor inter-rater agreement (*k* = -.022, *p* = .754). This indicates that the raters were not consistently applying the same (or similar) criteria to the rating of systematicity (Table 3).

Correlation between systematicity score and other measures of OCS

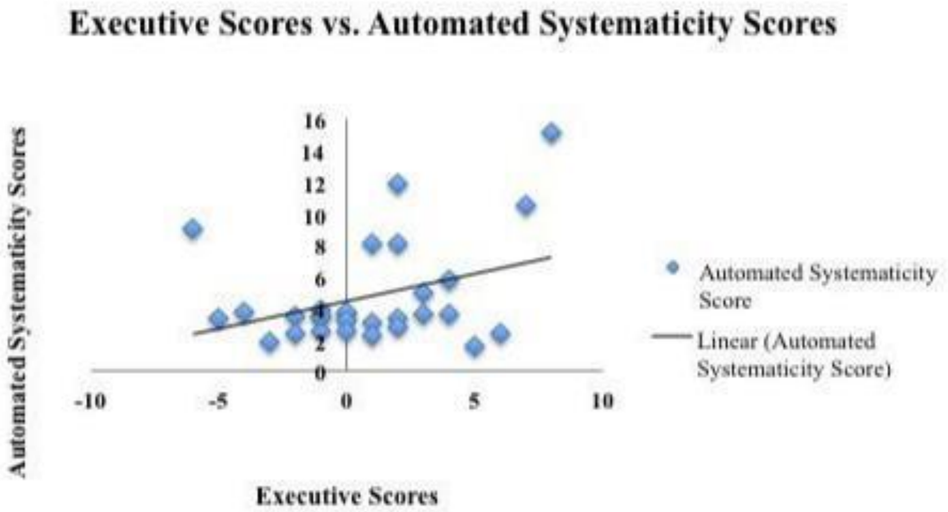
The automated systematicity scores were also correlated with the additional tests from the OCS, for each of the domains covered in the screen. For these correlations, outliers were explored using Tukey's Method (Boxplot) and participants were removed if there were outliers for the task. The removal of outliers did not result in any substantive impact on the overall conclusions of the analysis. There was a reliable correlation between the automated systematicity score ($\bar{x}$ = 4.71, SD= 3.3) and the executive measure from the OCS Trails tests (the cost in the switching task relative to the baselines); $\bar{x}$ = .86, SD = 3.38, r (27) = .357, p = .029) (Graph 3). There were no other reliable correlations between the systematicity measure and performance in the other domains of the OCS (see Table 4 for the r value and associated probability). The data suggest that systematicity was specifically related to executive dysfunction, and not to general effects of the lesion or other aspects of cognitive performance.



Graph 1. Displays a dissimilarity matrix graph (calculated on the distance between targets cancelled), produced based on the Euclidean distance between acute stroke patients' scores on the systematicity measure.



Graph 2. Displays a positive relationship between individual automated scores across acute stroke patients and expert 1 (*r* (26) = .501, *p* < .01 and expert 2 (*r* (26) = .391, *p* < .05) subjective ratings.



Graph 3. Displays a positive relationship between the automated systematicity scores against the executive score, obtained from the OCS Trails task (*r* (27) = .357, *p* < .05).

Table 4. *Correlations between the Automated Systematicity Score and OCS tests*

OCS tasks	*r*	*df*	*P* value
Language:			
Picture naming	- .11	28	.28
Number skills:	- .17	24	.2
Number writing			
Calculations			
Memory:	- .23	24	.13
Verbal memory			
Episodic memory			

DISCUSSION

In the present study, we derived a simple measure of the systematicity with which participants performed a cancellation task. Cancellation tasks are typically used to measure disorders of spatial attention, but performance can also reflect how organised a patient is. Our systematicity measure, based on a Nearest Neighbour calculation, provides an index of how organised a patient is, as the cancellation task is performed.

Here a group of 30 acute stroke patients performed a tablet-based cancellation task (the Broken Hearts test from the OCS; Demeyere et al., 2015). There was a reliable correlation between the automated systematicity scores and the systematicity score given by subjective raters. In addition, the automated systematicity scores correlated with a measure of executive function (the task switch cost) from the Trails test in the OCS. There were no correlations with the other cognitive domains of the OCS. Thus, the systematicity score's correlation with the executive function does not correlate with other domains of function, therefore, supporting the assertion that systematicity is a specific measure of planning, maintaining and updating a goal set rather than a general measure of cognitive functioning.

The organisation deficit we show here was also unrelated to impairments in spatial attention indexed by unilateral neglect (at least when the data were corrected for the absolute number of targets cancelled). The results highlight that a spatial organisation deficit can dissociate from problems in allocating attention across space.

The results indicate that a simple, easy-to-derive measure of systematicity in cancellation can be obtained and it can be shown to relate to the subjective ratings of systematicity and to a measure of executive function. This indicates that the automated systematicity score can serve as a useful addition to measurements of cancellation performance, over and above more standard measures of accuracy and spatial bias (Bickerton et al., 2011).

The measure can easily be built into computer-based (e.g., tablet PC) presentation schemes, giving useful extra information that is not easily derived from paper-and-pencil formats. It may also be that, in time, this scoring method can even replace the use of other measure of executive function, shortening the time taken for cognitive screens.

Study limitations

Normative data and the cut-off scores are the main limitation of this study. A sample of 52 neurologically healthy controls were recruited for the Broken Hearts with the intention of establishing an overall cut-off score for impairments on the automated systematicity score. However, as seen from Table 1, the availability of normative data would have been useful for the interpretability of patient's performance on the chosen tests in comparison to the neurologically healthy controls. In addition, it would have been interesting and informative to conduct an in-depth analysis by comparing the performance of healthy controls with acute stroke patients (with and without neglect) in consideration to the time taken to complete tasks between groups, in regards to systematicity measure.

The effect of age and education leads to the limitation in the established cut-off score. As noted from the participant demographic information, patient group age ranged from 44-91 (mean age = 76.30 years) and the average length of education was 11.45 years. The control group age ranged from 51-91 (mean age = 70.71) and the average length of education was 15.14 years. In the present study, we have only calculated one impairment score for the whole group (an overall cut-off score). Since, there is a difference in the age range and education between the healthy controls and stroke patients, it may be applicable to calculate age and education level matched cut-off scores. Unfortunately, the normative data sample here is small to make adjustments to in order to establish age and education level matched cut-off score. Therefore, it would be of great interest for the future to obtain a full set of OCS data on healthy participants (to explore the performance between healthy control performance and stroke patients) on a larger scale study (to the study effect of age and education in detail).

As mentioned in the general introduction, part 2 of the thesis consists of developing time efficient testing measures using singular tests. Therefore, the current chapter demonstrated how a visual cancellation task that is traditionally used to measure visual inattention and neglect is applicable to measure executive function using the Nearest Neighbour algorithm.

In the next chapter, we will discuss the development of scoring criteria for a Complex Figure Copy task that is typically used to measure visual and spatial construction and assess its utility as a measure of executive functioning.

CHAPTER 5

MEASURING EXECUTIVE FUNCTION THROUGH THE BCOS COMPLEX FIGURE TASK

ABSTRACT

INTRODUCTION: Complex figure tasks are popular neuropsychological tools for the assessment of visuospatial constructional ability and nonverbal memory skills. This report describes a qualitative scoring method that provides an index of executive measure for the BCoS Complex Figure Copy (Humphreys, Bickerton, Samson, & Riddoch, 2012). The proposed system provides scores on the presence, placement, and accuracy of visual features across Global and Local scales of processing (19 elements). **METHOD:** The validation is reported for reproductions drawn by stroke survivors at an acute stage (<3 months, *n*=100) after stroke. We evaluated the scores generated using the Global-Local Scoring System (GLSS) with ratings from two experienced neuropsychologists. The scores derived from the GLSS were also validated against measures of neglect, controlled attention and executive function (from the BCoS). **RESULTS:** The placement and accuracy scores from the GLSS correlated well with rule finding, a sustained attention index, and a working memory measure. There were also correlations between the GLSS scores and a cancellation measure of neglect. When the asymmetry of feature representation in the complex figure task was also taken into account, the scores from the placement score in the GLSS correlated with the overall cancellation score, which can index executive planning (Chapter 4). **CONCLUSION:** We conclude that the placement score on the Complex Figure Copy task can be used as an extra index of executive function.

INTRODUCTION

Complex figure drawing is traditionally used to evaluate visuospatial constructional ability and visual memory following a brain injury. It is one of the most widely used neuropsychological tests for the evaluation of visuospatial constructional ability and nonverbal memory skills under both clinical and experimental settings (Somerville, Tremont, & Stern, 2000). The task, usually, involves copying a complex geometric figure and then reproducing it from memory, either immediately, following a delay or both. Performance on the task provides data about several aspects of an individual's cognition including attention, concentration level, fine motor coordination, visuospatial perception, nonverbal memory and spatial organisation (Helmes, 2000). As the task taps several cognitive processes, it can be conceptualized as a key diagnostic task for the quick screening of cognition (Massa et al., 2015).

Massa et al., (2015) carried out a graphical model analysis on 287 stroke survivors, acquired from a large trial of the BCoS (the data for the present study is obtained from the same BCoS trial), to provide a description of the hierarchical associations between subscales and subtests of the BCoS. The relations between the different subtests in the BCoS were analysed at i) within-domain (tests within each domain were considered separately, e.g., language tests were considered separately from executive tests) and ii) across-domain (tests from all the domains were considered together). Massa et al., (2015) revealed that the relations between the tests according to the sub-domains of BCoS changed greatly when the tests were analysed across-domain. The cross-domain analysis accounted for several tests outside their given domain. Notably, the Complex Figure Copy task was one of the tests that formed connections, not only with tests within it’s given domain (praxis), but also with tests outside it’s given domain such as attention (specifically, spatial attention indices from Apple Cancellation) and, executive function (overall score from Rule Finding and Set Switching tests). Therefore, Massa et al., (2015) clearly supports the assertion that the complex figure task is associated with both attentional and executive skills.

Executive cognitive functions are required to manage goal-orientated behaviour, which is a core aspect of good performance at complex figure copying and reproduction (Shin, Kim, Cho, & Kim, 2003). Deficits in executive function are common post-stroke (Ballard et al., 2003; Pohjasvaara et al., 2002) and are known to reduce the effectiveness of stroke treatment (McDowd, Filion, Pohl, Richards, & Stiers, 2003; Mok et al., 2004). Being able to efficiently detect executive impairments, then, is important for early referral into appropriate rehabilitative services. However, one major constraint on early diagnosis is that the sensitive screening of cognition has often been difficult to achieve. Many neuropsychological assessments require prolonged testing, and this is often impractical in many clinical settings (see Bickerton et al., 2015, for discussion). There is a need for tests that can be decomposed to provide separate diagnoses of the different cognitive processes that may be involved. Here we examined whether a complex figure test, frequently used in neuropsychological screening, can be decomposed to reveal executive, as well as spatial and memorial cognitive processes.

To date, the Rey-Osterrieth Complex Figure (ROCF: Osterrieth, 1944; Rey, 1941) has probably been the most popular singular measure of visuoconstructional ability and non-verbal memory. Among the various ROCF administration procedures that exist, the Boston

Qualitative Scoring System (BQSS) (Stern et al., 1999) is perhaps the most comprehensive, guiding qualitative ratings based on the presence and accuracy of reproducing target elements, and the process of drawing itself (Stern et al., 1994). This scoring system purports to assess visuospatial organisation, visual memory and executive function by using multiple scores with well-defined criteria. However, there are no data on how well the measures match clinical judgements about planning/organisation as the task is undertaken, and there is no evidence on whether the planning/organisation measure can serve as a proxy for other indices of executive function.

In the present study, we put forward a set of novel scoring criteria, the Global-Local Scoring System (GLSS), to measure the ‘systematicity’ of performance[1] (see in this volume: Chapter 4), using the Complex Figure Copy test from BCoS (Humphreys, Bickerton, Samson, & Riddoch, 2012). In the scoring system, we utilise the notion of Global-Local processing, based on the proposal that complex figure copying involves the hierarchical decomposition and construction of perceptual units (see Kuschner, Bodner, & Minshew, 2009; Mcconley, Martin, BaÑos, Blanton, & Faught, 2006; Poreh & Shye, 1998). The perception and reproduction of global elements may reflect the overall ‘gist’ of a figure, while the reproduction of local elements may reflect the subsequent decomposition of the global form to incorporate appropriate local elements (cf. Navon, 1977; see also Poreh & Shye, 1998). Neuropsychological data from brain-injured patients, functional neuroimaging and transcranial magnetic stimulation (TMS) studies in healthy controls suggest some functional lateralisation of global and local processing, with global processing mediated by the right hemisphere and local processing by the left (Mevorach, Humphreys, & Shalev, 2005; Fink

---

[1] That is, how organised the construction process is.

et al., 1996; Lamb, Robertson, & Knight, 1989; Lamb, Robertson, & Knight, 1990; Robertson & Delis, 1986; Delis, Robertson, & Efron, 1986; although see Marshall & Halligan, 1995). For example, Fink et al. (1996) in a Positron Emission Tomography (PET) study with healthy, young participants found that attention to global figures was associated with activation within the right lingual gyrus, while attention to local figures activated within the left inferior occipital cortex. Here we evaluated whether a Global-Local Scoring procedure not only captured aspects of hierarchical processing but also the systematicity of reproduction.

The goals in the study were as follows: i) to develop a procedure for Global-Local scoring of a reproduced, complex figure; and ii) to elucidate whether executive function abilities can be derived from the GLSS. The relations between the Global-Local scores and executive functions were evaluated by assessing the performance of patients on several other independent measures of controlled attention and executive function, and iii) to determine which aspect(s) of the GLSS best reflect ‘systematicity’ in spatial organisation, an aspect of executive function (see in this Volume: Chapter 4). Successful measurement of executive function through complex figure copying can reduce the need to provide additional measures of executive processes in neuropsychological testing, making tests more clinically applicable (see Bickerton et al., 2015).

METHOD

Participants

The data were collected as part of a larger study, the Birmingham Cognitive Screen (BCoS: Humphreys et al., 2012). Stroke survivors were recruited into the study between November 2006 and January 2011 from 12 different hospitals in the West Midlands, England, U.K as part of the BCoS trial (http://www.bucs.bham.ac.uk). The stroke survivors were included if there are medically stable and within 3 months of their latest stroke. Diagnoses of stroke were confirmed through assessments by the clinical team at the given hospital. The exclusion criteria included: a) insufficient English to understand the basic instruction for assessments, b) lack of a concentration span that could cover at least 35 minutes, judged by the clinical team. Note that BCoS takes around 1 hour to administer but the design of the BCoS allows it to be completed in 2 parts, if or when needed (though in most cases the patients completed the screen in one session). Breaks were given for, if or when needed, for rest and to re-motivate performance. In addition, due to fatigue and/or other demands (e.g., medical tests or scheduled rehabilitation session) sometimes not all the sub-tests of the screen were completed.

For the purpose of the present study, we randomly selected a sample of 100 stroke patients who completed the Complex Figure Copy task (40 females and 60 males, 12 left-handed and 2 ambidextrous) from the 749 participants on the BCoS dataset. The patients' ages ranged from 27 to 93, with an average age of 70.02 (SD = 14.53). There was on average 10.78 years of education (SD = .71). The average time between test and post-stroke was 24.49 days (SD = 18.88). The clinical details of the patients (i.e., the type of stroke, lesion location and previous medical history) are presented in Table 1. This information was classified from the patient's clinical notes at the stroke ward.

In addition, a second examiner and two subjective raters were recruited to this study. The second examiner is a doctoral level researcher in the field of psychology who provided scores, using the detailed scoring algorithm, for the assessment of Inter-rater reliability (IRR). The subjective raters were experts in the field of neuropsychological assessment and had greater than 12 years of experience. These experts provided subjective ratings of how systematic each patient was on the reproduction of their BCoS complex figure (see Materials and procedure section for further information, page 157).

Procedure for data collection. Informed consent was obtained according to the approved ethics protocols of the U.K. National Research Committee. The neuropsychological assessments, BCoS battery was administered by trained examiners who were psychologists, occupational therapists and/ or stroke researchers (doctoral students or research assistants). All examiners attended a full day's BCoS training and successfully completed the given assessments as judged by the BCoS team. The first author did not participate in the BCoS study data collection. The first author's responsibilities in the data collection for the present study involved: i) selecting a study sample (*n*=100) from the BCoS data collection, ii) scoring each reproduction of the BCoS complex figure (*n*=100) as the first examiner for the present study, and securing iii) a second examiner as well as, iv) two subjective raters.

Table 1. *Patient’s Clinical details and Medical history*

Clinical and medical details	**Patients**
Type of stroke	
TIA	4
Subarachnoid Haemorrhage	1
Intracerebral haemorrhage	11
Ischemic stroke	79
Unknown	5
Lesion side	
Left	27
Right	39
Bilateral	14
Unknown	20
Previous medical history	
No known history	61
Previous stroke or TIA	32
Head injury	4
Dementia	2
Other	1

Note: TIA = Transient ischaemic attack

BCoS measures

The BCoS assesses 5 cognitive domains: i) attention and executive function, ii) language, iii) memory, iv) number skills and, v) praxis/actions. This screen can be further broken down into different functions within the main domains: i) spatial attention (measuring different forms of neglect and extinction) and controlled attention (measuring executive functions, sustained attention, response inhibition/suppression), ii) spoken and written language (involving words and numbers), ii) immediate and delayed memory, along with episodic memory, and iii) limb apraxia and constructional apraxia. Further information regarding BCoS is available at http://www.cognitionmatters.org.uk and the motivation in designing the BCoS, along with task descriptions, are provided in Humphreys et al. (2012). In total, there are 22 sub-tests, providing different sub-measures within. Along with the Complex Figure Copy test, the following tests were also chosen as independent assessments of task-relevant abilities: the Rule-Finding and Concept-Shifting task (testing executive function), the Auditory Attention task (taking measures of overall performance, false positive (inhibition) errors, sustained attention and working memory) and the Apple Cancellation task (a test of visuo-spatial attention (Bickerton et al., 2011) which is also sensitive to executive function (Chapter 4) (see below for more details).

1. ***Complex Figure Copy.*** Patients were administered the BCoS complex figure test copy condition, using the standardised procedure set out in the BCoS test manual (Humphreys et al., 2012). The BCoS complex figure is made up of a middle structure and additional structures to the left and right of this. The number of elements to the left and right were equated to balance the sensitivity to both left and right neglect (see Figure 1). The instruction to the patient was as follows:

“I will show you a figure. Please copy the figure the best you can”.

The patient was shown the space provided to re-draw the figure (usually, below the original complex figure). A maximum of 5 minutes was allowed for task completion and the time constraint was not disclosed to the patient.

