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**Assessing cognition post-stroke using virtual reality technology**

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## **Abstract**

Up to 70% of stroke survivors experience cognitive impairments. Assessing cognitive skills after stroke is critical to diagnose, to educate, and to tailor rehabilitation to maximise functional outcomes. The neuropsychological tests used to assess cognition are typically pen-and-paper based, which are often dependent on language skills for completion. Language impairments observed in stroke survivors with aphasia may confound non-linguistic cognitive performance in these pen-and-paper tests. The primary objective of this research was to develop a clinimetrically sound cognitive assessment for stroke survivors with or without aphasia.

A systematic review was conducted to determine whether studies that evaluated cognitive assessments in stroke included participants that represented the stroke population. Approximately two-thirds of the studies excluded individuals with communication problems, with a similar percentage of studies excluding individuals with cognitive impairments. This review highlighted the need for new and more feasible methods to assess cognition in the wider stroke population; particularly those with aphasia or cognitive impairment.

We developed a non-immersive virtual reality cognitive assessment for individuals with stroke (with or without aphasia) – the Cognitive Assessment for Aphasia App (C3A). This “aphasia-friendly” assessment incorporated computerised audio and visual feedback, practice opportunities, and intuitive functional tasks to minimise dependency on language skills for completion. Developing the C3A required the input from a multidisciplinary clinical and research team and stroke survivors. We targeted cognitive domains that are commonly affected in stroke and that influence functional outcomes. The C3A included a simple reaction time task to assess psychomotor skills and attention, a visual search task to assess visuospatial skills, a sequence copy task to assess visual memory, and a kitchen task to assess executive functioning.

A total of 97 participants were recruited (36 with aphasia, 29 stroke non-aphasia, 32 controls) from acute and inpatient rehabilitation settings and the community. All participants were assessed on the C3A and a battery of standard pen-and-paper cognitive tests typically used in stroke. Participants with aphasia and controls undertook the auditory comprehension sub-tests of the Comprehensive Aphasia Test. C3A performance

measures included latency and errors. Following successful trials of the C3A we sought to determine its feasibility and validity in stroke and controls.

Before analysing the C3A results, the association between language performance and the pen-and-paper cognitive tests in participants with aphasia and controls was explored. The association between language and a real-life measure of cognition (the Kettle Test) was also tested. All cognitive tests were significantly associated with auditory comprehension and naming performance (with up to 78% of variance explained), except for Star Cancellation and the Kettle Test. To measure non-linguistic cognitive performance in aphasia, the task instructions, stimuli, and response methods need to be modified to meet the needs of individuals with language impairments.

Evaluating the C3A started with exploring feasibility and user acceptance compared to standard cognitive pen-and-paper tests in stroke survivors (with and without aphasia) and controls. The C3A took approximately 20 minutes to complete. Only one participant with aphasia was unable to complete all C3A tasks, whereas 13 participants with aphasia were unable to complete all pen-and-paper tests. Only 13 of 95 respondents preferred the pen-and-paper tests to the C3A. This study demonstrated that the C3A was more feasible for stroke survivors than standard pen-and-paper tests, and it was also preferred by users across all three participant groups.

Demonstrating the validity of the C3A involved three lines of evidence. First, we established that C3A performance could distinguish between stroke participants and controls, but there was no difference in performance between stroke participants with and without aphasia. Second, construct validity for the C3A was examined by comparing performance with non-verbal pen-and-paper tests (in the absence of a criterion standard non-immersive virtual reality cognitive assessment). There were many significant associations with pen-and-paper tests, with errors made on the C3A kitchen task standing out as a particularly valid measure in stroke survivors with and without aphasia. Third, we identified robust ecological validity, with strong associations between C3A outcomes and scores on a functional cognitive outcome measure (FIM-cog).

Finally, the association between language performance and C3A performance in individuals with aphasia was explored. The C3A's reaction time task and sequence copy errors were not significantly associated with auditory comprehension and naming

performance. Kitchen task errors, designed to measure executive skills, were significantly associated with language performance. The “aphasia-friendly” kitchen task results support previous findings of co-occurring executive dysfunction in aphasia.

Historically, neuropsychological assessment of cognition has relied on linguistically-loaded pen-and-paper tasks, which are often not feasible for individuals with aphasia. We used non-immersive virtual reality technology to advance cognitive testing in stroke. Collectively, the studies included in this thesis provide evidence that the C3A is a feasible and valid measure of cognitive performance in stroke survivors with and without aphasia.