Global-Local scoring system scores in relation to other executive tasks

In order to examine the convergent validity of the Global-Local systematicity scores, the following tasks were selected from the BCoS cognitive screen:

2. ***Apple Cancellation test.*** The test consisted of 150 apple-stimuli randomly scattered, in an unstructured array, on an A4-page in a landscape orientation. Two-thirds of the apple stimuli were incomplete (apples with an opening on either the left or the right side; distractors), the remaining were complete apples (targets). The page was divided into a grid with 2 rows and 5 columns, creating 10 quadrants of equal size. In each quadrant, there were 5 targets and 10 distractors (5 apples with right side opening and 5 apples with left side opening). The grid was not visible to the participants but each section was designed to ensure an equal distribution of each type of apple across the page. The instruction for the patient as follows:

“I will show you a page with apples. Sometimes, the apple is full;
sometimes the apple is incomplete. Please cross out the full apples only.”

Prior to the actual test, patients were given an example to try first. The test sheet was placed in front of the patient who was asked not to move the page. A maximum of 5 minutes was allowed for the patient to complete the test. The construction of the page/test produced three scores: i) the overall accuracy, corresponding to the total number of targets (complete apples) selected, ii) a page-based asymmetry score for egocentric neglect, reflecting the difference between the total number of targets cancelled on the ride side of the page and the total number targets cancelled on the left side of the page (excluding the 2 middle quadrant) and ii) an object-based asymmetry score for allocentric neglect, corresponding to the number of non-targets (distractors) cancelled with a gap on the right side – the number of non-targets cancelled with a left side gap (see Bickerton et al., 2011).

3. ***Auditory Attention task.*** There were 6 words, presented 9 times, each. Half of the words were targets to respond to (i.e., 'no', 'hello' and 'please') and the remaining were closely related distractors ('yes', 'goodbye' and 'thanks'). All the chosen words had a high frequency of occurrence. These words were presented in a random order and occurred an equal number of times. The task was performed in 3 blocks. The instructions were as follows:

> *"You will hear a recording with a man saying different words. When the man says 'hello', 'please' or 'no' you have to tap on the table. When the man says something else, just ignore him. So, the three words you have to respond to are: hello, please and no."*

The patient was asked to repeat the words prior starting the test and in addition, a practice trial was conducted. Here, the practice was repeated until the patient made no errors and/or recalled all target words correctly (see Humphreys et al., 2012, for further details on the protocol of the test). This test produces 5 scores: i) Overall accuracy of selective attention, corresponding to the total number of correct responses, ii) Response inhibition, which corresponded to the total number of times the patient responded to a false positive (distractor), iii) Target omissions, corresponding to the total number of targets missed by the patient, iv) Sustained attention, corresponding to the difference between the correct response in block 1 and the number in block 3. This was a measure of how well individuals can sustain their attention across the blocks – in some cases - sustained attention index was not calculated since the test was stopped after block 1 or 2 (index was not applicable). Finally, working memory was scored, corresponding to the number of target words recalled at the end of the test.

4. ***Rule Finding and Concept Switching.*** The test consisted of 19 consecutive grids, made of 6 columns and 6 lines, creating rows. Most cells were grey, but 2 were red and 2 green. The objective was to predict the movement of a black marker, which moves across the grid. The black marker moved in a lawful manner but occasionally the rule was switched. The switch either operated along the prior dimension (i.e., moving in one direction another), or it operated across dimensions (i.e., switching from the position rule to a colour rule, where the black maker jumped between squares of the same colour). The instructions are as followed:

> *"The dot will move from a specific location on one page to a specific location on the next page. It can move everywhere and be positioned on either a grey or a coloured square. The dot does not move randomly but follows a pattern. However, the rule governing the*

pattern can change. Look carefully at how the dot moves on each trial. You have to anticipate and show me where the dot will move next. Please remain attentive so that you can keep track of the changes."

Patients were given a practice trial before the actual test (see Humphreys et al., 2012, for further information on the protocol of this test). The task measured the ability to find an abstract rule and to switch the rule across stimuli within and across dimensions. There were 18 trials and a maximum 15 seconds per trial (time constraint was not disclosed to the patient). As the task preceded the preceding page was always left visible in order to reduce memory demands. The test produced two scores: i) overall accuracy, corresponding to the total number of correct responses that were made (maximum score = 18), and ii) rule detection, corresponding to the number of rules that were applied correctly on the least 2 consecutive trials (maximum score = 3).

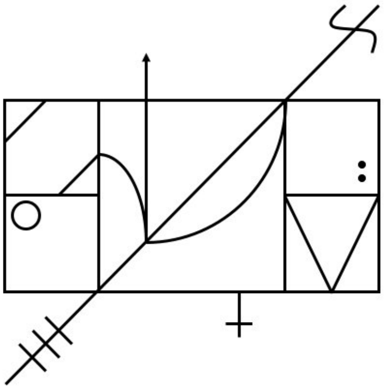
Introducing the Global-Local Scoring System

This system divides the figures into two sets of elements that are hierarchical in their relations to the structure of the figure (Figure 1). The Global elements include the large outline rectangle that further subdivides into the central square, four small squares (two on the left and right, respectively) and the main diagonal line. The Local elements comprised the shapes and line segments that form parts within the Global elements.

Defining the Global-Local Scoring System. The scoring system was based on a total of 19 elements (7 Global and 12 Local Elements). These elements were scored along 3 dimensions: the presence of the element, placement and shape accuracy. In this scoring system, presence reflects some reproduction of the element, even if placed in an incorrect spatial position or even if only partially accurate (see the Appendix B for detailed scoring criteria). Placement reflected whether the element is located in the correct spatial position (see Figure 2 for template). Finally, shape accuracy reflected whether the shape was accurate in terms of its spatial orientation, angles, and proportions. Note that shape accuracy may tap into integrative aspects of executive function where planning is necessary in order to successfully copy/integrate each element into its context (e.g., leaving enough space in order to not compress the shape).

Global-Local Scoring. The GLSS generated a total of 19 scores per dimension (presence, placement, shape accuracy). We will refer to these as the Dimensional scores (D-Presence, D-Placement and D-Accuracy). Second, the scores were divided according to whether they reflected Global (maximum score = 21) or Local (maximum score = 36) properties of the figure, a combination of the figure presence, placement and accuracy results. We will refer to this set of scores as Regional scores (R-Global and R-Regional). The Local elements were divided according to their spatial position into left (maximum score = 9), right (maximum score = 9) and middle (maximum score = 18). In respect to Local elements, an Asymmetry score was derived reflecting the difference between the local features on the right and the left side. We will refer to this score as Local-Asymmetry (L-Asymmetry). Finally, the Accuracy score reflected the overall accuracy and was the sum of all three dimensions across the 19 elements (generating a maximum score of 57), (see Table 2 for a summary of the scores and calculations). A higher the score reflects better performance (good systematicity).

Complete BCoS complex figure



Global elements (1-7) **Local elements (8-19)**

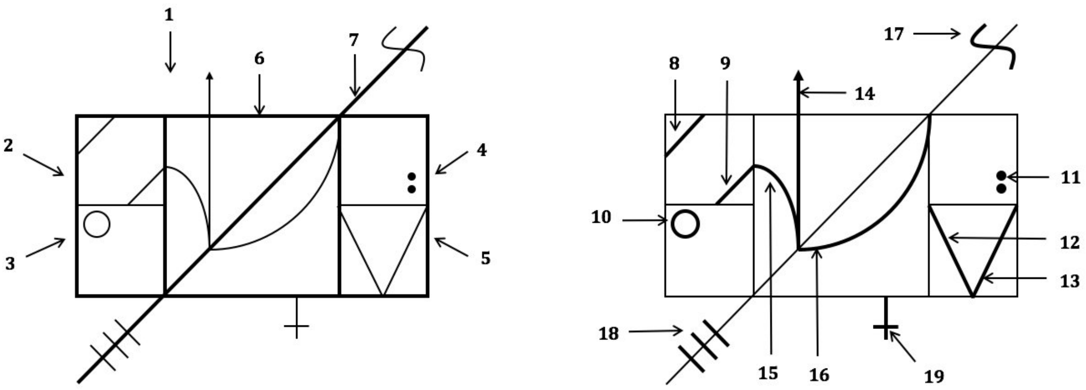


Figure 1. Division of the BCoS complex figure into Global-Local elements.

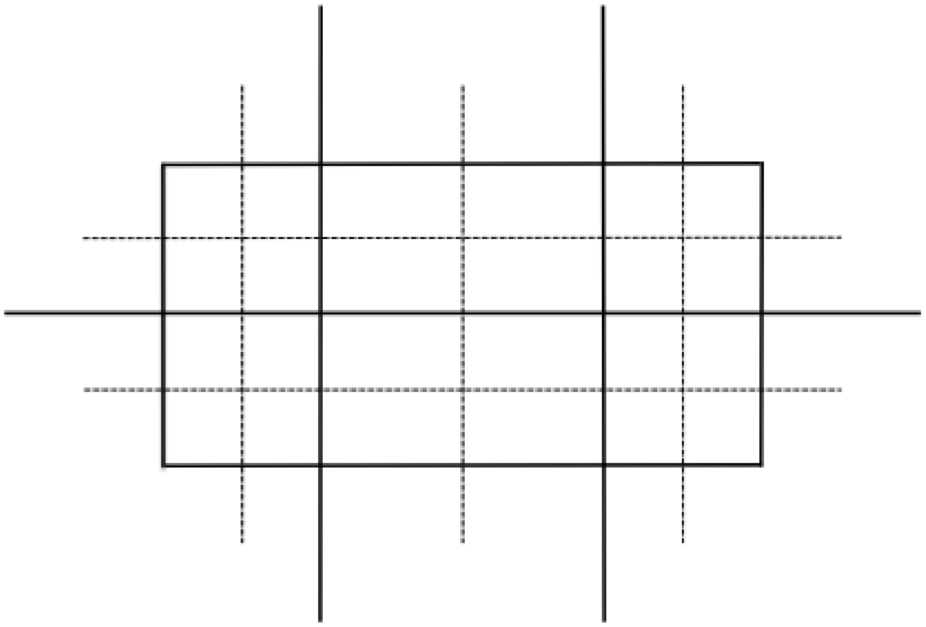


Figure 2. Precision template for Placement. The complex figure was divided into quadrants, which indicated the correct location for each Local element. The Local elements had to fall within the quadrant matching the figure to be given a correct placement score.

Table 2. *Scores and Calculations (Maximum Score)*

Scores	Calculations
Dimensional	
D-Presence	Global elements (7) + Local elements (12) = 19
D-Placement	Global elements (7) + Local elements (12) = 19
D-Accuracy	Global elements (7) + Local elements (12) = 19
Regional	
R-Global	Presence (7) + Placement (7) + Accuracy (7) = 21
R-Local	Presence (12) + Placement (12) + Accuracy (12) = 36 Left side (9) + Middle square (18) + Right side (9) = 36
L-Asymmetry	Sum of local element of local element scores on the Left side (9) *minus* the sum of the local elements scores on the Right side (9)
Overall Accuracy	Global (Presence, Placement, shape Accuracy: 21) + Local elements (Presence, Placement, shape Accuracy: 36) = 57

Note: **D** = Dimensional scores, **R** = Regional scores, **L** = Local elements. The GLSS generates a total of seven (main) scores (D-Presence, D-Placement, D-Accuracy, R-Global, R-Local, L-Asymmetry and an overall accuracy score). The scores were generated as a result of dividing local element per spatial positioning (left side, right side and middle square), these scores are as focus of asymmetry scores, to elicit spatial bias performances.

Inter-rater reliability and subjective ratings

Inter-rater reliability. The first examiner scored each reproduction of the BCoS complex figure (*n*=100) and the second examiner scored 30% of the sample for IRR. Both examiners scored, independently, clinically judged by the same detailed scoring criteria (for the Global-Local Scoring System criteria and the scoring sheet used, see Appendix B)

The IRR was not examined on the main seven scores of the GLSS. These scores are composite scores, calculated in combinations of different aspects of the scoring system, e.g., D-Presence score is the sum of presence of the element across the Global and Local regions and the R-Global score is the sum of all three dimensions (presence, placement and accuracy). Therefore, these scores did not reflect the independent scoring approach/clinical judgement by the examiners. Rather, the IRR was examined on a set of scores that were not contaminated by different aspects of the scoring system i.e., by dimensions (presence, placement and accuracy) across regions (Global and Local (divided into left side, right side, and middle Square)), respectively, (for Global-Local scoring sheet, see Appendix B).

In addition, the asymmetry score was not examined in the IRR assessment because the asymmetry rating is aimed to be a categorical rating calculated by the trained examiner during individual scoring rather than a score created by comparison to standard criteria, and therefore, the second examiner did not score asymmetry.

Subjective ratings. In addition to the above scores, the 30% of the samples were also given a ‘systematicity’ score based on a rating scale of 1 to 7; 1 being poor systematicity (no planning) and 7 good systematicity (well planned and organised reproduction). Here, the systematicity measure provided a form of overall Gestalt, likely reflecting both the Global and Local elements.

Two subjective raters gave these subjective ratings and, both raters followed the same protocol. Each subjective rater was given 30% of the samples and was asked to give a global rating on how 'systematic' each patient has performed the BCoS Complex Figure Copy task. Therefore, the subjective raters had to evaluate and give an overall (expert) rating on a scale of 1 to 7 to the reproduction (i.e., the end product of a coherent or piecemeal approach) of the BCoS complex figure drawn by a patient, on the basis of how well planned/organised was the reproduction. For example, a higher systematicity score would be achieved by drawing global elements such as the large rectangle drawn in one piece (rather than by quadrants), followed by other global features prior to drawing and/or filling with finer details such as the local elements. In general, this would be the normal tendency for such task to be approached and, completed in a logical and systematic manner. The systematicity score also accounted whether the figure was drawn within the boundaries of the page. Furthermore, the subjective raters were asked not to penalise the reproduction if the drawing was incomplete on one side (due to neglect), but rather to rate what was produced.

The second examiner and the two subjective raters only received patient's performance on reproduction of the Complex Figure Copy task. They were all blinded to one another's scores and to the results of other neuropsychological measures, as well as the patient's lesion and/or any clinical details. These individuals are all independent of the project.

DATA ANALYSIS

A series of analysis were conducted to examine the general performance on the BCoS Complex Figure Copy task as well as executive processes (e.g., planning/organisation approach) in regards to GLSS.

First, an IRR was conducted on a set of scores from the GLSS using Cohen's Kappa (k). Generally, k values range from -1 to + 1, with higher values representing better reliability (e.g., 1 represent a perfect agreement between raters) and lower values representing poor reliability (e.g., zero or values near zero indicates that the amount of agreement are to random chance). The adequacies of the kappa values were accepted using the guidelines described by Landis & Koch (1977).

Secondly, to evaluate the development of Global-Local scoring approach in respect to the performance on the BCoS Complex Figure Copy task, a Pearson correlation was conducted. The Pearson correlation examined the relationship between the systematicity ratings provided by the two individual subjective raters against the overall accuracy score derived from the GLSS. We conducted this analysis because the systematicity rating was on the reproduction of the BCoS complex figure i.e., the end product of coherent (e.g., drawing the global elements first, followed by local elements) or a piecemeal approach (e.g., drawing elements out of categorical order and, possibly, incomplete elements). In addition, since, the systematicity was considered in association with placement (reflecting the placement of elements in relationship with the adjoining context), we conducted another Pearson correlation using the expert ratings against one of the dimensional scores, D-Placement score, across the whole figure (maximum score = 19).

Finally, further Pearson correlations were conducted to examine the convergent validity of the GLSS. The seven main scores generated by the GLSS were validated against three other measures within BCoS that were chosen from domains that were to measure the same construct; executive function. A partial correlation coefficient was conducted between the overall score derived from the GLSS (overall accuracy, global and local) and the Apple Cancellation scores (overall accuracy, paged-based asymmetry, object-based asymmetry) using the asymmetry score were calculated from the BCoS complex figure as a control.

All *p* values were accepted at 0.5, unless, otherwise specified.

RESULTS AND DISCUSSION

Inter-rater reliability

The IRR for the copy condition i.e., the reproduction of the BCoS complex figure varied across the dimensions (presence, placement, and accuracy) by regions/divisions. The reliability for the Presence score was moderate on the global processing (k = .55) and substantial to almost perfect agreement on the local processing (k = .64 - .82) and. The reliability for the Placement score was fair for global processing (k = .56) and fair to moderate on local processing (k = .43 - .56). The reliability for the (shape) accuracy score indicated fair agreement across the Global-Local processing (k = .29 - 37) except for one division (local left side), which had moderate agreement (k = .55). For a summary of IRR for the Global-Local Scoring System, see Table 3.

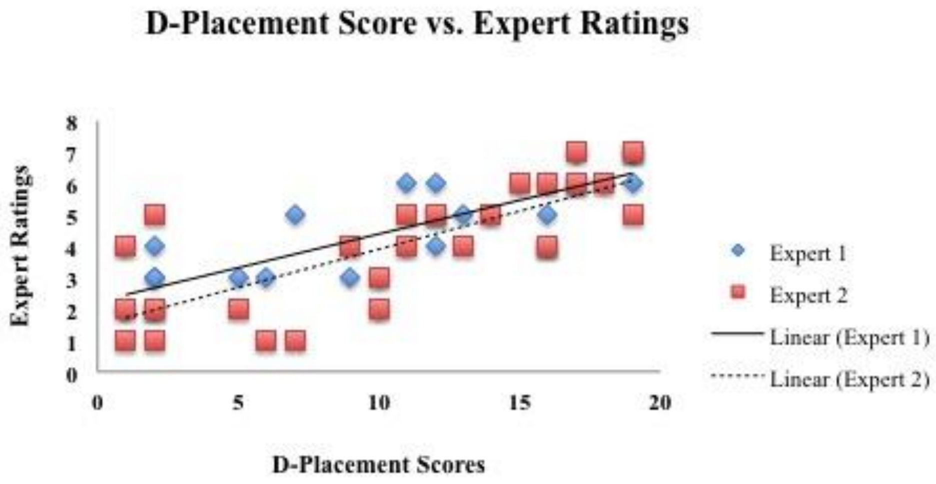
Table 3. *Inter-rater Reliability Across the Region per Dimension*

Regions	Kappa Statistics
	Copy condition
	Global elements
Presence	.55
Placement	.56
Accuracy *(shape)*	.29
	Local elements
Local left side	
Presence	.64
Placement	.50
Accuracy *(shape)*	.55
Local right side	
Presence	.82
Placement	.56
Accuracy *(shape)*	.37
Local middle square	
Presence	.66
Placement	.43
Accuracy *(shape)*	.36

Note: Interpreting Kappa values (Landis & Koch, 1997): < 0 = Poor agreement, 0.0 - 0.20 = Slight agreement, 0.21 - 0.40 = Fair agreement, 0.41 - 0.60 = Moderate agreement, 0.61 - 0.80 = Substantial agreement, 0.81 - 1 = Almost perfect agreement.