## **Declaration by author**

This thesis is composed of my original work, and contains no material previously published or written by another person except where due reference has been made in the text. I have clearly stated the contribution by others to jointly-authored works that I have included in my thesis.

I have clearly stated the contribution of others to my thesis as a whole, including statistical assistance, survey design, data analysis, significant technical procedures, professional editorial advice, and any other original research work used or reported in my thesis. The content of my thesis is the result of work I have carried out since the commencement of my research higher degree candidature and does not include a substantial part of work that has been submitted to qualify for the award of any other degree or diploma in any university or other tertiary institution. I have clearly stated which parts of my thesis, if any, have been submitted to qualify for another award.

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## **Publications during candidature**

### **Peer reviewed papers**

**Wall, K. J., Cumming, T. B., Koenig, S. T., Pelecanos, A. M., & Copland, D. A. (2017).** Using technology to overcome the language barrier: The Cognitive Assessment for Aphasia App. *Disability and Rehabilitation*, *19*(1), 1–12.  
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### **Statement of parts of the thesis submitted to qualify for the award of another degree**

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virtual reality, stroke, cognitive impairments, aphasia, neuropsychological tests, pen-and-paper tests, clinimetrics, user acceptance

## **Australian and New Zealand Standard Research Classifications (ANZSRC)**

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## **List of abbreviations**

ACE-R	Addenbrooke's Cognitive Examination-Revised
AMPS	Assessment of Motor and Process Skills
BIT	Behavioural Inattention Test
BNI	Barrow Neurological Institute Screen
BNT	Boston Naming Test
BMET	Brief Memory and Executive Test
BTT	Baking Tray Task
BVRT	Benton Visual Retention Test
C3A	Cognitive Assessment for Aphasia App
CAMCOG	Cambridge Cognitive Examination
CAT	Comprehensive Aphasia Test
CAMCOG	Cambridge Cognitive Examination
CCPT	Conners' Continuous Performance Test
CDT	Clock Drawing Test
CFAB	Chinese Frontal Assessment Battery
CLBT	Character-line Bisection Task
CLOX	Executive Clock Drawing Test
CST	Cognitive Screen Test
DLOTCA-G	Dynamic Lowenstein Occupational Therapy Cognitive Assessment -
DTVP-A	Developmental Test of Visual Perception - Adolescents and Adults
DVT	Digit Vigilance Test
EBLST	Exactly Bisected Line Selection Task
EFPT	Executive Function Performance Test
FIM-cog	Functional Independence Measure – total cognition score
FNSS	Frontal Network Syndrome Score
HVLT	Hopkins Verbal Learning Test
ICAS	Intelligent Cognitive Assessment System
ICH	Intracerebral Haemorrhage
IQR	Interquartile range
LACL	Large Allen Cognitive Levels
LAST	Language Screen Test
LOTCA	Loewenstein Occupational Therapy Cognitive Assessment
mLLT	modified Location Learning Test

MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
MSE	Memory Self-Efficacy
MVPT	Motor-Free Visual Perception Test
NAB	Neuropsychological Assessment Battery
NCS	Neurological Cognitive Status
NIHSS	National Institute of Health Stroke Scale
OL_RMBMT	Online Rivermead Behavioral Memory Test
OT-APST	Occupational Therapy Adult Perceptual Screening Test
RAVMT	Rey Auditory Verbal Learning Test
RBANS	Repeatable Battery for the Assessment of Neuropsychological Status
RBMT-CV	Rivermead Behavioral Memory Test-Chinese Version
R-CAMCOG	Revised–Cambridge Cognitive Examination
RDI	Recognition discrimination index
SART	Sustained Attention to Response Task
SD	Standard deviation
SDH	Subdural Haematoma
s-MMSE	standardized Mini Mental State Examination
SMQ	Short-term Memory Questionnaire
SNAP	Sunnybrook Neglect Assessment Procedure
TCS	Three Cities Test
TEA	Test of Everyday Attention
TICS	Telephone Interview for Cognitive Status
TOAST	Treatment of Acute Stroke Trial
TMT	Trail Making Test
Vmall	Virtual Mall
VMET	Virtual Multiple Errands Test
VRLAT	Virtual Reality Lateralized Attention Test
VRST	Visual Recognition Slide Test
WAIS	Wechsler Adult Intelligence Scale
WAIS-III	Wechsler Adult Intelligence Scale III
WCST	Wisconsin Card Sorting Test
WMS-III	Wechsler Memory Score III
UFOV	Useful Field of View

# Chapter 1: Introduction

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Chapter 1 provides a brief introduction to the thesis. Section 1.1 summarises the background and rationale for this research project, section 1.2 outlines the aims of the thesis, and section 1.3 provides an overview of the thesis structure.