Relationship between the Global-Local scoring and the subjective ratings

The data revealed strong positive correlations between the overall accuracy score ($\bar{x}$ = 32.87, SD = 15.86) and each expert rater (rater 1: $\bar{x}$ = 4.53, SD = 1.68), *r* (28) = .815, *p* < .001; rater 2: $\bar{x}$ = 4.07, SD = 1.95), *r* (28) = 807, *p* < .001. Also, an IRR was examined between expert rater 1 and expert 2, which revealed a fair agreement between the two expert ratings (k = .22). Therefore, this aspect of the data indicates that, despite differences in individual clinical judgement, the Global-Local measure is capable of capturing planning/organisation, the systematicity of a reproduced complex figure. In addition, the Pearson correlation between the expert ratings and the D-Placement scores also revealed a strong correlation between the D-Placement score ($\bar{x}$ = 10.67, SD = 6.32) and both raters (expert 1: *r* (28) = 812, *p* < .001; expert 2: *r* (28) = .789, *p* < .001) (Graph 1).



Graph 1. Displays a positive relationship between the D-Placement scores (maximum score: 19) derived from the Global-Local Scoring System and the subjective ratings (scale of 1 to 7; 1 being poor systematicity and 7 being good systematicity) from both experts raters (Expert 1: r (28) = .812, and Expert 2: r (28) = .789, both at *p* < .001)

Global-Local scores in relation to BCoS tasks (attention and executive function)

Summary statistics for the relevant score of the selected BCoS sub-tests are, also, presented in Table 4. All Pearson correlation coefficients between the Global-Local scores and the representative scores from the BCoS subtests are shown in Table 5. The Partial correlation coefficients between the scores derived from the GLSS and the Apple Cancellation scores are shown in Table 6. For these correlations, the probability level was set at $p < .025$ to correct for multiple comparisons.

Rule Finding and Concept Switching. Both scores, overall accuracy and the number of rules detected, from the Rule Finding and Concept Switching task showed a moderate positive correlation with six of the complex figure scores (D-Presence, D-Placement, D-Accuracy, R-Global, R-Local and overall accuracy; see Table 4). The complex figure asymmetry score (R-Asymmetry) derived from the GLSS (the sum of the score on the left side *minus* the sum of elements on the left side) did not correlate with either the rule finding accuracy ($r = .169$, $p > .025$) or the number of rules detected ($r = .164$, $p > .025$). Thus, the relations between the presence, placement and shape accuracy scores and the Rule Finding and Concept Shifting task were independent of spatial neglect. Since Rule Finding and Concept Switching demands executive abilities, the strong correlation with the Global-Local measures provides validation that complex figure performance can be used as an index of executive function.

Auditory Attention task. The overall accuracy on the Auditory Attention task positively correlated with all six main complex figure scores, but not the complex figure asymmetry score (see Table 5). The number of false positives on the Auditory Attention task also correlated negatively with all six main scores, except the asymmetry score. Interestingly, the sustained attention index positively correlated only with the complex figure asymmetry measure (r = .262, p = .014). Also, the working memory score on the Auditory Attention test also showed a weak positive correlation with D-Placement (r = .220, p = .017).

These data indicate that the Global-Local measures related to overall performance, responses to false positive and working memory for targets on the Auditory Attention task - the latter factors reflecting the executive functions of inhibiting responses to distractors and maintaining goal related information in mind (cf. Miyake, Friedman, Rettinger, Shah, & Hegarty, 2001). In contrast, the relations between the complex figure asymmetry score and the sustained attention index fits with the idea that spatial attention is critically reliant on sustained attention and that this is independent of specific aspects of reproducing global and local elements (Robertson, et al., 1997).

Apple Cancellation. The scores for the complex figure showed some correlations with the Apple Cancellation task. Notably, overall accuracy on the cancellation task positively correlated with all seven complex figure scores, though complex figure asymmetry showed a weak positive correlation compared to the other six scores (see Table 5). In contrast, both asymmetry scores of the cancellation task, false positive (cancelling distractor apples with a gap on one side, reflecting egocentric neglect) and as well as the page-based asymmetry score (number of apples cancelled on the left side the number of apples cancelled on the right side, reflecting allocentric neglect) negatively correlated with the complex figure asymmetry score (see Table 5).

Given the correlation between the overall Apple Cancellation scores and the Global-Local scores, we conducted a partial correlation by controlling the asymmetry score from the complex figure, to ensure that the overall correlation did not reflect the effects of neglect. The overall accuracy score from the Apple Cancellation task strongly correlated with D-Presence ($r = .624$, $p < .01$), D-Placement ($r = .648$, $p < .01$), D-Accuracy ($r = .594$, $p < .01$), R-Global ($r = .628$, $p < .01$), R-Local ($r = 651$, $p < .01$) and the overall accuracy on the Complex Figure Copy task ($r = .672$, $p < .01$). There were no other significant correlations (see Table 6).

The consistent relationship between the Global-Local scores and the accuracy scores from the Apple Cancellation, even with neglect on the complex figure controlled, demonstrates that the Global-Local scores are not affected by neglect.

Table 4. *Summary statistics for Global-Local Scoring System and other BCoS sub-tests*

Task	Score (n)	Range	$\bar{x}$	SD
Complex figure				
	Accuracy (100)	2-52	*29.86*	*14.06*
	D-Presence (100)	1-19	*14.45*	*5.13*
	D-Placement (100)	0-19	*9.73*	*5.62*
	D-Accuracy (100)	0-16	*5.68*	*4.41*
	R-Global (100)	0-20	*11.57*	*5.39*
	R-Local (100)	0-34	*18.29*	*9.39*
	L-Asymmetry (100)	(-9)-7	- *.98*	*3.05*
Apple cancellation				
	Accuracy (97)	0-50	33.86	15.77
	False positive Right (97)	0-40	2.19	5.76
	False positive Left (97)	0-40	3.12	6.23
	Page-based asymmetry (97)	(-15)-19	1.04	5.63
	Object-based asymmetry (97)	(-12)-17	.87	4.1
Auditory attention				
	Accuracy (93)	8-54	39.07	15.25
	False positive (93)	0-20	4.22	5.42
	Omission (93)	0-23	4.34	4.86
	Sustained attention index (71)	(-3)-8	1.42	2.4
	Working memory (93)	0-3	2.419	.81
Rule finding and switching				
	Accuracy (93)	0-17	4.55	5.24
	Rules detected (93)	0-3	.84	1.1

Table 5. *Correlation Coefficient between the Global-Local scores and the BCoS test scores*

Global-Local Scores	D-Presence	D-Placement	D-Accuracy	R-Global	R-Local	L-Asymmetry	Overall Accuracy
Apple cancellation							
Accuracy	**.646****	**.652****	**.558****	**.648****	**.639****	**.266****	**.673****
FPr	- .018	- .057	- .083	- .011	- .077	.189	- .056
FPl	- .121	- .158	- .153	- .123	- .163	- .064	- .156
Page-asymmetry	-.124	- .088	- .062	- .147	- .067	- .518**	-.01
Object-asymmetry	- .16	- .156	- .116	- .168	- .14	- .353**	- .157
Auditory attention							
Accuracy	**.345****	**.397****	**.384****	**353****	**.400****	- .025	**.402****
FP	- .230*	- .304**	-.272**	- .302**	- .260**	.103	- .289**
Omission	- .111	- .124	- .132	- .095	- .141	.029	- .13
Sustained attention Index	- .019	- .209	- .198	- .077	- .186	**.262***	- .154
Working memory	.12	**.220***	.202	.166	.194	- .051	.193
Rule finding and switching							
Accuracy	**.340****	**.480****	**.421****	**.350****	**.471****	.169	**.450****
Rules detected	**.310****	**.455****	**.417****	**.328****	**.450****	.164	**.428****

Note: **FPr** = False positive right side distractors, **FPl** = False positive left side distractors, **FP** = False positive. * $p < 0.025$, ** $p < 0.01$.

Bold type |r| > 0.2

Table 5. *Partial Correlation Coefficient between the Global-Local scores and the Apple Cancellation scores*

Global -Local scores	Apple Cancellation scores				
				Asymmetry scores	
	Accuracy	FPr	FPl	Object-based	Page-based
D-Presence	***.624*****	- .062	- .011	- .01	- .089
D-Placement	***.648*****	- .082	- .151	- .032	- .124
D-Accuracy	***.594*****	- .074	- .157	- .106	- .144
R-Global	***.628*****	- .054	- .112	- .044	- .102
R-Local	***.651*****	- .087	- .161	- .051	- .133
Overall accuracy	***.672*****	- .079	- .15	- .05	- .127

Note: **FPr** = False positive right side distractors, **FPl** = False positive left side distractors. **$P < 0.01$, Bold type $|r| > 0.2$

CONCLUSION

We propose an automated system for scoring performance on a Complex Figure Copy task, reflecting the reproduction of both global and local aspects of the figure – the Global-Local Scoring System. We showed that there was good agreement between independent examiners using the system and that an overall measure of accuracy on the GLSS correlated with ratings given by experienced neuropsychologists on how ‘systematic’ a patient was in his/her reproduction. We conclude that the GLSS is reliable and can reflect holistic impressions of how planned drawing behaviour is.

We further showed that the GLSS generated measures that largely correlated with indices of executive function derived independently from other tests in the BCoS battery: the Rule Finding and Concept Switching task, and the Auditory Attention task (particularly the overall score, the number of false positive responses to distractors and a measure of working memory). These correlations are unlikely to reflect the general effects of the brain lesion. With the exception of the spatial asymmetry measure of reproducing local elements, there were no correlations with indices of spatial neglect in the Apple Cancellation task. The lack of correlations with the neglect measure, and the reliable correlations with the measures reflecting executive functions, suggest that the GLSS captures aspects of executive function – such as the ability to plan ahead, to inhibit immediate action and to keep the goal in mind. Even though complex figure tasks are typically interpreted as measures of visuospatial and constructional ability, our results indicate that significant aspects of construction performance are linked to executive functions (planning, goal maintenance, inhibiting action) of brain-injured patients, and these executive aspects of performance can be derived independently of factors such as neglect.

In a recent lesion-symptom mapping study of complex figure drawing, Chechlacz et al. (2015) argued for distinctions between several functional components of copying complex figures. For example, they found an association between poor positioning of elements and lesions to both posterior (lingual gyrus and calcarine fissure) and more anterior sites (insula), suggesting that the effects stemmed from poor visuospatial coding. Our current analysis indicates that positioning errors are also related to executive functions such as planning, and this may explain the link between these errors and more anterior lesions involving the insula. In addition, Chechlacz and colleagues noted that spatial asymmetries in complex figure copying were correlated with damage to posterior parietal cortex. Our results concur with these data; indicating that poor spatial positioning in drawing can dissociate from spatial asymmetries and that the asymmetries are typically linked to spatial neglect (and lesions associated with neglect; Chechlacz et al., 2015). Chechlacz and colleagues also found that poor reproduction of global aspects of a complex figure were associated with right hemisphere lesions while poor reproduction of local elements was linked to left hemisphere damage (see also Fink et al., 1996; Lamb et al., 1989, 1990, for effects of left hemisphere damage, and Doyon & Milner, 1991; Lamb et al., 1990; for effects of right hemisphere damage).

Interestingly, we did find that spatial asymmetries in the complex figure task were related to a measure of sustained attention in the Auditory Attention test from BCoS. Spatial neglect has been linked to impairments in sustained attention (Robertson, et al., 1997).

Rehabilitation aimed at improving sustained attention has had beneficial effects on neglect (Robertson, Tegnér, Tham, Lo, & Nimmo-Smith, 1995). Our data fit with the argument that poor sustained attention may underlie at least some impairment in spatial attention; in particular, if reduced sustained attention particularly affects the right hemisphere (Robertson et al., 1997), then a reduction in this factor may limit attention to the left, and a right bias emerges in spatial reproduction.

In sum, the GLSS demonstrates both, a way of systematically scoring complex figure performance and linking this to aspects of executive function. This may be utilised in the design of future test batteries which use complex figure copying as a way of quickly assessing several cognitive functions (see Massa et al., 2015), with some particular measures able to signal executive dysfunction.

Study limitations

We note two main limitations of the present study that are of future interest.

One is that the measurement of systematicity relied upon the summation of a presence, placement and accuracy for both local and global scores. It should be recognised that a method of simple summation does not control for variation in methodological/psychometric properties of the composite indices. An alternative approach might have been to use item response theory to create composite scores that control for item response and discrimination.

The second limitation concerns the adequacy of IRR between the Global-Local ratings provided by the two independent examiners. Out of the 12 scores used to examine the IRR, only one score (the presence score for local left side) was excellent as it reached 0.81-1 (almost perfect agreement) and rest of the scores were within 0.61-0.80 (substantial agreement) or lower, especially the accuracy ratings across the Global-Local aspects. The, overall, moderate agreement in the data raise concerns as to whether the discrepancy in the data: i) due to an ambiguity in the written guidelines of the detailed scoring criteria, therefore, it was difficult for the second examiner to comprehend in order to apply for each element when scoring, or ii) both examiners employed different interpretation of the guidelines. In such case, securing a third independent examiner for IRR is a prospect, since, an overall good agreement between the second and third examiner is an indication that the guidelines in the scoring criteria need further revision. In contrast, disagreements between all three examiners will indicate, either: i) unreliable qualitative scoring system and or ii) qualitative methods are largely dependent on the individual clinical judgment.

Consequently, the latter statement brings us to the next chapter, Chapter 6. In this chapter, we will be developing an automated scoring criterion for a complex figure task to measure executive function, as well as the general performance (e.g., visuospatial constructional abilities and visual memory). This will be a pilot study, involving a smaller study sample and a different complex figure, were the primary goal of the study is to demonstrate the principle of a novel technique to measure systematicity.

CHAPTER 6

MEASURE OF SYSTEMATICITY IN A VISUOSPATIAL TASK: PILOT STUDY

ABSTRACT

INTRODUCTION: In a Complex Figure Copy task, a participant is asked to copy the given complex figure (made of geometric shapes) and reproduce it from memory (in some assessments). These assessments are used to evaluate visuospatial constructional ability and visual memory, as well as aspects of executive function (EF) in research and clinical environment. However, majority of these assessments are scored manually in a subjective manner. Consequently, the scoring and data collection for these measures are time-consuming and potentially increase the risk of human error. **METHOD:** We present a pilot study, demonstrating the principle of a novel technique; an automated scoring system to measure the construction organisation (the 'systematicity' index) while a participant progresses drawing the given figure. We evaluated stroke survivors at a chronic stage (*n*=16) after stroke using the tablet version of Oxford Cognitive Screen-Dementia (OCSd). **RESULTS:** We showed that the scores generated by the 'automated Global-Local Scoring System' (aGLSS) correlates with the overall cancellation performance, which in return can index executive planning (Chapter 4). There also was a correlation between the systematicity scores generated using the aGLSS with another measure of EF (performance on the trails test from the OCSd). **CONCLUSION:** Although, the study demonstrates that this automated systematicity score can be a useful addition to the traditional measures used for scoring complex figure assessments, there are some limitations to the study which have been addressed.

INTRODUCTION

Deficits in executive function are common post-stroke (Ballard et al., 2003; Pohjasvaara, et al., 2002), reported to occur in around 19% to 75% of stroke victims, depending on the diagnostic criteria (Ballard et al., 2003; Leśniak, Bak, Czepiel, Seniów, & Członkowska, 2008; Nys et al., 2007; Pohjasvaara, et al., 2002; Rasquin et al 2004; Zinn, Bosworth, Hoenig, & Swartzwelder, 2007). Although, spontaneous recovery occurs, persistent executive deficits are frequently observed in individuals (Rasquin et al 2004). In return, the executive deficits impact stroke rehabilitation, and reduce the effectiveness of stroke treatment (McDowd, Filion, Pohl, Richards, & Stiers, 2003; Mok et al., 2004), with a higher risk of functional dependence (Leśniak et al., 2008; Pohjasvaara et al., 2002). As a result, individuals with executive deficits are often affected by a reduced capacity to successfully engage in important activities of daily living, including self-care, academic pursuits/failure to return to work, poor participation in social activities (Slick, Lautzenhiser, Sherman, & Eyrl, 2006; McDowd et al., 2003; Ownsworth & Shum, 2008).

Because of the severity of executive deficits, it is of great concern to clinicians and researchers to use sensitive testing measures, not only to detect and/or diagnose deficits in executive function, but also to provide detailed information to develop potential rehabilitation methods. In addition, executive dysfunction has been reported, as an excellent predictor of long-term outcomes (Nys et al., 2005) and should be identified at an early stage post-stroke to maximise the effect of stroke treatment. This indicates the need for a test measure that is time efficient (provide separate diagnoses of the different cognitive processes), practical in clinical settings and to be administered during the acute stage post-stroke for early diagnosis.

One type of test that is commonly used in clinical practice is the Complex Figure Copy (CFC) tests. These tests require the participant to draw a figure (usually, composed of geometric shapes), as accurately as possible, with the figure either the placed in front of them (copy condition) or removed out of sight to demand visual memory (immediate/ delayed condition). Performance on these tasks may reflect the patient's ability of different cognitive functioning including visuospatial constructional, nonverbal memory and, executive functioning, particularly organisational skills (Helmes, 2000; Shin, Park, Park, Seol, & Kwon, 2006; Watanabe et al., 2005) as well as other data such as the adequacy of attention, level of concentration and fine motor-coordination (Helmes, 2000). Rey-Osterrieth Complex Figure (ROCF: Osterrieth, 1944; Rey, 1941) is one of the widely used CFC tests in clinical practice, traditionally used to measure visuo-constructional ability and non-verbal visuospatial memory skills (Somerville, Tremont, & Stern, 2000). However, with the development of the Boston Qualitative Scoring System (BQSS), ROCF has been shown to measure executive functioning (particularly planning and organisation skills) through a set of comprehensive guidelines with a well-defined scoring criteria and templates to support scoring (Somerville et al., 2000). Though, BQSS use informative guides and templates to produce a very comprehensive score, the scoring process itself is time consuming as one drawing takes an average of 5 to 15 minutes to mark. In addition, the planning/organisation aspects of executive function (EF) were recorded using pre-printed flow charts and coloured pens (changed in time intervals) to track the drawing steps. This increases the administration time and the amount of labour that is required.