## 1.1 Background and Current Gap in Research and Clinical Practice

Stroke is the second most common cause of death and the third most common cause of disability worldwide. Approximately 40,000-48,000 stroke episodes occur in Australia every year and the number of survivors living with physical and cognitive impairments is predicted to increase due to the aging population (Naco, Gjerci, Xinxo, & Kruja, 2014; Senes, 2006). Up to 70% of stroke survivors experience cognitive impairments (Lindén, Skoog, Fagerberg, Steen, & Blomstrand, 2004). The post-stroke cognitive profile is heterogeneous and often involves multiple interconnected cognitive processes, including attention, memory, language, executive functioning and visuospatial skills (Frankel, Penn, & Ormond-Brown, 2007; Fucetola, Connor, Strube, & Corbetta, 2009). In a population-based study, Barker-Collo and Feigin (2006) examined the association between domain specific deficits in cognition and a range of functional outcomes at five years post-stroke. Visuospatial skills, visual memory and information processing speed were independently associated with activity limitations and quality of life issues over and above the impact of age, depression and stroke. The association between cognitive status and activities of daily living is verified in the literature (Akbari, Ashayeri, Fahimi, Kamali, & Lyden, 2011; Wagle et al., 2011), including the influence of mild cognitive deficits on executing more complex, instrumental activities of daily living (Gold, 2012).

International guidelines for stroke management recommend that all patients should be assessed for cognitive deficits following a stroke using validated and reliable tools (National Institute for Health and Care Excellence, 2013; National Stroke Foundation, 2010; Scottish Intercollegiate Guidelines Network, 2010; Stroke Foundation of New Zealand and New Zealand Guidelines Group, 2010). Many cognitive assessments have been developed and applied to the stroke population. A review by Lees, Fearon, Harrison, Broomfield, and Quinn (2012) explored contemporary studies to determine the frequency of using various cognitive assessments post-stroke. Of the 408 included studies, 300

different cognitive assessments were identified; the most commonly used was the Mini-Mental State Examination (MMSE) (36%). Pen-and-paper cognitive assessments, such as the MMSE, are often heavily dependent on linguistic skills for completion (Osher, Wicklund, Rademaker, Johnson, & Weintraub, 2008). This approach often requires individuals to understand verbal or written instructions and to respond verbally or in writing to answer questions. Linguistically-loaded cognitive assessments create access barriers for individuals with post-stroke aphasia, and non-linguistic cognitive results may be confounded by language deficits.

Aphasia is observed in up to 30% of stroke survivors (Engelter et al., 2006). Individuals with aphasia have poorer functional outcomes (Gialanella, 2011), they are less likely to return to work and social activities (Carod-Artal & Egido, 2009), and they have higher health care costs (Dickey et al., 2010) compared to stroke survivors without aphasia. Non-linguistic cognitive impairments (e.g., attention, memory and executive functioning) may co-occur with aphasia, which can adversely impact rehabilitation (Harnish & Lundine, 2015; Lambon Ralph, Snell, Fillingham, Conroy, & Sage, 2010). Excluding individuals with aphasia from assessment can result in their cognitive impairments being overlooked, while assessing them with language-reliant tasks may result in misleading findings. To ensure accurate evaluation, clinicians need access to valid and reliable tools to measure cognitive performance in individuals with post-stroke aphasia.

The purpose of assessing cognition has shifted from determining the likely aetiology of brain dysfunction (Sbordone & Long, 1998), to predicting everyday functioning and guiding rehabilitation needs. Ecological validity is now considered in the theoretical development of cognitive assessments, as demonstrated by the Behavioural Assessments of the Dysexecutive Syndrome (Norris & Tate, 2000). Technological advances have enabled the development of novel approaches to assess post-stroke cognitive skills, such as virtual reality (Buxbaum, Dawson, & Linsley, 2012; Rand, Katz, & Tamar Weiss, 2007). Advantages of virtual reality include improved ecological validity, the capacity to provide multisensory input and feedback to enhance learning (Johansson, 2012; Tinga et al., 2016), and the precision of computerised performance measures. However, it is unknown whether advances in technology assist in overcoming the barriers associated with pen-and-paper assessments or whether they create alternative barriers for stroke survivors.