In this thesis (Chapter 5), we introduced the Global-Local Scoring System (GLSS) that was developed to measure an aspect of executive functioning, the ‘systematicity’ in construction organisation, using the BCoS Complex Figure Copy task (Humphreys, Bickerton, Samson, & Riddoch, 2012). The data revealed that the summary scores generated by GLSS were in convergence with clinical judgements, from two expert neuropsychologists, on how well planned/organised the patient’s performance was in the copy task. In addition, one of the six scores generated by the GLSS, the placement score established significance in correlation with the overall cancellation score, which can index executive planning in visual cancellation task (see in this Volume: Chapter 4), thus, providing evidence that the placement score can also index executive planning. In this study, we described an approach to systematically score complex figure performance and a particular aspect of the system (placement score) that can indicate potential executive dysfunction (‘systematicity’ index of spatial organisation), making the BCoS complex figure task as a time efficient cognitive test (i.e., derive multiple measures from a single test). However, various aspects of the GLSS have produced low inter-rater reliability (IRR). Note, that these qualitative scoring systems are performed by hand in what tends to be subjective manner and therefore, the interpretation of the guidelines for each element are open to interpretation (as different people interpret specific guidelines differently). This may lead to inconsistency between ratings.

A more efficient way of assessing planning/organisation would be the computerisation of the CFC, were drawing of each element and the order in which each element is drawn can be recorded without the risk of human error. Such a method would provide an objective and consistent result as well as be practical in clinical settings, particularly, by saving clinicians from undertaking tedious tasks.

The present study

In this study, we piloted a new scoring procedure that could be a potential solution, an automated measure of construction organisation (the 'systematicity' index) using the Figure Copy test from Oxford Cognitive Screen – Dementia (OCSd). The OCSd version of CFC was used to demonstrate this procedure, as opposed to the BCoS version of CFC (pencil-and-paper version). The reason being, OCSd Figure Copy was already computerised, along with other OCSd sub-tests in the tablet-version of a screen.

The computerisation of CFC has several advantages, for one, it provides an unobtrusive method for recording the constructional process of a drawing. Secondly, computerisation is capable of recording the dynamic data of a patient's performance, such as how well planned/organised a patient has undertaken the task (without being resource-and-labour intensive). In previous studies, this dynamic data has shown to contain valuable information on simpler neuropsychological copy test (Fairhurst & Smith, 1991). This introduces new and/or interesting possibilities of research to analyse CFC data, beyond the commonly existing paper-and-pencil CFC paradigms.

The first step in this automation is categorising the OCSd Figure Copy elements to facilitate the automated scoring criteria, therefore, the Global-Local processing (same paradigm used to categorise the BCoS CFC for GLSS; Chapter 5 for details on the hierarchical proposal) was used to categorise the elements of OCSd Figure Copy. However, with the availability of the dynamic data, we assessed the construction process of the CFC in relation to an 'automated Global-Local Scoring System' (aGLSS) algorithm, designed to index whether patients approached the construction of the figure in a context dependent manner (by drawing the outlines/border of the shape, followed by filling in the details), indicating highly systematic constructional process or by a context-independent manner (start with a detail and move to the outlines/border of the shape at a later stage, in random order), indicating poor systematicity in constructional processing.

To clarify, OCSd is a dementia based cognitive screen (see method section for details, page 181). However, the primary goal of the present study is to demonstrate the principle of an automated 'systematicity' scoring system in CFC, by correlating the scores with an established 'systematicity' measure, the Nearest Neighbour measure (see in this Volume: Chapter 4). We also evaluated whether our measure of construction organisation linked to other executive measures using a Trails task. OCSd consists of the required tests (search organisation task and the trails), along with other tests that are represented to the stroke profile (e.g., language assessment and memory tests) to evaluate the aGLSS in respect to measure of EF. Furthermore, the patient sample analysed in the present study includes the performance of chronic stroke patients, representing the stroke population. Our data and choice of materials, therefore, seem adequate for the purpose of the study – a pilot study where a novel research instrument is pre-tested to examine whether i) executive function can be assessed using automated scoring system and ii) identify short-comings in the study design, which could be addressed in preparation for the major study.

METHOD

Participants

Sixteen chronic stroke patients were recruited from a participant panel from Cognitive Neuropsychology Centre (CNC) in the Department of Experimental Psychology, University of Oxford. The patients' ages ranged from 42 to 80 years, with an average age of 59.94 years (SD = 12.2). The average length of education was 13.36 years (SD = 3.18). There were 4 females and 12 males; of them 15 were right-handed. The mean time post-stroke was 1.58 years (SD = 1.60). Lesion locations for the group were: 10 left hemisphere patients, 5 right hemisphere patients and 1 bilateral. This information was obtained from their clinical record that was taken upon the initial recruitment into the CNC patient panel, along with written informed consent.

Procedure for data collection

Informed consent was obtained according to the approved ethics protocols of the UK Research Ethics Committee and the Oxford University ethics procedure. The patient data in this study was collected as part of a large research trial, OCS trial, by trained examiners at the Cognitive Neuroscience Centre (CNC), Oxford University. The trained examiners were research assistants and doctoral researchers involved in the trial. The first author, who is also a trained examiner for the OCSd trial, did not participate in the data collection of the patient sample presented in the present study. The first author's responsibilities in the data collection for the present study involved: i) organisation and the preparation of the 16 samples used, ii) scoring each reproduction of the OCSd Figure Copy, following the automated Global-Local algorithm (for details see page 181 and 187-9 for the algorithm) and the search organisation of the OCS cancellation (*n*=16) using the 'Nearest Neighbour' algorithm (see Chapter 4).

Materials and procedures

OCSd neuropsychological examination. The Oxford Cognitive Screen - Dementia (OCSd) is a short cognitive screen, designed to detect cognitive impairments in patients diagnosed with dementia (currently, a research study based at Oxford University). The screen is dementia-specific and consists of 11 sub-tests that cover different domains including Attention and Executive functioning, Language, Memory, and Praxis. Note, this is a dementia-specific cognitive screen reflecting cognitive profile of dementia, however, as mentioned in the introduction (page 179), the tasks within the screen will be used to demonstrate a (potential) novel/alternative procedure to measure systematicity (planning/organisational aspect of executive functioning) using a complex figure task. The OCSd was conducted in the CNC, where the OCSd screen was presented in an electronic version, 'Tablet PC'. The OCSd tasks were implemented in Matlab using PsychToolbox (Brainard, 1997; Pelli, 1997). The OCSd screen was run on Window Surface Pro tablet (10.6-inch display) and the patient used a stylus to complete the tasks. All OCSd tasks were presented in a portrait format with an exception of the Selection tasks, presented in a landscape format. The following tests from OCSd were chosen for the purpose of this study. Table 1 presents the summary statistics of the chosen tests.

As mentioned above, all OCSd tasks were implemented in Matlab, including the Figure Copy task. However, the automated Global-Local algorithm was not inherent as part of the original OCSd screen, for it to be scored in real time. Therefore, for the purpose of this ‘pilot’ study, each patient’s performance on the Figure Copy test was extracted separately as an animation/video, to be analysed later. These videos illustrated the construction processes of the figure by each participant (from beginning to end) in black on a white background/space. Using these video data, the first author scored the performance of each OCSd Figure Copy (*n*=16), following the criteria of the automated Global-Local Scoring System (page 187-189). The automated Global-Local Scoring System was developed by the first author, however, the OCSd program (including the extraction of raw data) was developed as part of the OCS trial. In addition, the ‘Nearest Neighbour’ algorithm was also not inherent as part of the original OCSd screen (see Chapter 4 for details), and therefore, visual ‘plots’ were utilised to score the search organisation of the OCSd cancellation (‘Selection’ task, page 183-4).

1. Figure Copy test. The OCSd Figure Copy is made of two structures (right and left) both of which are joined to each other, vertically (see Figure 1). The numbers of elements in the left and right structure were equated to balance the sensitivity to both left and right spatial biases in patient performance/neglect. The Figure Copy test was administered to the stroke patients, from the CNC patient panel, in a quiet testing room, using the standard procedure set out in the OCSd test manual. To note, the OCSd Figure Copy test consists of two components: i) *Copy condition* (were the patients were presented with a test screen displaying the OCSd figure on the top half of the screen and a blank space at the bottom half) and, ii) *Recall condition (*were the patients were required to reproduce the same figure immediately after, but this time from memory). For the purpose of this study, we only analysed the data for the Copy condition. The instructions for the Copy condition, to the patient was as follows:

"I will show you a drawing. Your task is to use the pen to copy in the space underneath it"

Upon reading out the instructions, the patients were presented with a test screen displaying the OCSd figure and shown the space provided to re-draw the figure (below the original figure). The performance was timed.

2. Executive assessments. To assess the relationships between the systematicity score (derived from the automated Global-Local Scoring System) and executive function, the performance of the chronic stroke patients on the OCSd Selection and trails tasks were used:

***2.1** Selection.* The OCSd selection test is a visuospatial task typically used to measure unilateral neglect. The test was characterised by a range of pseudo-random fruits (targets) and vegetables (distractors) stimuli scattered across an A4 page, in a landscape orientation. The fruits and vegetables are separated under a kitchen category that resulted in three kinds of fruit (apple, banana, pear) and three kinds of vegetable (bell pepper, cabbage, carrots). The total area of the test screen was divided into 10 quadrants, 2 central (top and bottom), 4 left (far and near, top and bottom) and 4 right (far and near, top and bottom). Each quadrant contained 6 stimuli made of 3 targets and 3 vegetables, making a total of 30 targets and 30 distractors, per test screen. The test screen was positioned in front of the patient, at the participant's midline on the desk and the patient was instructed to 'tap' (select) only the fruits while ignoring the vegetables, using the stylus pen.

The overall accuracy score corresponded to the total number of targets selected (maximum score = 30). The asymmetry score for spatial neglect (failing to cancel fruit items on one side of the page) corresponded to the difference between the numbers of selected targets on the right side and the number of targets selected on the left side of the page (excluding the 2 central columns: maximum score = 24). Positive values on the asymmetry score indicated that more targets were selected on the right than the left side of the page (left neglect) and negative values indicated the opposite (right neglect).

The test consists of two parts: i) *Feedback condition (*were the previously selected stimuli are visible for the patient during the course of the task) and ii) *No Feedback condition (*were the previously selected stimuli are not visible for the patient during the course of the task). Both conditions were timed; each patient was given a maximum of three minutes to complete each condition. The time limit was not disclosed to the patient before the test, the display was automatically closed at the end of the three minutes. For the purpose of the present study, we only analysed the data for the Feedback condition, to correlate against the systematicity score generated from the Figure Copy performance.

2.1 Trails. The OCSd task requires participants to draw connecting lines between different geometric shapes (circles and squares). The test consists of three components, two of them are baselines: i) connecting circles in decreasing order of size, in the presence of square distractors, and ii) connecting squares in the increasing order of size, in the presence of circle distractors. The baselines are compared with iii) a switch task, that is a shape switching condition in which participants draw a trail alternating between circles and squares, with circles going in descending order of size and squares in ascending order of size. The shapes are positioned randomly, in the central section of the screen. Therefore, the participant can draw the correct trail without crossing any other shapes.

There were eight circles and eight squares on the test screen. Score of 1 was given for each correct connection. However, if an error is made, but subsequent performance is corrected, the correct connection is automatically acknowledged. Patients scored 1 for each correct connection for the baseline task (maximum score = 7, each), and for the switch task (maximum score = 15). Executive score is the result of total number of correct connections in the baseline tasks versus switched. The subtraction of performance in the switch task from that in the baselines assess the effect of task switching with effects of processing speed and eliminate spatial biases in patient performance. Performance is timed.

3. Language assessment. The *Picture Naming* was selected from the language domain of the OCSd as it is typically used to assess the level of expressive language. The test requires the patient to recognise and name stimuli with low frequency names. There were four grey shaded hand drawn pictures (dolphin, kangaroo, corn, cherries); each picture is positioned in the central section of the test screen and was presented to the patient, individually. A score of 1 was given for each correct answer (maximum score = 4). Self-correction was permitted and the final answer was taken as the patient’s response.

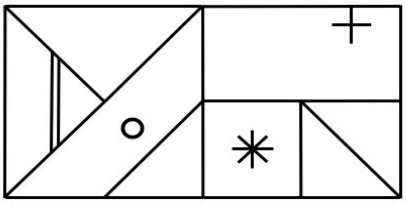
4. Memory. The *Recall and Recognition* task from the Memory domain was chosen to represent the memory domain. This test consists of two parts:

i) *Verbal memory* - at the beginning of OCSd, a list of words was given to patients to read, they were reminded to remember the words as they will be asked to reproduce them at a later stage. There were five words (bicycle, mist, wardrobe, teacher, and rectangle) to remember and the patient was required to recall all the words. If the patient was unable to free *recall*, all the words correctly, a verbal recognition test was given for each missed or erroneous word. The verbal recognition test is presented as a multiple-choice response, where, for each target word, the patient was shown a screen with four options distributed vertically; one correct response and three semantically related distractors. Each word on the screen was read out aloud by the examiner and the patient was requested to choose the correct response. A score of 1 was given for each target word recalled correctly. The total score reflected the number of total correct responses after the multiple-choice options (maximum score = 5).

i) *Episodic memory* - visual episodic memory was assessed through recognition of previously encountered items (pictures/words) during the first part of OCSd. The patient was asked four questions and a multiple-choice response was shown on the test screen with four options, one target and three visually/semantically related distractors, distributed vertically in a portrait format. Out of the four questions, three were based on picture stimuli and one verbal (for this question, the examiner read the responses loudly), and the patient was asked to point to the correct response. A score of 1 was given for each correct answer (maximum score = 4).

For this study, we summed the two memory scores (maximum score = 9) that correlated with the systematicity score.

Complete OCSd complex figure



Global elements (1-7) **Local elements (8-19)**

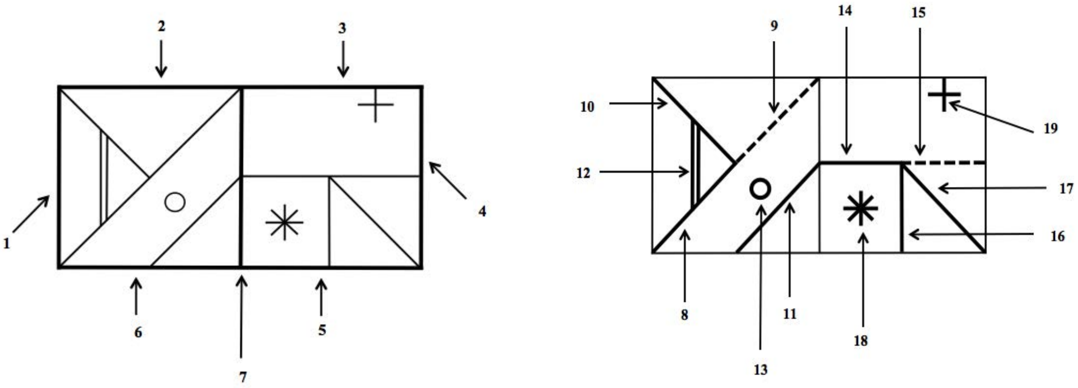


Figure 1. Division of the OCSd complex figure into aGLSS Global elements[1] and Local elements[2]

---

[1] 1=Left vertical border line, 2=Left top horizontal border line, 3=Right top horizontal border line, 4=Right vertical border line, 5=Right bottom horizontal border line, 6=Left bottom horizontal border line, 7=Central vertical border line.

[2] 8=Left large diagonal border line 1, 9=Left large diagonal border line 2, 10=Left small diagonal line 1, 11=Left small diagonal line 2, 12=Left parallel line, 13=Left circle, 14=Right horizontal line 1, 15=Right horizontal line 2, 16=Right vertical line, 17=Right diagonal line, 18=Right asterisk, 19=Right cross.

Introducing the automated Global-Local Scoring System

The automated Global-Local system divides the OCSd Figure Copy into two sets of elements with the assumption that the OCSd Figure Copy construction process should be organised in a hierarchical manner. Therefore, the automated Global-Local Scoring System categorised the OCSd Figure Copy elements into Global and Local elements to facilitate the scoring (see Figure 1). There are 19 elements; of which 7 of the elements are Global (the lines that represent/make up the outlines of the left and right structures) and 12 of the Local elements (the lines within the Global structures that form geometric shapes within the Global structures).

automated Global-Local Scoring System. This scoring system used a three-point scale approach to evaluate the construction process of each patient's performance on the OCSd Figure Copy task. Each of the elements drawn were scored along a three-point scale, ranging from a 0 to 1; 0 being no/poor systematicity and 1 being good systematicity reflecting good planning/organisation ability. Therefore, for each element drawn (the target element), we provided a score by assessing whether i) the patient completed the target element without moving to any another element (new element/another element that was drawn previously but incomplete; *score of 1*), ii) the patient moved to another element within the same category (e.g., global to global elements), before completing the target element and returning to complete the target element at a later stage (*score of 0.5*) and, ii) the patient moved to another element across the category (e.g., global to local elements), before completing the target element and returning to complete the target element (*score of 0*). In addition, if a drawn element is incomplete (the patient did not return to complete the element, also a *score of 0* is given).

Perseveration (recognisably inappropriate repetition of an element) took two forms: i) repetition of elements within the element, and ii) replication of an element elsewhere in the figure. In such cases, differentiating between the perseveration, self-permitted corrections or the target is ambiguous and is often open to interpretation, therefore, 3-Point scale acknowledged the reproduction of the element close to the original. However, each perseveration is recorded as a new element, denoting a number in order of elements drawn. Fragmentation (integration of an individual element such as whether the element was drawn as a whole unit) also took two forms: i) individual element was drawn in strokes without moving to another element before completion, ii) the element was split; the patient moved to another element and returned for completion. The former fragmentation was discounted as this form of fragmentation can be a result of habit and latter was recorded as a new element. The final systematicity score was calculated by summing the score for each of the elements (19) in the 3-Point scale divided by the total number of elements drawn, including perseveration and fragmented (split) lines. The final automated systematicity score reflected the global coherence of the patient's planning/organisation.

DATA ANALYSIS

The aGLSS was examined using a sample of 16 drawings of the OCSd figure copy produced by chronic stroke patients attending the CNC patient panel, Oxford University. The systematicity score derived from the aGLSS was validated against an existing measure chosen to index the same underlying function (i.e., the 'systematicity' in cancellation performance, generated using the nearest neighbour measure, see this Volume: Chapter 4).

In addition, we also report correlations whether our measure of construction organisation linked to an index of executive control taken from a ‘trails’ test of executive function in the OCSd. We also evaluated the automated global-local scoring approach against the performance of the other aspects of cognition (memory and language domain), demonstrated by lack of correlations with measures that are not thought to underlie the same function. Summary statics of for the chosen tests are presented in Table 1. For these correlations, participants were removed if they were outliers for the task (identified using Tukey’s (1977) method).

Table 1. Summary Statistics of *OCSd Subtest Scores for Chronic Stroke Patients*

Sub-tests	Measure	Mean	SD
		Statistic scores	
Figure copy			
Global		5.5	2.48
Local			
	Left Square	5.94	.25
	Right Square	5.88	0.5
	Asymmetry	.06	.25
Selection			
	Accuracy	29.25	1.39
	False positive	.13	.34
	Asymmetry	0	.37
		Dynamic scores	
Figure copy:			
automated Global-Local score		.74	.18
Selection:			
Nearest neighbour score		2.51	0.87
Sub-tests used for validation			
Trails	Executive score	-3.94	4.95
Picture naming	Overall accuracy	3.56	.63
Memory:		7.75	1.24
i. Verbal Score	Overall accuracy	4.5	.73
ii. Episodic Score	Overall accuracy	3.25	.68

RESULTS

Correlations between aGLSS systematicity score and ‘systematicity’ score of cancellation performance.

A Pearson correlation was conducted to assess the relationship between the automated systematicity score on the OCSd Figure Copy (copy condition) (derived from the aGLSS approach) and systematicity scores for cancellation performance on the OCSd Selection task (feedback condition) (derived using the Nearest Neighbour approach). There was a negative correlation between the automated systematicity score between the Figure Copy condition ($\bar{x}$ = .78, SD = .12) and the cancellation performance from the Selection test ($\bar{x}$ = 2.53, SD = .90), *r* (13) = - .451, *p* = .046, one outlier was omitted. This indicates that high systematicity scores generated from aGLSS (indicating systematic drawing organisation) were associated with low scores on the Nearest Neighbour measure (indicating high systematic performance in search organisation).

Correlations between systematicity score and other measures of OCd

Furthermore, the automated systematicity scores derived from aGLSS were correlated with other sub-tests from the OCSd. There was a reliable correlation between the automated systematicity score of the Figure Copy ($\bar{x}$ = .74, SD = .18) and the executive measure from the OCSd Trails tests (the cost in the switching: $\bar{x}$ = - 3.94, SD = 4.95), *r* (14) = - .471, *p* = .033. There were no other correlations between the systematicity measure and performance in the other domains of the OCSd; Picture Naming score in the language domain ($\bar{x}$ = 3.56, SD = .63), *r* (14) = - .025, *p* = .464) and Memory ($\bar{x}$ = 7.75, SD = 1.24), *r* (14) = .105, *p* = .349. Though, the results suggest that systematicity can be assessed using the aGLSS, this being a pilot study, the specificity and sensitive related to executive dysfunction is in need of further research analysis. This will be discussed as limitations of the study in that are of future interest.

DISCUSSION

Complex Figure Copy tasks are one of the widely used tests in clinical and research settings to evaluate neurological dysfunction in visual perception, non-verbal memory, and executive function. A patient is asked to copy the complex figure and then reproduce it from memory (for the purpose of this study, we only analysed the copy condition of the test). The test is typically administered as a pen-and-paper neuropsychological test and as a result, the drawings are scored manually in a subjective manner, raising concerns for its reliability and consistency.

In the present study, we demonstrated a principle for an automated systematicity measure, aGLSS, to provide an index of how well planned/organised a patient performed the CFC task. We evaluated this, aGLSS, approach on a sample of 16 chronic stroke patients performing a computerised Figure Copy task selected from the OCSd screen. There was a correlation between the automated systematicity score on the Figure Copy test scores derived using the aGLSS and the automated systematicity scores from the Selection task measured through the Nearest Neighbour scoring system. Also, there was a significant correlation between the automated systematicity for the Figure Copy and the measure of executive function (the cost of task switching) from the Trails test in the OCSd. There were no correlations with tests from other cognitive domains of the OCSd (memory and language). The data suggests that the systematicity score generated from the aGLSS approach can measures executive function, particularly organisation. Furthermore, the study has demonstrated that this automated systematicity score can be a useful addition to the traditional measurements used for scoring CFC tasks, providing a time efficient evaluation on the construction organisation of the drawing process itself without the risk of human error in recording the drawing process or interrupting patient's performance to change the colour of the marker.

However, the generalisation of these findings to a stroke population is confined by insufficient statistical analysis and the small sample size (*n*=16). Further work is needed for the replication of these results. On that note, it should be recognised that this is a pilot study, thus there will be potential practical problems in the research procedure to be addressed, as well as study limitations, when the study is to be replicated in a larger-full scale study. These issues are discussed in turn.

Study limitations

The study utilised a dementia based cognitive screen. Though, the choice of sub-tests and the patient sample were adequate for the purposes of study; both, Dementia and Stroke consists of different cognitive profiles and the sub-tests are designed and scored accordingly. Therefore, the use of a stroke based cognitive screen would have been suitable for the study, for consistency in validation. In the major study, it would be more beneficial and informative to using stroke specific cognitive screen/sub-tests to validate the aGLSS systematicity measure. The choice of tests for validation brings us to our next limitation, the sub-test that was used to validate the ‘systematicity’ aspect of aGLSS measure, that is, the Selection test from OCSd. In the previous studies (see in this Volume: Chapter 4 and Chapter 5), we utilised expert opinions for the convergence of systematicity of which was not conducted in this study. Rather, we applied the Nearest Neighbour approach on the OCSd Selection task and validated the systematicity between the search organisation and constructional organisation. To emphasise, the use of the Nearest Neighbour approach (Chapter 4) across a different form of visual cancellation and cross validation against another executive measure (the proposed systematicity measure from aGLSS) implies that the Nearest Neighbour measure can be applicable across different forms of visual cancellation tasks. However, this limitation could be considered as a research problem to be addressed in the larger study, where experts are included to provide a systematicity score that is “how systematically each patient performed the Figure Copy task”. Here, the experts can rate how well the patient planned/organised the drawing take on a scale of 1 to 10; 1 being no/poor organisation and 10 being good organisation. Subsequently, these ratings will be correlated with the aGLSS systematicity score for stronger convergence evidence for the relationship between the aGLSS score and the score given by the subjective raters on how well planned/organised the patient performance is. Thus, a high aGLSS score will correlate with a high systematicity score given by the subjective rater, indicating good planning/organisation in the constructional processing. In addition, the data from experts may provide interesting and valuable information from a clinical perspective on constructional organisation.

On a final note, an interesting avenue of research for the larger study is the method utilised in selecting the validation tests. The use of factor analysis, particularly, principle component analysis appears to provide a highly reliable theoretical base to confirm relationships between tests of which measure the same construct or a different construct. This is a procedure that is to be explored further and possibly change the paradigm of the study.

CHAPTER 7

CONCLUSIONS AND GENERAL COMMENTS

The overall aim of this thesis was to develop measures of planning/organisation, (the ‘systematicity’ index), using performance-based cognitive tests that are suitable for the stroke population.

According to the Anderson (2002) model of executive function, the Executive Control System, systematicity is a coupling of the planning and organisation skill from executive function. Here, the organisation ability involves the strategic arrangement of complex information to reach the end (intended) goal, and planning ability involves an individual’s ability to formulate goals, devise strategies and or sequence of steps/actions to achieve the end goal. Fundamentally, planning, along with initiation, inhibition, self-monitoring/regulation, are all aspects of executive functions involved in goal-directed behaviour. Therefore, an impairment in systematic organisation, that is, when the ability to organise has been compromised, will result in inefficient planning resulting in developing inefficient and ineffective strategies to achieve the end (intended) goal, through goal-directed behaviour.

Apraxia is a disorder of higher motor cognition, where an individual is unable to perform (previously) learnt goal-directed behaviours, and it is also one of the common cognitive deficits that occur after a stroke. Ideational apraxia (IA) is a classification of limb apraxia, characterised by the inability in performing a sequence of actions/multi-action in the specific manner and order necessary to attain the end goal. Therefore, IA is a disorder of systematicity, since the clinical manifestation of IA exhibits the inability to organise and develop efficient planning to perform goal directed behaviours to achieve the end goal. Accordingly, such apraxic disorders reduces the functional independence of an individual, and in return impact the psychological wellbeing of that individual, increasing the burden of the caregiver. The importance of assessing and identifying apraxic disorders is apparent. However, the test measures currently in use to assess apraxia, especially, IA (to assess multi-action sequencing in everyday living) either, do not measure the underlying cognitive causes of disorganisation (ADL measures) or are not appropriate for stroke patients as they are language-laden (the Key Search and Zoo Map tests from Behavioural Assessment of the Dysexecutive Syndrome (BADS: Wilson, Alderman, Burgess, Emslie, & Evans, 1996; Wilson, Evans, Emslie, Alderman, & Burgess, 1998) in which the complex instructions/rules of the tests may compete for limited working memory resources required for planning.

Therefore, in this thesis we set out to develop measures of planning/organisation (the ‘systematicity’ index) suitable to be utilised within the stroke population. The candidate measure was designed to be unbiased (the score only reflected the overall planning/organisational ability in an individual), nonverbal (maximise the patient assessment) and time-efficient (where one cognitive test can produce several measures of cognitive deficits, in a single performance). The successful development of multi-dimensional cognitive instruments will provide sustainable and easily interpretable result for the clinicians and or the examiners (researchers, the rehab staff etc.,) in an environment with limited time.

This thesis comprised of five empirical studies, across two parts that aimed to explore the variation of cognitive deficits of stroke patients (Part 1) and development of measures of planning/organisation for stroke population (Part 2).

Part 1: Assessing the underlying factors in the cognitive profile of stroke patients

In Study 1 (see in this Volume: Chapter 2), using a Principle Component Analysis (PCA) with a varimax rotation (pairwise deletion to control missing data) on the sub-acute (<3 months, *n*=763) and chronic stage post-stroke patients (~9 months, *n*=349), the PCA revealed seven factors, which largely reflected the hypothesised theoretical Birmingham Cognitive Screen (BCoS: Humphreys, Bickerton, Samson, & Riddoch, 2012) latent variable structure, for both patient samples.

The **Sub-acute** sample (64.26% total variance) reflected seven primary factors; the largest factor being ‘Left hemisphere lesion’ (as a result of neuro-anatomically clustered variables) and the rest of the factors were better associated with specific cognitive components (‘Memory’, ‘Spatial attention’, ‘Controlled attention’, ‘Attention to detail’, ‘Response suppression/Executive function’ and ‘Attentional to capacity during selection’). The **Chronic** sample (61.51% total variance) reflected specific cognitive components, where some of the factors matched the sub-acute sample (‘Memory’, ‘Controlled attention’ and ‘Response suppression’), while others were a result of a clear fractionation of cognitive processes (‘Language’, ‘Praxis’, ‘Spatial attention’ and ‘Visual-attention capacity after left hemisphere lesion’). The study revealed that the cognitive profile after stroke changes from the sub-acute to a chronic phase, and that domain-specific cognitive deficits become more evident over time.

In study 2 (see in this Volume: Chapter 3), another PCA was conducted using varimax rotation on the difference score, to evaluate the underlying factors that contribute in the changes of cognitive performance between two test periods, the sub-acute and the chronic stage post-stroke. For this study, the same BCoS dataset as Chapter 2 was used, however, only consisting of patients who participated in the initial session (sub-acute, <3 months) and the follow up session (chronic, ~9 months) post-stroke. Therefore, the difference score was calculated by comparing the differences in the scores from the sub-acute (initial testing, <3 months) and to chronic stage post-stroke (follow-up, ~9 months).

Here, nine factors were retained from the PCA analysis. Factor 1 (‘Motor output process of post-stroke’) was the largest factor, consisting of variables associated with physical abilities reflecting improvement in motor functioning post-stroke. Rest of the factors were associated with specific components of cognition (‘Memory’, ‘Competition for selection’, ‘Attention to local detail’ and ‘Spatial attention’) where some of the factors represented distinguishing neuropsychological syndromes by dissociating within domain. For example, language domain divided into two factors (‘Speech output’ and ‘Verbal retrieval’) and controlled attention/executive function also loaded into two factors (‘Working memory’ and ‘Sustained attention’), consistent with the BCoS design (to distinguish between processes) based on the theoretical fractionation of cognitive processes.

One of marked similarities in the latent variable structures reported in Study 1 and Study 2 was the factor ‘Spatial attention’, made of variables from two spatial attention tasks, Apple Cancellation test and Complex Figure Copy test (from the BCoS). Both tests are made up of multiple different components, deemed to provide multiple measures. In addition, both tasks are nonverbal and singular. Appropriately, both tasks were utilised in developing stroke specific measures of planning/organisation, the ‘systematicity’ measure (Part 2).

Part 2: Developing executive measures for stroke

In study 3 (see in this Volume: Chapter 4), we demonstrated an algorithm to measure organisation in a visual cancellation task (*n*=30 acute stroke patients). The principle of the technique was demonstrated in a computerised cancellation task, the Broken Hearts test from Oxford Cognitive Screen (OCS: Demeyere, Riddoch, Slavkova, & Humphreys, 2015). OCS is the shorter version of BCoS. Therefore, the Broken Hearts was a replica of the Apple Cancellation, but differed by the selection of stimuli. The measure correlated with expert opinions of how systematic a patient is during cancellation as well as with a measure of executive function (performance on the trails test from the OCS). In addition, a *t*-test between neglect and non-neglect patients indicated that the measure was not significantly affected by spatial biases. This measure of systematicity was named, the 'Nearest Neighbour".

The additional information provided by this measure indicates that the score is a useful clinical addition to standard indices of spatial attention (Bickerton, Samson, Williamson, & Humphreys, 2011).

In Study 4 (see in this Volume: Chapter 5), we demonstrated a qualitative scoring method to measure organisation in a visuo-constructional task (*n*=100 chronic patients). The principle of the technique was demonstrated in a pencil-and-paper version of a Complex Figure Copy task from BCoS. The proposed system provides scores on the presence, placement and accuracy of visual features across Global and Local scales of processing (19 elements). The scores derived from this measure were validated against measures of neglect, controlled attention and executive function (from the BCoS). The scores, especially, the placement score and the overall accuracy score from this measure correlated well with the rule finding, sustained attention index, working memory as well as the neglect scores. In addition, when spatial asymmetry was controlled in the complex figure task, the placement score from the systematicity measure correlated with the overall cancellation score from the Apple Cancellation task, which can index executive planning (see in this Volume: Chapter 4, the development of measure of organisation in cancellation, the 'systematicity' in cancellation performance). This measure of systematicity was named, the 'Global-Local Scoring System' (GLSS).

From this study, the placement score on the complex figure task was found to be a good indicator of planning/organisation aspect of executive function. Therefore, used as an extra index of executive function to aid in clinical assessments. However, the overall reliability (the inter-rater reliability: IRR) for the GLSS was low, raising concerns with current subjective scoring that is tend to be done manually by human scorers.

Therefore, in Study 5 (see in this Volume: Chapter 6), we demonstrated an algorithm to measure organisation in a visual constructional task (*n*=16 chronic stroke patients), of which could be a potential solution to the IRR concerns. The principle of the technique was demonstrated in a computerised visual constructional task, the Figure Copy test from the Oxford Cognitive Screen-Dementia (OCSd). The same Global-Local processing, as Chapter 6, was used to categorise the Figure Copy elements. Rather than using expert opinions to provide evidence of systematicity, the Nearest Neighbour measure was applied to a cancellation task (also from OCSd), which revealed a significant correlation. In addition, the measure also correlated with another measure of executive function (performance on the trails test from the OCd). This measure of systematicity was named, the ‘automated Global-Local Scoring System’ (aGLSS).

The additional information provided by this measure indicates that the score is a useful clinical addition to standard measures of Complex Figure Copy, providing an index of ‘systematicity’ in spatial organisation. However, this was a pilot study consisting of a very low number of stroke patient samples and inadequacy in statistical analysis. Therefore, the results need to be reproduced in a larger sample.

In summary, this thesis has marshalled measures of planning/organisation (the ‘systematicity’ index) that are suitable to be used within the stroke population: i) The Nearest Neighbour measure (see in this Volume: Chapter 4), demonstrated to measure planning aspect of executive function by correlating with expert opinions of how systematic a patient is during cancellation as well as with a measure of executive function (performance on the trails test from the OCS), ii) the Global-Local Scoring System (GLSS), the placement score demonstrated to index executive planning as it correlated with the overall cancellation score from the Apple Cancellation performance, when spatial asymmetry was controlled in the Complex Figure Copy (see in this Volume: Chapter 5). Finally, iii) the automated Global-Local Scoring System (aGLSS), demonstrated to measure executive aspect of planning/organisation as the analysis revealed a significant correlation between the Nearest Neighbour measure and the performance on the trails test from the OCSd (see in this Volume: Chapter 6). However, this is a pilot study to demonstrate a novel principle, and therefore, in order for the results to be conclusive, the study needs to be replicated in a larger sample. This would be potential interest for future research.

In consideration to the study limitations, the aforementioned measures have the demonstrated to have a potential to measure planning/organisation (the ‘systematicity’ index) using performance-based, language reduced/nonverbal tasks that could be used in a stroke population. In addition, these measures can be beneficial to the clinicians in terms of in saving time (by being time-efficient) and providing direct scores, without complicating the interpretation of the results.

Future research

It would be beneficial to replicate the pilot study (see in this Volume: Chapter 6) in a larger stroke sample; whereby, a validated index of ‘systematicity’ in spatial organisation (aGLSS) can be a reliable measure, which can be used in clinical settings, particularly at the acute stage of stroke. The easy administration can be an advantage in the acute stage, where executive deficits can be detected favouring the clinicians in respect of their time. In addition, recruitment of control data for performance comparison against the stroke patients would further assist in developing a cut-off score for the (aGLSS) ‘systematicity’ index. Another aspect of this thesis that is worthwhile to be explored further is the BCoS dataset using Confirmatory Factor Analysis to test the theoretical base of the BCoS structure. These are some of the many future proposals that could complement the content produced in this thesis.

REFERENCE

Alexander, M. P., & Stuss, D. T. (2000). Disorders of frontal lobe functioning. In *Seminars in neurology* (Vol. 20, No. 04, pp. 427-438).

Alvarez, J. A., & Emory, E. (2006). Executive function and the frontal lobes: a meta-analytic review. *Neuropsychology review*, *16*(1), 17-42.

Anderson, P. (2002). Assessment and development of executive function (EF) during childhood. *Child neuropsychology, 8*(2), 71-82.

Anderson, T. W., & Rubin, H. (1956). Statistical inference in factor analysis. In *Proceedings of the third Berkeley symposium on mathematical statistics and probability* (Vol. 5, pp. 111-150).

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. *Trends in cognitive sciences, 8*(4), 170-177.

Baddeley, A. (1996). Exploring the central executive. *The Quarterly Journal of Experimental Psychology Section A: 49*(1), 5-28.

Baddeley, A. (2000). The episodic buffer: a new component of working memory?. *Trends in cognitive sciences*, *4*(11), 417-423.