There is a pressing need to overcome the challenges in assessing non-linguistic cognitive skills in post-stroke aphasia. Improving the diagnostic accuracy for cognitive impairments will enable clinicians to better educate patients and their families, and to tailor appropriate rehabilitation to maximise functional outcomes and quality of life for stroke survivors.

## **1.2 Aims of this Research**

This research originates from clinical experience, where it was perceived that assessing non-linguistic cognitive performance in individuals with aphasia was complex, given the lack of clinimetrically sound cognitive assessments designed for post-stroke aphasia. Clinimetrics is a methodological discipline that focuses on the quality of clinical measurements (Feinstein, 1983), with important features including validity, reliability, and feasibility. The aims of the research were to:

- determine if studies evaluating the clinimetric properties of cognitive assessments used in stroke included participants that represent the broader stroke population,
- explore how much variability in performance on pen-and-paper cognitive tests and a real-life measure of cognition is associated with auditory comprehension and naming performance in post-stroke aphasia,
- develop a non-immersive virtual reality cognitive assessment for stroke survivors that is designed to be inclusive of post-stroke aphasia (called the Cognitive Assessment for Aphasia App – C3A),
- evaluate feasibility and user acceptance of the C3A in stroke survivors (with and without aphasia) and controls,
- determine if C3A performance can differentiate between stroke survivors (with and without aphasia) and controls. Second, examine the association between the C3A and pen-and-paper non-verbal cognitive tests in stroke survivors (with and without aphasia). Third, to evaluate ecological validity for the C3A by comparing the C3A performance outcomes with a functional measure of cognitive performance, and
- determine the association between C3A performance and auditory comprehension and naming performance in post-stroke aphasia.



### **1.3 Overview of the Thesis Structure**

This doctoral thesis consists of two primary phases. Phase 1 consists of background information pertaining to cognitive tests and the association to language. This includes a systematic review (chapter 2) where the included studies evaluated the clinimetric properties of cognitive assessments. The eligibility criteria used in the included studies were synthesised to report the profile of stroke survivors typically excluded in these studies. This systematic review identified the different approaches to assessing cognition and quantified the gap in current research and clinical practice for assessing cognition in specific stroke subgroups. Phase 1 also details a study (chapter 3) that explored the association between language (auditory comprehension and naming) and cognition in aphasia and controls using a neuropsychological battery and a real-life measure of cognitive performance recommended in stroke.

Phase 2 of this thesis consists of studies that described and evaluated the newly developed C3A. Chapter 4 reports the development of the C3A and the study explored the feasibility and user acceptance of the assessment in stroke and controls. Chapter 5 details the study that validated the C3A in stroke survivors with and without aphasia. Finally, chapter 6 reports the study that explored the association between auditory comprehension and naming and C3A performance in post-stroke aphasia.

This thesis has been submitted under The University of Queensland's definition of a "partial thesis by publication". Chapter 2, 3 and 4 have been published and chapters 5 and 6 are currently being submitted for publication. Publication details and a linking paragraph are reported at the beginning of each chapter. Published chapters replicate the content of the publication, but this thesis has been formatted to be consistent with the American Psychological Association (APA) guidelines, 6th edition.

## Chapter 2: Assessing Cognition after Stroke. Who Misses Out?

### A Systematic Review

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Chapter 2 details a systematic review, which included studies that evaluated the clinimetric properties of cognitive assessments in stroke. This systematic review serves as a background to the different approaches of cognitive testing post-stroke, and the findings identified the most prominent barriers to cognitive testing in specific stroke subgroups. The results were an important part of the rationale for this research project.

The content of this chapter has been published in a paper entitled “Assessing cognition in stroke. Who misses out? A systematic review” in the *International Journal of Stroke* (Wall, Cumming, Isaac & Copland, 2016; see [Appendix A](#) for URL link to the published manuscript).

The content included in this chapter replicates the published manuscript, but the formatting was modified to match the style of this thesis.

## 2.1 Abstract

**Background:** Cognitive impairments post-stroke are common. Assessment of cognition typically involves pen-and-paper tasks, which are often reliant on linguistic and motor function, creating barriers for many stroke survivors. The characteristics of stroke survivors excluded from cognitive assessments have never been investigated.

**Aims:** (1) to determine if the stroke samples included in studies evaluating clinimetric properties of cognitive assessments represent the stroke population, (2) to identify the different modes of cognitive assessments, and (3) to ascertain whether the different modes of cognitive assessments influence the stroke samples used in the studies.

**Summary of review:** We systematically reviewed studies that evaluated at least one clinimetric property of a cognitive assessment in adult stroke survivors from January 2000 to October 2013. Eligibility criteria, reasons for drop-outs and missing data were extracted. A theming process was employed to synthesise the data. From the initial yield of 3,731 articles, 109 were included. Six broad categories describing reasons for exclusion were identified. Cognitive impairments were the most common (68%), then communication issues (62%), endurance problems (42%), sensory loss (39%), psychiatric illness (38%) and motor limitations (27%). The most prevalent assessment mode was pen-and-paper (73%), then virtual reality (11%), computer (6%), observational functional performance (5%), informant (3%) and telephone (3%). Regardless of mode, issues with cognition and communication were the most frequently used exclusion criteria.

**Conclusions:** Our findings indicate that cognitive assessments are not tested in representative stroke samples. Research is needed to identify valid and reliable cognitive assessments that are feasible in a wider range of stroke survivors.

**Key words:** clinimetrics, cognitive assessment, neuropsychological assessment, pen-and-paper, stroke, systematic review

## 2.2 Introduction

Up to 70% of stroke survivors experience cognitive impairments (Lindén et al., 2004). Cognitive impairments can adversely impact activities of daily living (Kihun & Wanhee, 2012; Oneş, Yalçinkaya, Toklu, & Çağlar, 2009), the ability to return to work (van Es et al., 2011), as well as being a prognostic indicator for dependency (Narasimhalu et al., 2011) and poor survival (Melkas et al., 2009; Patel, Coshall, Rudd, & Wolfe, 2002). Thus, identification of post-stroke cognitive impairments is critical to plan rehabilitation and optimise patient functional outcomes (Bode, Heinemann, Semik, & Mallinson, 2004; Hachinski et al., 2006).

Cognitive processing is heterogenous and performing daily tasks often involves multiple inter-related cognitive domains, including attention, language, memory and executive functioning (Frankel et al., 2007; Fucetola et al., 2009). Cognitive assessments need to detect deficits in these domains to guide rehabilitation goals. Due to the complexity of measuring cognitive performance, many different assessments have been developed and applied in the stroke population. A review by Lees et al. (2012) searched contemporary studies to identify cognitive assessments used post-stroke. Of the 408 studies identified, 300 different cognitive assessments were described; the most commonly used was the Mini-Mental State Examination (MMSE) ( $n = 108$ ).

Pen-and-paper based cognitive assessments, such as the MMSE and many neuropsychological assessments, commonly rely on linguistic skills for completion. This mode of assessment often requires patients to understand verbal or written instructions, and respond verbally or in writing to answer questions. Up to 30% of patients experience aphasia post-stroke (Engelter et al., 2006) and administering pen-and-paper assessments for this stroke subgroup is often impractical. If cognitive tasks require written or drawn responses, patients with upper-limb paresis – representing over 60% of stroke survivors (Broeks, Lankhorst, Rumping, & Prevo, 1999) – may not be able to complete the required tasks. While it is recognised that specific stroke subgroups are often excluded from studies evaluating the clinimetric properties (validity, reliability and feasibility) of cognitive assessments (Alvan, 1983), this has never been quantified.

In addition to pen-and-paper assessments, other modes have been developed to assess cognition post-stroke. These modes include computer assessments (Cumming,

Brodthmann, Darby, & Bernhardt, 2012; Shopin et al., 2013), virtual reality (Buxbaum et al., 2012) and observational functional performance (Cederfeldt, Widell, Andersson, Dahlin-Ivanoff, & Gosman-Hedström, 2011). Virtual reality can be described as using computer hardware and software to create simulations for users to interact with objects and events that resemble the real world (Lam, Man, Tam, & Weiss, 2006). Observational functional performance assessments measure cognition while patients undertake tasks involving everyday activities. It is not known whether different modes of cognitive assessment influence patient samples used in clinimetric studies post-stroke. Alternative modes of cognitive assessment may provide clinicians with additional resources to enable flexibility in the selection of tools for assessing cognition, which are most appropriate to the individual.