Baddeley, A. (2002). Fractionating the central executive. In D. T. Stuss & R.T. Knights (eds.), *Principles of frontal lobe function* (pp. 246-260). New York: Oxford University Press

Ballard, C., Stephens, S., Kenny, R., Kalaria, R., Tovee, M., & O'Brien, J. (2003). Profile of neuropsychological deficits in older stroke survivors without dementia. *Dementia and Geriatric Cognitive Disorders, 16,* 52–56.

Barker-Collo, S., & Feigin, V. (2006). The impact of neuropsychological deficits on functional stroke outcomes. *Neuropsychology Review, 16,* 53–64.

Beaumont, J. Graham (2012). Introduction to neuropsychology (2nd ed.). New York: The Guilford Press

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

Bickerton, W. L., Riddoch, M. J., Samson, D., Balani, A. B., Mistry, B., & Humphreys, G. W. (2012). Systematic assessment of apraxia and functional predictions from the Birmingham Cognitive Screen. *Journal of Neurology, Neurosurgery & Psychiatry, 83,* 513–521.

Bickerton, W. L., Samson, D., Williamson, J., & Humphreys, G. W. (2011). Separating forms of neglect using the Apples Test: Validation and functional prediction in chronic and acute stroke. *Neuropsychology, 25,* 567–580.

Black, S., Ebert, P., Leibovitch, F., Szalai, J. P., Blair, N., & Bondar, J. (1995, April). Recovery in hemispatial neglect. In *Neurology*, *45* (4), pp. A178-A178. 34 Beacon Street, Boston, MA 02108-1493: Little Brown Co.

Brainard, D. H. (1997). The Psychophysics Toolbox. *Spatial Vision*, *10*(4), 433 - 436.

Brocki, K. C., & Bohlin, G. (2004). Executive functions in children aged 6 to 13: A dimensional and developmental study. *Developmental neuropsychology*, *26*(2), 571-593.

Campbell, D. C., & Oxbury, J. M. (1976). Recovery from unilateral visuo-spatial neglect?. *Cortex*, *12*, 303-312.

Cantagallo, A., Maini, M., & Rumiati, R. I. (2012). The cognitive rehabilitation of limb apraxia in patients with stroke. *Neuropsychological rehabilitation*, *22*(3), 473-488.

Cassidy, T. P., Lewis, S., & Gray, C. S. (1998). Recovery from visuospatial neglect in stroke patients. *Journal of Neurology, Neurosurgery & Psychiatry*, *64*(4), 555-557.

Chechlacz, M., Mantini, D., Gillebert, C. R., & Humphreys, G. W. (2015). Asymmetrical white matter networks for attending to global versus local features. *Cortex*, *72*, 54-64.

Chechlacz, M., Rotshtein, P., Bickerton, W. L., Hansen, P. C., Deb, S., & Humphreys, G. W. (2010). Separating neural correlates of allocentric and egocentric neglect: Distinct cortical sites and common white matter disconnections. *Cognitive Neuropsychology, 27* (3), 277-303.

Chechlacz, M., Rotshtein, P., Roberts, K. L., Bickerton, W. L., Lau, J. K., & Humphreys, G. W. (2012). The prognosis of allocentric and egocentric neglect: evidence from clinical scans. *PLoS One*, *7*(11), e47821.

Colombo, A., De Renzi, E., & Gentilini, M. (1982). The time course of visual hemi-inattention. *Archiv für Psychiatrie und nervenkrankheiten*, *231*(3), 539-546.

Comrey, L. A., & Lee, H.B., (1992). A first course in factor analysis (2nd ed.). Hillside, NJ: Lawrence Erlbaum Associates.

Corbetta, M., & Shulman, G. L. (2011). Spatial neglect and attention networks. *Annual review of neuroscience, 34,* 569.

Corbetta, M., Ramsey, L., Callejas, A., Baldassarre, A., Hacker, C. D., Siegel, J. S., ... & Connor, L. T. (2015). Common behavioral clusters and subcortical anatomy in stroke. *Neuron*, *85*(5), 927-941.

Crone, E. A., Wendelken, C., Donohue, S. E., & Bunge, S. A. (2005). Neural evidence for dissociable components of task-switching. *Cerebral cortex*, *16*(4), 475-486.

Dalmaijer, E. S., Van der Stigchel, S., Nijboer, T. C., Cornelissen, T. H., Husain, M., (2015). CancellationTools: All-in-one software for administration and analysis of cancellation tasks. *Behaviour Research Methods, 47*(4), 1065-1075.

Damasio, A. R, Tranel, D., & Rizzo, M. (2000). Disorders of complex visual processing. In Mesulam, M. M (Ed.) Principles of Behavioural and Cognitive Neurology (2nd ed.) (pp.332-372). New York: Oxford University Press

Damasio, A. R. (1995). Toward a Neurobiology of Emotion and Feeling: Operational Concepts and Hypotheses. *The Neuroscientist*, *1*(1), 19-25.

de Haan, E. H., Nys, G. M., & Van Zandvoort, M. J. (2006). Cognitive function following stroke and vascular cognitive impairment. *Current Opinion in Neurology, 19* (6), 559–564.

Delis, D. C., Robertson, L. C., & Balliet, R. (1983). The breakdown and rehabilitation of visuospatial dysfunction in brain-injured patients. *International Rehabilitation Medicine, 5*(3), 132-138.

Delis, D. C., Robertson, L. C., & Efron, R. (1986). Hemispheric specialization of memory for visual hierarchical stimuli. *Neuropsychologia*, *24*(2), 205-214.

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

Diamond, A. (2013). Executive functions. *Annual review of psychology*, *64*, 135-168.

Donkervoort, M., Dekker, J., & Deelman, B. (2006). The course of apraxia and ADL functioning in left hemisphere stroke patients treated in rehabilitation centres and nursing homes. *Clinical rehabilitation*, *20*(12), 1085-1093.

Donkervoort, M., Dekker, J., Stehmann-Saris, F. C., & Deelman, B. G. (2001). Efficacy of strategy training in left hemisphere stroke patients with apraxia: A randomised clinical trial. *Neuropsychological rehabilitation*, *11*(5), 549-566.

Donovan, N. J., Kendall, D. L., Heaton, S. C., Kwon, S., Velozo, C. A., & Duncan, P. W. (2008). Conceptualizing functional cognition in stroke. *Neurorehabilitation and Neural Repair, 22*(2), 122–135.

Doricchi, F., & Galati, G. (2000). Implicit semantic evaluation of object symmetry and contralesional visual denial in a case of left unilateral neglect with damage of the dorsal paraventricular white matter. *Cortex*, *36*(3), 337-350.

Dovern, A., Fink, G. R., & Weiss, P. H. (2012). Diagnosis and treatment of upper limb apraxia. *Journal of Neurology*, *259*(7), 1269–1283.

Doyon, J., & Milner, B. (1991). Right temporal-lobe contribution to global visual processing. *Neuropsychologia, 29*(5), 343-360.

Edwards, D. F., Hahn, M. G., Baum, C. M., Perlmutter, M. S., Sheedy, C., & Dromerick, A. W. (2006). Screening patients with stroke for rehabilitation needs: Validation of the post-stroke rehabilitation guidelines. *Neurorehabilitation and Neural Repair, 20*(1), 42–48.

Elliott, R. (2003). Executive functions and their disorders: Imaging in clinical neuroscience. *British medical bulletin, 65*(1), 49-59.

Fabrigar, L. R., Wegener, D. T., MacCallum, R. C., & Strahan, E. J. (1999). Evaluating the use of exploratory factor analysis in psychological research. *Psychological methods*, *4*(3), 272.

Fairhurst, M. C., & Smith, S. L. (1991). Application of image analysis to neurological screening through figure-copying tasks. *International journal of bio-medical computing*, *28*(4), 269-287.

Fink, G. R., Halligan, P. W., Marshall, J. C., Frith, C. D., Frackowiak, R. S. J., & Dolan, R. J. (1996). Where in the brain does visual attention select the forest and the trees?. *Nature, 382*(6592), 626-628.

Floyd, F. J., & Widaman, K. F. (1995). Factor analysis in the development and refinement of clinical assessment instruments. *Psychological assessment*, *7*(3), 286.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*(3), 189–198.

Fure, B., Bruun Wyller, T., Engedal, K., & Thommessen, B. (2006). Cognitive impairments in acute lacunar stroke. *Acta Neurologica Scandinavica*, *114*(1), 17–22.

Gioia, G. A., Isquith, P. K., & Guy, S. C. (2001). Assessment of executive functions in children with neurological impairment. In R. J. Simeonsson & L. Rosenthal (eds.), *Psychological and developmental assessment: Children with disabilities and chronic conditions* (pp. 317-356). New York: Guilford Press.

Goldenberg, G. (2003) The neuropsychological assessment and treatment disorders of voluntary movement. In: Halligan P, Kischka U, Marshal JC (eds.) Handbook of clinical neuropsychology (pp. 387-400). Oxford University Press, Oxford.

Goldenberg, G. (2008) Apraxia. In: Goldenberg G, Miller BL (eds.) Neuropsychology and behavioural neurology (pp.323-338). Elsevier, Amsterdam.

Goldenberg, G. (2013). *Apraxia - The cognitive side of motor control*. Oxford, New York: Oxford University Press.

Goldenberg, G., & Hagmann, S. (1998). Therapy of activities of daily living in patients with apraxia. *Neuropsychological Rehabilitation*, *8*(2), 123-141.

Grafman, J., & Litvan, I. (1999). Importance of deficits in executive functions. *The Lancet, 354*(9194), 1921-1923.

Granger, C. V., Hamilton, B. B., Keith, R. A., Zielezny, M, & Sherwin, F. S. (1986). Advances in functional assessment for medical rehabilitation. *Topics in Geriatric Rehabilitation, 1*(3), 59–74.

Gross, R. G., & Grossman, M. (2008). Update on apraxia. *Current neurology and neuroscience reports*, *8*(6), 490-496.

Hamilton, B. B., Granger, C. V., Sherwin, F. S., Zielezny, M., & Tashman, J.S, (1987). A uniform national data system for medical rehabilitation. In: Fuhrer MJ (editor): Rehabilitation Outcomes: Analysis and Measurement (pp. 137–147). Baltimore: Paul H. Brooks.

Hanks, R. A., Rapport, L. J., Millis, S. R., & Deshpande, S. A. (1999). Measures of executive functioning as predictors of functional ability and social integration in a rehabilitation sample. *Archives of Physical Medicine and Rehabilitation*, *80*(9), 1030 - 1037.

Heilman, K. M., & Rothi, L. J. G. (1993) Apraxia. In: Heilman KM, Valenstein E, editors. *Clinical neuropsychology* (3rd ed.) (pp. 141–63). New York: Oxford University Press.

Helmes, E. (2000). Learning and memory. *Neuropsychological assessment in clinical practice: A guide to test interpretation and integration*, 293-334.

Heyder, K., Suchan, B., & Daum, I. (2004). Cortico-subcortical contributions to executive control. *Acta psychologica*, *115*(2), 271-289.

Hillis, A. E., Newhart, M., Heidler, J., Barker, P. B., Herskovits, E. H., & Degaonkar, M. (2005). Anatomy of spatial attention: insights from perfusion imaging and hemispatial neglect in acute stroke. *Journal of Neuroscience*, *25*(12), 3161-3167.

Hsieh, S., Schubert, S., Hoon, C., Mioshi, E., & Hodges, J. R. (2013). Validation of the Addenbrooke's Cognitive Examination III in frontotemporal dementia and Alzheimer's disease. *Dementia and geriatric cognitive disorders*, *36*(3-4), 242-250.

Humphreys, G. W., & Riddoch, M. J. (1994). Attention to within-object and between-object spatial representations: Multiple sites for visual selection. *Cognitive Neuropsychology*, *11*(2), 207-241.

Humphreys, G. W., Bickerton, W. L., Samson, D., & Riddoch, J. (2012). The Birmingham Cognitive Screen (BCoS) Psychology Press.

Humphreys, G. W., Forde, E. M., & Riddoch, M. J. (2001). The planning and execution of everyday actions.

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

Husain, M., Mannan, S., Hodgson, T., Wojciulik, E., Driver, J., & Kennard, C. (2001). Impaired spatial working memory across saccades contributes to abnormal search in parietal neglect. *Brian*, *124*(5), 941- 952.

Jaillard, A., Naegele, B., Trabucco-Miguel, S., LeBas, J. F., & Hommel, M. (2009). Hidden dysfunctioning in sub-acute stroke. *Stroke, 40*, 2473-2479.

Karnath, H. O., & Rorden, C. (2012). The anatomy of spatial neglect. *Neuropsychologia*, *50*(6), 1010-1017.

Karnath, H. O., Rennig, J., Johannsen, L., & Rorden, C. (2011). The anatomy underlying acute versus chronic spatial neglect: A longitudinal study. *Brain*, *134*(3), 903–912.

Kelly, T. (2000). The development of executive function in school-aged children. *Clinical Neuropsychological Assessment*, *1*, 38-55.

Kleinman, J. T., Newhart, M., Davis, C., Heidler-Gary, J., Gottesman, R. F., & Hillis, A. E. (2007). Right hemispatial neglect: frequency and characterization following acute left hemisphere stroke. *Brain and cognition*, *64*(1), 50-59.

Kuschner, E. S., Bodner, K. E., & Minshew, N. J. (2009). Local vs. global approaches to reproducing the Rey Osterrieth complex figure by children, adolescents, and adults with high-functioning autism. *Autism Research*, *2*(6), 348-358.

Laeng, B. (2006). Constructional apraxia after left or right unilateral stroke. *Neuropsychologia*, *44*(9), 1595-1606.

Lamb, M. R., Robertson, L. C., & Knight, R. T. (1989). Attention and interference in the processing of global and local information: Effects of unilateral temporal-parietal junction lesions. *Neuropsychologia*, *27*(4), 471-483.

Lamb, M. R., Robertson, L. C., & Knight, R. T. (1990). Component mechanisms underlying the processing of hierarchically organized patterns: inferences from patients with unilateral cortical lesions. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *16*(3), 471.

Landis, J. R., Koch, G. G. (1977). The measurement of observer agreement for categorical data. Biometrics, 159-174.

Lehto, J. E., Juujärvi, P., Kooistra, L., & Pulkkinen, L. (2003). Dimensions of executive functioning: Evidence from children. *British Journal of Developmental Psychology*, *21*(1), 59-80.

Leiguarda, R. C., & Marsden, C. D. (2000). Limb apraxias: higher-order disorders of sensorimotor integration. *Brain*, *123*(5), 860-879.

Leśniak, M., Bak, T., Czepiel, W., Seniów, J., Czlonkowska, A. (2008). Frequency and prognostic value of cognitive disorders in stroke patients. *Dementia Geriatric Cognitive Disordorders,* *26*(4), 356-363.

Levin, H. S., Culhane, K. A., Hartmann, J., Evankovich, K., Mattson, A. J., Harward, H.,... & Fletcher, J. M. (1991). Developmental changes in performance on tests of purported frontal lobe functioning. *Developmental neuropsychology*, *7*(3), 377-395.

Lezak, M. D. (1982). The problem of assessing executive functions. *International Journal of Psychology*, 17(1-4), 281-297.

Lezak, M. D. (1995). *Neuropsychological Assessment.* New York: Oxford University Press.

Luria, A. (1973). *The working brain.* New York: Basic Books.

Mahoney, F. I., & Barthel, D. W. (1965). Functional evaluation: the Barthel Index: a simple index of independence useful in scoring improvement in the rehabilitation of the chronically ill. *Maryland state medical journal*, 14, 61-65.

Malhotra, P., Jäger, H. R., Parton, A., Greenwood, R., Playford, E. D., Brown, M. M.,... & Husain, M. (2005). Spatial working memory capacity in unilateral neglect. *Brian*, *128* (2), 424 - 435.

Mark, V. W., Woods, A. J., Ball, K. K., Roth, D. L., & Mennemeier, M. (2004). Disorganized search on cancellation is not a consequence of neglect. *Neurology, 63*(1), *78-84.*

Marsh, E. B., & Hillis, A. E. (2008). Dissociation between egocentric and allocentric visuospatial and tactile neglect in acute stroke. *Cortex, 44*(9), 1215-1220.

Marshall, J. C., & Halligan, P. W. (1995). Seeing the forest but only half the trees?. *Nature, 373*(6514), 521

Massa, M. S., Wang, N., Bickerton, W-L., Demeyere, N., Riddoch, M. J., & Humphreys, G. W. (2015). On the importance of cognitive profiling: A graphical modelling analysis of domain-specific and domain-general deficits after stroke. *Cortex*, *71*, 190-204.

Mathuranath, P. S., Nestor, P. J., Berrioes, G, E., Rakowicz, W., & Hodges, J. R. (2000). A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. *Neurology, 55*(11), 1613-1620.

McConley, R., Martin, R., BaÑos, J., Blanton, P., & Faught, E. (2006). Global/local scoring modifications for the Rey-Osterrieth Complex Figure: Relation to unilateral temporal lobe epilepsy patients. *Journal of the International Neuropsychological Society*, *12*(03), 383-390.

McDowd, J. M., Filion, D. L., Pohl, P. S., Richards, L. G., & Stiers, W. (2003). Attentional abilities and functional outcomes following stroke. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 58*(1), P45-P53.

Medina, J., Kannan, V., Pawlak, M. A., Kleinman, J. T., Newhart, M., Davis, C., ... & Hillis, A. E. (2009). Neural substrates of visuospatial processing in distinct reference frames: evidence from unilateral spatial neglect. *Journal of Cognitive Neuroscience*, *21*(11), 2073-2084.

Mevorach, C., Humphreys, G. W., & Shalev, L. (2005). Attending to local form while ignoring global aspects depends on handedness: evidence from TMS. *Nature neuroscience*, *8*(3), 276-277.

Mevorach, C., Humphreys, G. W., & Shalev, L. (2006). Opposite biases in salience-based selection for the left and right posterior parietal cortex. *Nature Neuroscience, 9*(6), *740-742.*

Mioshi, E., Dawson, K., Mitchell, J., Arnold, R., & Hodges, J. R. (2006). The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. *International journal of geriatric psychiatry*, *21*(11), 1078-1085.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex “frontal lobe” tasks: A latent variable analysis. *Cognitive psychology*, *41*(1), 49-100.

Miyake, A., Friedman, N. P., Rettinger, D. A., Shah, P., & Hegarty, M. (2001). How are visuospatial working memory, executive functioning, and spatial abilities related? A latent-variable analysis. *Journal of experimental psychology: General*, *130*(4), 621.

Mok, V.C.T., Wong, A., Lam, W.W.M., Fan, Y.H., Tang, W.K., Kwok, T., ... & Wong, K.S. (2004). Cognitive impairment and functional outcome after stroke associated with small vessel disease. Journal of Neurology, Neurosurgery and Psychiatry, *75*(4), 560–566.

Moon, Y.-S., Kim, S.-J., Kim, H.-C., Won, M.-H., & Kim, D.-H. (2004). Correlates of quality of life after stroke. *Journal of the Neurological Sciences, 224*, 37–41.

Narasimhalu, K., Ang, S., De Silva, D. A., Wong, M. C., Chang, H. M., Chia, K. S., ... & Chen, C. (2009). Severity of CIND and MCI predict incidence of dementia in an ischemic stroke cohort. *Neurology*, *73*(22), 1866-1872.

Narayanan, N. S., Prabhakaran, V., Bunge, S. A., Christoff, K., Fine, E. M., & Gabrieli, J. D. (2005). The role of the prefrontal cortex in the maintenance of verbal working memory: an event-related FMRI analysis. *Neuropsychology*, *19*(2), 223.

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I.,... Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society, 53*(4), 695–699.

Navon, D. (1977). Forest before trees: The precedence of global features in visual perception. *Cognitive psychology*, *9*(3), 353-383.

Nichols-Larsen, D. S., Clark, P. C., Zeringue, A., Greenspan, A., & Blanton, S. (2005). Factors influencing stroke survivors' quality of life during subacute recovery. *Stroke, 36*(7), 1480–1484.

Nijboer, T. C. W, Van de Port, I., Schepers, V., Post, M., & Visser-Meily, A. (2013b). Predicting functional outcome after stroke: the influence of neglect on Basic Activities in Daily Living. *Frontiers in Human Neuroscience, 7.*

Nijboer, T. C., Kollen, B. J., & Kwakkel, G. (2013a). Time course of visuospatial neglect early after stroke: a longitudinal cohort study. *Cortex*, *49*(8), 2021-2027.

Norman, D. A., & Shallice, T. (1986). Attention to action. In R. J. Davidson, G. E. Schwartz., & D, E. Shapiro (eds.), *Consciousness and self-regulation* (Vol. 4, pp. 1-14). New York: Plenum Press.

Nouri, F. M., & Lincoln, N. B. (1987). An extended activities of daily living scale for stroke patients. *Clinical rehabilitation*, *1*(4), 301-305.

Nys, G. M. S., Van Zandvoort, M. J. E., De Kort, P. L. M., Jansen, B. P. W., De Haan, E. H. F., & Kappelle, L. J. (2007). Cognitive disorders in acute stroke: prevalence and clinical determinants. *Cerebrovascular Diseases*, *23*(5-6), 408-416.

Nys, G. M. S., van Zandvoort, M. J. E., De Kort, P. L. M., Jansen, B. P. W., Van Der Worp, H. B., Kappelle, L. J., & de Haan, E. H. F. (2005). Domain-specific cognitive recovery after first-ever stroke: A follow-up study of 111 cases. *Journal of the International Neuropsychological Society*, *11*, 795–806.

Nys, G. M. S., Van Zandvoort, M. J. E., De Kort, P. L. M., Van der Worp, H. B., Jansen, B. P. W., Algra, A., ... & Kappelle, L. J. (2005). The prognostic value of domain-specific cognitive abilities in acute first-ever stroke. *Neurology*, *64*(5), 821-827.

Nys, G. M., van Zandvoort, M. J., van der Worp, H. B., de Haan, E. H., de Kort, P. L., Jansen, B. P., & Kappelle, L. J. (2006). Early cognitive impairment predicts long-term depressive symptoms and quality of life after stroke. *Journal of the Neurological Sciences, 247*(2), 149–156.

O'donnell, J. P., Macgregor, L. A., Dabrowski, J. J., Oestreicher, J. M., & Romero, J. J. (1994). Construct validity of neuropsychological tests of conceptual and attentional abilities. *Journal of Clinical Psychology*, *50*(4), 596-600.

Ochipa, C., RothiI, L. J. G., & Heilman, K. M. (1992). Conceptual apraxia in Alzheimer's disease. *Brain*, *115*(4), 1061-1071.

Olson, C. R. (2003). Brain representation of object-centered space in monkeys and humans. *Annual review of neuroscience*, *26*(1), 331-354.

Osterrieth, P. A. (1944). Le test de copie d'une figure complexe. *Archives de Psychologie*, *30*, 206-356.

Ota, H., Fujii, T., Suzuki, K., Fukatsu, R., & Yamadori, A. (2001). Dissociation of body- centered and stimulus-centered representations in unilateral neglect. *Neurology*, *57*(11), 2064-2069.

Ownsworth, T., & Shum, D. (2008). Relationship between executive functions and productivity outcomes following stroke. *Disability and rehabilitation*, *30*(7), 531-540. Oxford University Press.

Patel, M., Coshall, C., Rudd, A. Wolfe, C. (2003). National history of cognitive impairment after stroke and factors associated with its recovery. *Clinical Rehabilitation, 17*(2), 158-166.

Paul, S. L., Sturm, J. W., Dewey, H. M., Donnan, G. A., Macdonell, R. A., & Thrift, A. G. (2005). Long-term outcome in the North East Melbourne Stroke Incidence Study: Predictors of quality of life at 5 years after. *Stroke, 36*(10) 2082-2086

Pelli, D. G. (1997). The VideoToolbox software for visual psychophysics: Transforming numbers into movies. *Spatial Vision*, *10*(4), 437- 442.

Petreska, B., Adriani, M., Blanke, O., & Billard, A. G. (2007). Apraxia: a review. *Progress in brain research*, *164*, 61-83.

Pohjasvaara, T., Leskelä, M., Vataja, R., Kalska, H., Ylikoski, R., Hietanen, M., ... & Erkinjuntti, T. (2002). Post- stroke depression, executive dysfunction and functional outcome. *European Journal of Neurology, 9*(3), 269–275.

Pohjasvaara, T., Mäntylä, R., Salonen, O., Aronen, H. J., Ylikoski, R., Hietanen, M.,... Erkinjuntti, T. (2000). How complex interactions of ischemic brain infarcts, white matter lesions, and atrophy relate to poststroke dementia. *Archives of Neurology, 57*(9), 1295–1300.

Poreh, A., & Shye, S. (1998). Examination of the global and local features of the Rey Osterrieth complex figure using faceted smallest space analysis. *The Clinical Neuropsychologist*, *12*(4), 453-467.

Rasquin, S. M., Lodder, J., Ponds, R. W., Winkens, I., Jolles, J., & Verhey, F. R. (2004). Cognitive functioning after stroke: a one-year follow-up study. *Dementia and geriatric cognitive disorders*, *18*(2), 138-144.

Rey, A. (1941). L'examen psychologique dans les cas d'encéphalopathie traumatique. (Les problems.). *Archives de Psychologie*, *28*, 215-285.

Riddoch, M. J., & Humphreys, G. W. (1983). The effect of cueing on unilateral neglect. *Neuropsychologia*, *21*(6), 589-599.

Riddoch, M. J., Humphreys, G. W., Luckhurst, L., Burroughs, E., & Bateman, A. (1995). “Paradoxical neglect”: spatial representations, hemisphere-specific activation, and spatial cueing. *Cognitive Neuropsychology*, *12*(6), 569-604.

Roberts, A. C., & Wallis, J. D. (2000). Inhibitory control and affective processing in the prefrontal cortex: neuropsychological studies in the common marmoset. *Cerebral Cortex*, *10*(3), 252-262.

Robertson, I. H., Manly, T., Beschin, N., Daini, R., Haeske-Dewick, H., Hömberg, V., ... & Weber, E. (1997). Auditory sustained attention is a marker of unilateral spatial neglect. *Neuropsychologia*, *35*(12), 1527-1532.

Robertson, I. H., Tegnér, R., Tham, K., Lo, A., & Nimmo-Smith, I. (1995). Sustained attention training for unilateral neglect: theoretical and rehabilitation implications. *Journal of Clinical and Experimental Neuropsychology*, *17*(3), 416-430.

Robertson, L. C., & Delis, D. C. (1986). 'Part-whole' processing in unilateral brain-damaged patients: dysfunction of hierarchical organization. *Neuropsychologia*, *24*(3), 363-370.

Roby-Brami A, Hermsdörfer J, Roy AC, Jacobs S (2012). A neuropsychological perspective on the link between language and praxis in modern humans. *Philosophical Transactions of the Royal Society B: Biological Sciences, 367*(1585), 144-160.

Rothi, L. J. G., & Heilman, K. M. (eds.). (2014). *Apraxia: the neuropsychology of action*. Psychology Press.

Rumiati, R. I., Papeo, L., & Corradi-Dell'Acqua, C. (2010). Higher-level motor processes. *Annals of the New York Academy of Sciences*, *1191*(2010), 219–241.

Rushworth, M. F. S., Walton, M. E., Kennerley, S. W., & Bannerman, D. M. (2004). Action sets and decisions in the medial frontal cortex. *Trends in cognitive sciences*, *8*(9), 410-417.

Samuelsson, H., Jensen, C., Ekholm, S., Naver, H., & Blomstrand, C. (1997). Anatomical and neurological correlates of acute and chronic visuospatial neglect following right hemisphere stroke. *Cortex*, *33*(2), 271-285.

Shallice, T. (1988). *From neuropsychology to mental structure*. Cambridge: Cambridge University Press.

Shin, M. S., Kim, Y. H., Cho, S. C., & Kim, B. N. (2003). Neuropsychologic characteristics of children with attention-deficit hyperactivity disorder (ADHD), learning disorder, and tic disorder on the Rey-Osterreith Complex Figure. *Journal of child neurology*, *18*(12), 835-844.

Shin, M. S., Park, S. Y., Park, S. R., Seol, S. H., & Kwon, J. S. (2006). Clinical and empirical applications of the Rey–Osterrieth complex figure test. *Nature protocols*, *1*(2), 892.

Slick, D. J., Lautzenhiser, A., Sherman, E. M., & Eyrl, K. (2006). Frequency of scale elevations and factor structure of the Behaviour Rating Inventory of Executive Function (BRIEF) in children and adolescents with intractable epilepsy. *Child Neuropsychology, 12*(3), 181-189.

Smania, N., Girardi, F., Domenicali, C., Lora, E., & Aglioti, S. (2000). The rehabilitation of limb apraxia: A study in left-brain–damaged patients. *Archives of physical medicine and rehabilitation*, *81*(4), 379-388.

Somerville, J., Tremont, G., & Stern, R. A. (2000). The Boston qualitative scoring system as a measure of executive functioning in Rey-Osterrieth complex figure performance. *Journal of Clinical and Experimental Neuropsychology*, *22*(5), 613-621.

Stephens, S., Kenny, R. A., Rowan, E., Kalaria, R. N., Bradbury, M., Pearce, R.... Ballard, C. G. (2005). Association between mild vascular cognitive impairment and impaired activities of daily living in older stroke survivors without dementia. *Journal of the American Geriatrics Society, 53(1),* 103–107.

Stern, R. A., Javorsky, D. J., Singer, E. A., Singer Harris, N. G., Somerville, J. A., Duke, L. M., ... & Kaplan, E. (1999). The Boston Qualitative Scoring System for the Rey-Osterreith Complex Figure (BQSS): Manual. Lutz, Florida: Psychological Assessment Resources.

Stern, R. A., Singer, E. A., Duke, L. M., Singer, N. G., Morey, C. E., Daughtrey, E. W., & Kaplan, E. (1994). The Boston qualitative scoring system for the Rey-Osterrieth complex figure: Description and interrater reliability. *The Clinical Neuropsychologist, 8*(3), 309-322.

Stevens, J. (2002). Applied multivariate statistics for the social sciences (4th ed.). Mahwah, NJ: Lawrence Erlbaum Associates.

Stone, S. P., Patel, P., Greenwood, R. J., & Halligan, P. W. (1992). Measuring visual neglect in acute stroke and predicting its recovery: the visual neglect recovery index. *Journal of Neurology, Neurosurgery & Psychiatry*, *55*(6), 431-436.

Stuss, D. T., & Benson, D (1984). Neuropsychological studies of the frontal lobes. *Psychological Bulletin*, *95*(1), 3-28.

Stuss, D. T., & Benson, D. F. (1986). *The frontal lobes*. New York: Raven Press.

Stuss, D. T., Alexander, M. P., Floden, D., Binns, M.A., Levine, B., McIntosh, A. R., et al. (2002). Fractionation and localisation of distinct frontal lobe processes: Evidence from focal lesions in humans. In D.T. Stuss & R.T. Knights (eds.), *Principles of frontal lobe function*. New York: Oxford University Press.

Stuss, D. T., Shallice, T., Alexander, M. P., & Picton, T. W. (1995). A multidisciplinary approach to anterior attention functions. *Annals of the New York Academy of Sciences*, *769*, 191-211

Tukey, J. W. (1977). Exploratory data analysis.

van Zandvoort, M. J. E., Kessels, R. P. C., Nys, G. M. S., de Haan, E. H. F., & Kappelle, L. J. (2005). Early neuropsychological evaluation in patients with ischaemic stroke provides valid information. *Clinical Neurology and Neurosurgery*, *107*, 385–392.

Verdon, V., Schwartz, S., Lovblad, K. O., Hauert, C. A., & Vuilleumier, P. (2009). Neuroanatomy of hemispatial neglect and its functional components: a study using voxel-based lesion-symptom mapping. *Brain*, *133*(3), 880-894.

Wade, D. T., Legh-Smith, J., & Hewer, R. L. (1985). Social activities after stroke: measurement and natural history using the Frenchay Activities Index. *International rehabilitation medicine, 7*(4), 176-181.

Walker, R., & Young, A. W. (1996). Object-based neglect: An investigation of the contributions of eye movements and perceptual completion. *Cortex*, *32*(2), 279-295.

Warren, M., Moore, J. M., & Vogtie, L. K. (2008). Search performance of healthy adults on cancellation tests. *American Journal of Occupational Therapy, 62, 588–594.*

Watanabe, K., Ogino, T., Nakano, K., Hattori, J., Kado, Y., Sanada, S., & Ohtsuka, Y. (2005). The Rey–Osterrieth Complex Figure as a measure of executive function in childhood. *Brain and Development*, *27*(8), 564-569.

Weintraub, S. (2000). Neuropsychological assessment of mental state. In: Mesulam, M. M., editor. Principles of Behavioural and Cognitive Neuropsychology. New York: Oxford University Press

Weintraub, S., & Mesulam, M. M. (1988). Visual hemispatial inattention: stimulus parameters and exploratory strategies. *Journal of Neurology, Neurosurgery & Psychiatry*, *51*(12), 1481-1488.

Welsh, M. C., Pennington, B. F., & Groisser, D. B. (1991). A normative-developmental study of executive function: A window on prefrontal function in children. *Developmental neuropsychology*, *7*(2), 131-149.

Wilson, B. A., Alderman, N., Burgess, P. W., Emslie, H., & Evans, J. (1996). *Behavioural assessment of the dysexecutive syndrome*. Thames Valley Test Company, UK

Wilson, B. A., Evans, J. J., Emslie, H., Alderman, N., & Burgess, P. (1998). The development of an ecologically valid test for assessing patients with a dysexecutive syndrome. *Neuropsychological rehabilitation*, *8*(3), 213-228.

Wilson, B., Cockburn, J., & Halligan, P. W., (1987). *Behavioural inattention test*. Thames Valley Test Company, UK

Woods, A. J., & Mark, V. W. (2007). Convergent Validity of executive organisation measures on cancellation. *Journal of Clinical and Experimental Neuropsychology, 29*(7), 719-723.

Zinn, S., Bosworth, H. B., Hoenig, H. M., & Swartzwelder, H. S. (2007). Executive function deficits in acute stroke. *Archives of physical medicine and rehabilitation*, *88*(2), 173-180.

Zinn, S., Dudley, T. K., Bosworth, H. B., Hoenig, H. M., Duncan, P. W., & Horner, R. D. (2004). The effect of poststroke cognitive impairment on rehabilitation process and functional outcome. *Archives of Physical Medicine and Rehabilitation, 85,* 1084– 1090.

Zwinkels, A., Geusgens, C., van de Sande, P., & van Heugten, C. (2004). Assessment of apraxia: inter-rater reliability of a new apraxia test, association between apraxia and other cognitive deficits and prevalence of apraxia in a rehabilitation setting. *Clinical Rehabilitation*, *18*(7), 819-827

APPENDIX A

BCoS TASK DESCRIPTIONS

The Birmingham Cognitive Screen (BCoS) is a clinical test instrument that is specifically designed to provide an overall ‘cognitive profile’ for stroke patients. The battery consists of 22 sub-tests covering five primary domains that can be affected by stroke and are likely to have a direct impact on everyday life: i) attention and executive functions, ii) language, iii) number skills, iv) memory and v) praxis. The BCoS sub-tests are aimed, and clustered accordingly, to assess domain-specific abilities (abilities that are primarily affecting only one area of cognition mentioned above) and domain-general processes (processes that affect abilities outside the target area such as impairment in executive functioning which can impact performances in language, memory etc.).

The sub-tests are designed to be (a) *Inclusive*, making the tests ‘aphasic and neglect friendly’ (for the non-language tests, BCoS uses high-frequency short words and forced-choice testing procedures where possible, and, for non-spatial attention tasks, the stimuli are centred on the page) and (b) *Time-efficient*, where possible, single the tests are designed to measure multiple cognitive processes.

1. ATTENTION AND EXECUTIVE FUNCTIONS

1.1 Auditory attention task

The task consists of pre-recorded words. There are total of six high-frequency words presented nine times each, across three blocks. Half of the words are target words to respond to, and the other half are distracter words to be ignored. Each target word (‘no’, ‘hello’, ‘please’) has a closely related distracter (‘yes’, ‘goodbye’, ‘thanks’). The words are presented in random order, each being preceded an equal number of times by a 2 second, 3 second or 4-second silence gap. The task is for the patient to respond to the target words and not the related distractors (a measure of *selective attention*). In addition, the task being performed in three blocks provides a measure of how well patients can *sustain their attention* across the blocks. At the end of the task, each patient is asked to recall the target and distractor words that provides a measure of whether they can store items in memory over the short-term when they are engaged in another activity (*working memory*).

1.2 Rule finding and concept switching

The stimulus is a set of grids, and each grid is made of 6 rows and 6 columns. The cells (formed by the grid) are mostly grey colour with 2 red and 2 green cells. Within the grid lays a black dot (marker). The task is for the patient to learn to predict the proceeding movement of the marker across the grid. Note, the marker does not move randomly, it always moves lawfully but then switches the rule. The switching rule operates along either single dimension (position) or across dimensions (switch from position to colour). The task measures the patient's ability to find an abstract rule and their ability to switch rule across stimuli within and across dimensions.