The aim of this systematic review was to: (1) determine if the stroke samples included in clinimetric studies represent the stroke population, (2) identify the different approaches to cognitive assessment in stroke, and (3) ascertain whether the different modes of cognitive assessment influence the stroke samples used in the studies.

## **2.3 Methods**

The PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-analyses; Moher, Liberati, Tetzlaff, & Altman, 2009) were applied according to the needs of this systematic review.

### **2.3.1 Search Strategy**

To identify contemporary studies evaluating the clinimetric properties of cognitive assessments post-stroke we searched articles published between January 2000 and October 2013 from Cochrane, CINAHL, Embase, Ovid Medline, AMED, APA PsycNET. Unpublished literature was also searched using Google Scholar and a variety of grey literature sources. The start date of the year 2000 was chosen so that results reflect current practice, and this start date is consistent with a previous review that identified contemporary cognitive and mood assessments post-stroke (Lees et al., 2012). The search strategy was developed in collaboration with a research librarian at The University of Queensland using MeSH headings and keywords associated with “stroke”, “cognition”, in combination with “assessment”, “screen” and “test”. An example of the full search strategy, using Ovid Medline, can be viewed in [Appendix B](#). The reference lists of the included articles were reviewed for further potential studies.

### **2.3.2 Study Selection**

Research examining the clinimetric properties of cognitive assessments or screening tools for stroke survivors were included for review if they met the following criteria: (1) participants were aged 18 or above; (2) cognitive assessments included at least one cognitive domain of attention, language, memory, visual perception, executive function; or a quantitative, standardised measure of cognition using real life activities. Studies were excluded from the review if: (1) a single case study design was used; (2) the assessment was not dedicated to cognition, despite containing some cognitive information (e.g., severity or disability rating scales, such as the National Institute of Health Stroke Scale or Functional Independence Measure); (3) if stroke data were not reported separately from other neuropathology, and authors could not provide this information upon request.

Titles and abstracts identified in the searches were independently reviewed by two authors (K. W. and M. I.) against the pre-determined eligibility criteria. Articles that appeared to meet the inclusion criteria, or were unclear, were retained for further full-text review. Disagreements between reviewers were resolved by consensus or by referral to a third reviewer (T. C.).

### **2.3.3 Data Extraction**

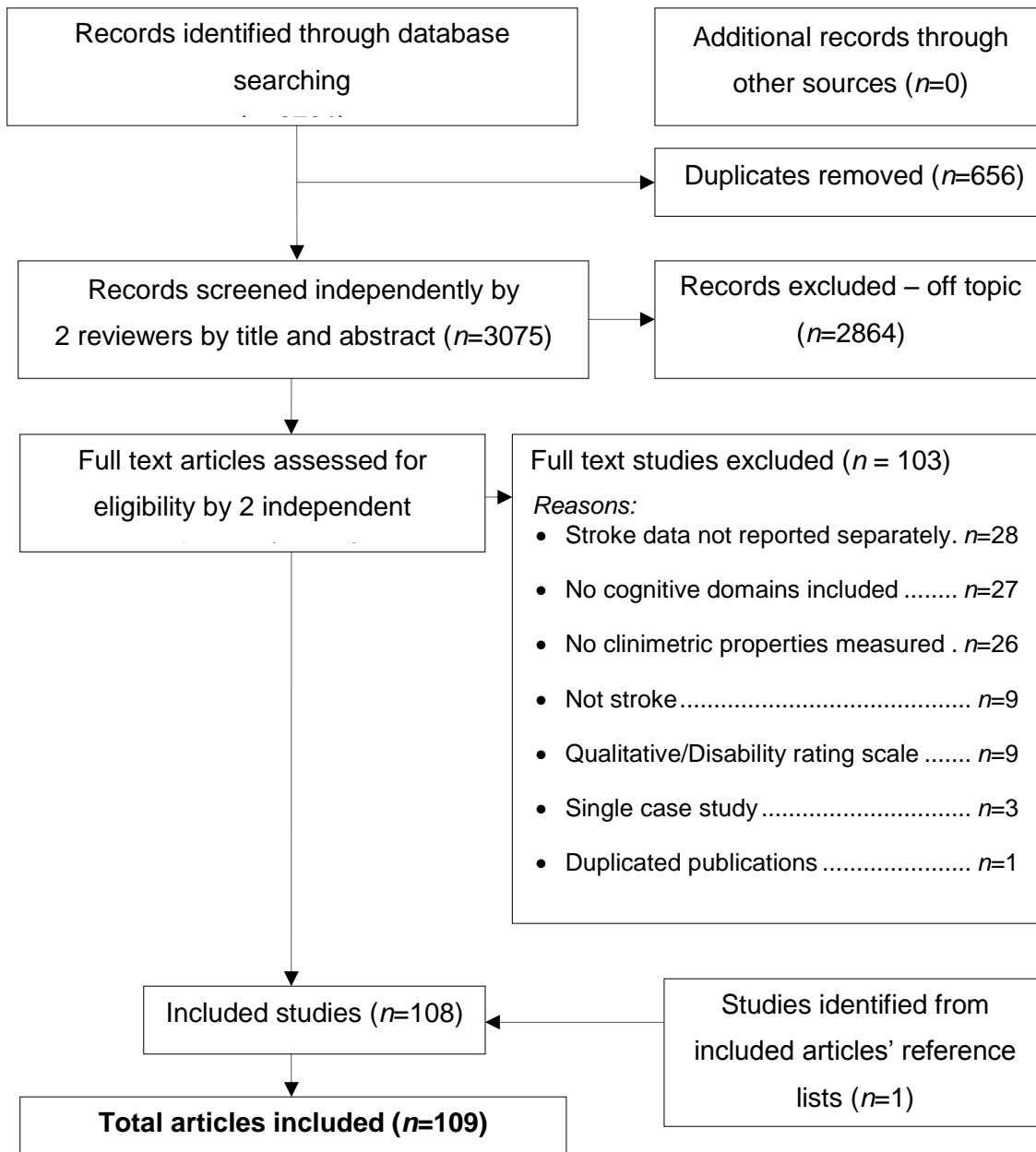
Data were extracted using a standardised form for each included article. Information included citation details, participant characteristics, time post-stroke onset, stroke subtypes, stroke severity, name of cognitive assessments or screens, mode of delivery, mode of reference standard used and clinimetric properties measured. The descriptive eligibility criteria, reasons for drop-outs and missing data were extracted verbatim, and associated quantitative data were recorded. Authors were contacted for additional information when quantitative information, reasons for drop-outs, or missing data were not reported.