1.3 Apple cancellation

The task consists of complete (target) and incomplete (distractors) apples broken either on the right or left side. The apple stimuli are scattered on an A4 page presented in landscape orientation. The page is structured into 10 invincible quadrants; 2 central (top and bottom), 4 left (far and near, top and bottom) and 4 right (far and near, top and bottom). Each quadrant contains 15 apples (5 complete and 10 incomplete; 5 broken on the right and 5 broken on the left side). The task is for the patient to cancel (strike out) the target apples while ignoring the distractor apples. *Egocentric* neglect is measured by whether the patient has omitted targets on one side of the page. *Allocentric* neglect is measured by whether the patient has responded to false positive by cancelling a distractor.

1.4 Visual extinction

The task consists of 4 unilateral left visual stimuli (finger movements by the examiner), 4 unilateral right and 8 bilateral items. The patient is to point and/ orally recognise which side (left or right; upper or lower) the examiner is moving their finger. The patient's performance is recorded according to whether unilateral stimuli are omitted (providing a measure of neglect or a field defect), and whether there is a spatially selective drop in detection on one side when two stimuli relative to one stimulus are presented (providing a measure of extinction).

1.5 Tactile extinction

The task consists of 4 unilateral left stimuli (taps on the participant's hands by the examiner), 4 unilateral right and 8 bilateral items. The patient is to recognise and tell the examiner which hand/side the examiner tapped. Patient performance is recorded per as for visual extinction.

2. LANGUAGE

2.1 Picture naming

The task consists of 14 grey sketches of items (half living and half non-living). Half of these items have a long name in English (6-9 letters), and the other half of the items have a short name in English (3-5 letters). The patient is to name each sketch correctly.

2.2 Sentence construction

The stimuli for the task consists of a photograph of a person carrying out an action and two words printed below the photograph. The task is for the patient to construct a sentence that describes what the person in the photograph is doing, using the two printed words below the photograph.

2.3 Sentence reading

The task consists of 2 sentences including both regular and exception words, along with suffixed and prefixed words. Each sentence is presented in several lines (3-5 lines), aligned at the centre of the page – designed to avoid contamination by neglect (left and right) and sensitive to problems in visual disorientation.

2.4 Reading nonwords

There are 6 pronounceable nonwords, 5-6 letters long. These words are presented at the same time (3 words per page). The patient is to read each word, respectively. The test measures the patient's ability to use phonological procedures in reading, and at the same time, lexical procedures are measured through reading exception words.

2.5 Writing words and nonwords

The task consists of 4 familiar words and 1 nonword. The patient is to write each word as the examiner reads them out individually. The task measures the patient's ability to generate spellings lexically (for exception words) and phonologically (for the nonwords).

2.6 Instruction comprehension

This is a qualitative measure based on the clinical judgment of the examiner. The examiner is asked to evaluate and rate how well the patient understands the instruction on four target tasks (these tasks are chosen as their instruction cannot be deduced by just the visual presentation of the material). Also, the examiner is to consider the number of times the instruction has to be repeated.

3. NUMER SKILLS

3.1 Number/price/time reading

The task consists of 9 set of numbers; 3 complex numbers (with units of hundreds and thousands, additive and multiplicative relations, and embedded zeros), 3 prices (in sterling pounds and pence) and 3 times (with the digital representation of hours and minutes). The patient is to recognise and read the numbers in their correct concept. The use of prices and time provides a functional measure of numbers in everyday situations.

3.2 Number/price writing

The task consists of 5 sets of numbers (2 complex numbers and 3 prices), the same manner as for the number/price reading task. The patient is to write down each number in the correct concept, as the examiner reads them out, individually.

3.3 Calculation

There are 4 complex calculations (addition, subtraction, multiplication and division). The patient is to answer each calculation (verbally or written) correctly as they are read out, individually, by the examiner. The test measures the patient's ability in basic number processing, whether the patient can code and respond to numbers.

4. MEMORY

4.1 Orientation

The task is divided into 3 parts to assess: i) personal information (semantic autobiographic knowledge), ii) orientation in time and space, iii) awareness of deficits (nosognosia). All 3 parts are verbal questions and, forced-choice testing in the modality of multiple-choice (four choice responses) is given when needed such as when there is no response by the patient, an error by the patient or cases where the patient is aphasic (preventing a verbal response).

4.2 Story recall and recognition

The task is designed around a story and, the story consists of 15 segments. First the story is read out loud to the patient and, subsequently, the patient is asked to recall the segments immediately then after a delay. Both recall and recognition measures are taken. Recall measure is the patient's ability to recall the segments without any cue (free recall), and for the recognition measure (multiple-choice), a question is presented for every segment in the story that the patient has initially missed or recalled incorrectly. Each multiple-choice consists of one correct response and three incorrect responses to the question. Poor recall and recognition in the immediate recall reflect encoding deficit in the patient. In addition, poor recall but improved recognition (i.e., when a cue is provided) reflects retrieval deficit in the patient. The Large drop in performance between immediate recall/recognition and delayed recall/recognition reflects problems in forgetting/consolidation.

4.3 Task recognition

The task is a measure of visual memory. The task consists of 10 questions, and each question is presented in the multiple-choice modality, where the patient is asked which of the stimuli/actions they had previously encountered (during the assessment). The multiple-choice is made of one correct response and three incorrect responses (distractors). The distractors are closely related to the correct response (for example same action but on a different material).

5. PRAXIS

5.1 Complex figure copy

The stimulus for the task is a composite figure that contains three structures, middle, and additional structures on the left and right. Also, there are additional features (elements) anchored to each structure. The number of elements on the left and right is equated to balance the probability of left and right neglect. The patient is to copy the figure accurately in the space provided (below the original image). The scoring measures constructional apraxia and the presence of visual neglect.

5.2 Multi-step object use

The task requires the patient to perform a sequence of actions using the target objects (2 batteries and a torch) in the presence of multiple objects to carry out an instruction (light the torch). The target objects are placed with distractor objects. The instruction is given verbally (in writing and the examiner speaking) and pictorially - to avoid problems in any modality. The task measures selection and sequences of goal-directed behaviours.

5.3 Gesture production

The task is performed with the least affected hand of the patient, where the patient is requested to produce 6 familiar actions, 3 intransitive (communicative) actions and 3 transitive (object-oriented) actions, on examiner’s verbal command. All actions can be executed within a single step-sequence (e.g., be quite). The patient is to produce actions to names.

5.4 Gesture recognition

The task requires the patient to recognise 6 actions, 3 intransitive and 3 transitive actions that are acted out by the examiner. The examiner performs each action individually, accompanied by a multiple-choice response (1 target and 3 distractors). The stimuli are presented as written words and read aloud by the examiner. The patient is to recognise the correct meaning/word that matches the action produced by the examiner.

5.5 Gesture imitation

The task involves 4 meaningless actions performed by the examiner. Two actions involved a sequence of 2 hand positions in relation to the head and 2 involve a single finger position. The patient is to mimic these actions with the least affected hand.

Table A1. *BCoS Sub-tests Scores (variables) used in Exploratory Factor Analysis (EFA)*

Sub-tests Scores		Label
1	**ATTENTION & EXECUTIVE FUNCTIONS**	
1.1	**Auditory attention**	
	Sum of correct responses	*Auditory attention*
	Sum of response to distractor words (false positives)	*Auditory attention (FP)*
	Sum of omitted target words	*Auditory attention (Omission)*
	The difference between the 1st block and the last block. There is a total of 3 blocks, and if stopped after 1st or 2nd block, Index= N/A (non-applicable)	*Auditory attention (Sustained attention Idx.)*
	Sum of words recalled at the end of the test	*Auditory attention (Working memory)*
1.2	**Rule finding & concept switching**	
	Sum of correct responses (movements)	*Rule finding*
1.3	**Apple cancellation**	
	Sum of incomplete apples (false positives) with the RIGHT side opening	*Apple cancellation (FP Right)*
	Sum of incomplete apples (false positives) with the LEFT side opening	*Apple cancellation (FP Left)*
	Sum of complete (target) apples cancelled on the right side of the page *minus* the sum of targets on cancelled the left side of the page	*Apple cancellation (Egocentric neglect)*
	Sum of false positives with LEFT side opening *minus* the of number false positives with RIGHT side opening	*Apple cancellation (Allocentric neglect)*
1.4	**Visual extinction**	
	Sum of left unilateral correct detections *minus* number of left bilateral correct detections	*Left visual extinction*
	Sum of right unilateral correct detections *minus* number of right bilateral correct detections	*Right visual extinction*
1.5	**Tactile extinction**	
	Sum of left unilateral correct detections *minus* number of left bilateral correct detections	*Left tactile extinction*
	Sum of right unilateral correct detections *minus* number of right bilateral correct detections	*Right tactile extinction*
2	**LANGUAGE**	
2.1	**Picture naming**	
	Sum of pictures named correctly	*Picture naming*
2.2	**Sentence construction**	
	Sum of correct uses of the given stimuli	*Sentence construction*
2.3	**Sentence reading**	
	Sum of words read correctly. This score was calculated by summing the accuracy of both sentences, for an overall reading score	*Sentence reading*

Table A1. (CONTINUED)

2.4	**Reading nonwords**	
	Sum of nonwords read correctly	*Nonword reading*
2.5	**Writing words and nonwords**	
	Sum of words and nonwords written correctly	*Word/nonword writing*
3.	**NUMBER SKILLS**	
3.1	**Number/price/ time reading**	
	Sum of items read correctly	*Number reading*
3.2	**Number writing**	
	Sum of items written correctly	*Number writing*
3.3	**Calculation**	
	Sum of correct calculations	*Calculation*
4.	**MEMORY**	
4.1	**Story recall and recognition - Immediate recall**	
	Sum of items recalled freely ONLY	*Immediate free recall*
	Sum of items recalled using forced-choice testing. This score was calculated by summing the free recall & recognition total score	*Immediate recognition*
4.2	**Story recall and recognition - Delayed recall**	
	Sum of items recalled freely ONLY	*Delayed free recall*
	Sum of items recalled using forced-choice testing. This score was calculated by summing the free recall & recognition total score	*Delayed recognition*
4.3	**Task recognition**	
	Sum of correct items recognised. If some tests were NOT presented to the participant, a modified score is given in respect to the total number of task completed by the participants.	*Task recognition*
5.	**PRAXIS**	
5.1	**Gesture production**	
	Sum of actions produced accurately	*Gesture production*
5.2	**Gesture recognition**	
	Sum of actions recognised correctly	*Gesture recognition*
5.3	**Meaningless gesture imitation**	
	Sum of scores for hand and finger posture imitated correctly	*Gesture imitation*
5.4	**Multi-step object use**	
	Sum of correct steps taken to successfully complete the given instruction	*Multiple object use*
5.5	**Complex figure copy**	
	Sum of elements drawn correctly across the 3 structures (left, middle and right) according to the BCoS scoring criteria	*Complex figure copy*
	Sum of scores on the LEFT side structure *minus* the total number of scores on the RIGHT side structure	*Complex figure copy (Asymmetry)*

APPENDIX B

Global-Local Scoring System for BCoS Complex Figure Copy

Administration and Scoring Instructions

The Global-Local Scoring System is a qualitative scoring method designed to score the BCoS Complex Figure Copy task systematically. The system provides scores on presence, placement and accuracy of visual features across Global and Local scales of processing (19 elements). The total score is 57 points with higher scores indicating better performance.

These general instructions are designed to make scoring clear for the examiner. Please read them carefully before starting to score.

GENERAL INSTRUCTION

- Score in the order of elements given in the description, and score each element independently.
- By scoring each element independently, each element should be proportional to its adjoined element and/ or the square the element is within.
- Try not to penalise an error more than ones. For example, in the global elements if or when one of the horizontal lines that divides a rectangle into two small squares is longer than 1/8 from the edge of the large square, reduce accuracy score for ONLY 1 of the two small squares, preferably, the first square given in the description.

PRESENCE

Global elements: Presence of only a part of the global element, provide a score of 1

Local elements: Presence of a mark resembling target shape in the correct location/ a shape that resembles the target shape (at least part of it) elsewhere, provide a score of 1

PLACEMENT

Global elements: Presence of fragmentation and/ or absence of elements that are direct to the current element, evaluate the current element with another associated element(s).

Local elements: Divide each square into 4 equal quadrants for precision

ACCURACY

Global elements: Lines should not fall short or extend more than ⅛ of the square or the rectangle.

Local elements: Lines should not fall short or extend more than ¼ of the edge of the square the element is placed within.

Table B1. *Description of Global-Local Scoring System*

GLOBAL ELEMENTS	
1. Large rectangle	
Presence	Any mark or shape resembling the target shape (this is the global container which anchors all other elements).
Placement	Evidence of no closing-in behaviour (e.g., copy is made close to or on top of the original figure).
Accuracy	4 lines meeting at a right angle forming a rectangle shape. The horizontal lines should be longer than the vertical lines.
2. Left top small square	
Presence	Any mark or shape resembling the target shape.
Placement	Attached to the upper left side of the middle square.
Accuracy	4 lines (approximately equal length) meeting at right angle forming a square. The height and width are in proportion to the middle square, roughly ¼ of the middle square.
3. Left bottom small square	
Presence	Any mark or shape resembling the target shape.
Placement	Attached to the lower left side of the middle square.
Accuracy	4 lines (approximately equal length) meeting at right angle forming a square. The height and width are in proportion to the middle square, roughly ¼ of the middle square.
4. Right top small square	
Presence	Any mark or shape resembling the target shape.
Placement	Attached to the upper right side of the middle square.
Accuracy	4 lines (approximately equal length) meeting at right angle. The height and width are in proportion to the middle square, roughly ¼ of the middle square.
5. Right bottom small square	
Presence	Any mark or shape resembling the target shape.
Placement	Attached to the lower right side of the middle square.
Accuracy	4 lines (approximately equal length) meeting at right angle and forming a square. The height and width are in proportion to the middle square, roughly ¼ of the middle square.

6. Middle square	
Presence	Any mark or shape resembling the target shape.
Placement	Between the left and the right side of the small squares.
Accuracy	4 lines (unequal length) meeting at right angle and forming a square shape rather than a rectangle. The height and width should be proportion to the small squares at the right and left side.
7. Middle diagonal Line	
Presence	Any mark or shape resembling the target shape.
Placement	Middle square where the tails falls within the lower left (tail) and upper right (tail) corners of the middle square.
Accuracy	A fairly straight diagonal line across the middle square in the correct orientation. Both tails are roughly ½ of the diagonal distance of the middle square (not less than ¼ or more than ¾).
LOCAL ELEMENTS	
	LEFT SIDE SQUARES
8. Top parallel line	
Presence	Any shape resembling the target shape.
Placement	The line falls within the top left corner of the top square.
Accuracy	Fairly straight diagonal line in the correct orientation. Roughly parallel to the bottom parallel line.
9. Bottom parallel line	
Presence	Any shape resembling the target shape.
Placement	The line falls within the bottom right corner of the top square.
Accuracy	Fairly straight diagonal line in the correct orientation. Roughly parallel to the top parallel line.
10. Circle	
Presence	Any shape resembling the target shape.
Placement	Top left corner of the bottom square.
Accuracy	The form is a closed circle with no filling inside. Oval, tear drop forms or presence of obvious straight lines are incorrect, score 0.
	RIGHT SIDE SQUARES
11. Double dots	
Presence	Any shape resembling the target shape.

Placement	The dots fall within the lower right corner of the top square.
Accuracy	2 dots, one above each other (vertically parallel). The dots are solid, round or small circles with some attempts to fill in (provide a score of 1 even if one dot is filled).
12. Left diagonal line	
Presence	Any shape resembling the target shape.
Placement	The diagonal line falls within the left side of the square; top end falls at the top left corner of the bottom square, while the bottom end falls roughly at the centre of the lower horizontal line of the bottom square.
Accuracy	A fairly straight diagonal line in the correct orientation. No obvious curves or twisted shapes.
13. Right diagonal line	
Presence	Any shape resembling the target shape.
Placement	The diagonal line falls within the right side of the square; top end falls at the top right corner of the bottom square, while the bottom end falls roughly at the centre of the lower horizontal line of the bottom square.
Accuracy	A fairly straight diagonal line in the correct orientation. No obvious curves or twisted shapes.
	MIDDLE SQUARE
14. Arrow with shaded head	
Presence	Any shape resembling the target shape (vertical line and/or the triangle shaped arrow head).
Placement	Falls on the left side of the middle square; the triangular shape should be above the left half of the middle square with the vertical line extending to meeting the Main diagonal line.
Accuracy	Presence of both, the vertical line and a triangular shape in the correct formation/orientation. A triangular shape with a sign of an attempt to fill the middle.
15. Left curve	
Presence	Any mark or shape resembling the target shape.
Placement	Falls on the left side of the middle square; starts just below ¼ way down the left side of the middle square and ends at the meeting point between the vertical line from the arrow and the Middle diagonal line. In the absence of the meeting point, the line ends roughly at the bottom half of the Middle square.
Accuracy	A concave downward in the right orientation.

	No obvious straight lines or steepness.
16. Right curve	
Presence	Any mark or shape resembling the target shape.
Placement	Falls on the right side of the middle square; the top should touch roughly the top corner of the middle square while the bottom end should touch the meeting point of the Middle diagonal line and the arrow/left curve. In the absence of the meeting point/left curve, the line should end roughly ¾ on the left half of the Middle square.
Accuracy	A concave upward in the right orientation. The curve is, roughly, symmetrically balanced.
17. "S" shape	
Presence	Any mark or shape resembling the target shape.
Placement	The shape is above (or at least half) the right top square.
Accuracy	A complete "S" shape close to the correct orientation (of any angle within 90 degrees). Proportional to the top right square.
18. 3 Parallel lines	
Presence	Any shape resembling the target shape.
Placement	The shape is below (or at least half) the left bottom square.
Accuracy	Consist of 3 short lines roughly parallel to each other in the correct orientation. 3 short parallel lines falls (or at least half) on the left tail of Main diagonal line.
19. Cross	
Presence	Any mark or shape resembling the target shape.
Placement	Below the right half of the middle square.
Accuracy	A shape of a cross, where the vertical line is longer than the horizontal line. The horizontal line falls in the bottom half of the vertical line.

Table B2. *Global-Local Scoring System Score Sheet*

Participant ID: Date:				
	Presence	**Placement**	**Accuracy**	**Comment**
GLOBAL ELEMENTS				
1. Large rectangle				
2. Left upper square				
3. Left lower square				
4. Right upper				
5. Right lower				
6. Middle square				
7. Main diagonal				
Total				
LOCAL ELEMENTS				
LEFT SIDE SQUARES				
8. Top parallel line				
9. Bottom parallel line				
10. Circle				
Total				
RIGHT SIDE SQUARES				
11. Double dot				
12. Left diagonal line				
13. Right diagonal line				
Total				
MIDDLE SQUARE				
14. “S” Shape				
15. 3 Parallel lines				
16. Arrow				
17. Left Curve				
18. Right curve				
19. Cross				
Total				
Dimension scores				
Asymmetry score: (Left *minus* right)				
Total score				