### **2.3.4 Data Synthesis**

Theming of the different modes of cognitive assessments and reasons for exclusions were independently undertaken by two authors (K. W. and T. C.). To ensure rigor of the descriptive synthesis, an inductive process was used where no predetermined themes were used, and categories evolved from the raw data (Boyatzis, 1998). Agreement was achieved following comparison and discussion of the categories until consensus was reached. The frequency of the categories was reported according to the mode of cognitive assessment.

## 2.4 Results

From the 3,731 articles identified in the searches, 109 studies met the inclusion criteria (total  $n$  participants = 12,037). The search strategy and results can be viewed in a flow diagram in [Figure 2.1](#). Details of the study characteristics for the included articles are shown in [Appendix C](#).



**Figure 2.1** Flow chart of search results



Despite a range of exclusion criteria used in the individual studies, recurring criteria between studies was common. [Table 2.1](#) displays the six broad categories and associated sub-categories that emerged. Even though there was overlap in the meaning between categories, the criterion used in the individual studies was only assigned to a single category. To illustrate, an exclusion criterion for patients who were “unable to follow commands” could be allocated to either “general language” or “aphasia”. If the authors did not specify aphasia, this criterion was assigned to the “general language” sub-category. Also, many authors excluded patients with recurrent stroke. This was assigned to the “cognition” category as it was assumed the reason for this exclusion was due to the possibility of pre-morbid cognitive impairment.

**Table 2.1** Identified categories and sub-categories used to exclude participants in the studies

<p><b>Cognition</b></p> <ul style="list-style-type: none"> <li>• Dementia</li> <li>• General cognition</li> <li>• Visual-perceptual deficits</li> <li>• Other neurology</li> <li>recurrent stroke</li> </ul>	<p><b>Communication</b></p> <ul style="list-style-type: none"> <li>• Aphasia</li> <li>• General language</li> <li>• Non-native language</li> <li>• Motor speech</li> </ul>	<p><b>Endurance</b></p> <ul style="list-style-type: none"> <li>• Attention</li> <li>• Fatigue/endurance</li> <li>• Reduced consciousness</li> <li>• Medically unstable</li> </ul>
<p><b>Sensory</b></p> <ul style="list-style-type: none"> <li>• Hearing</li> <li>• Visual</li> </ul>	<p><b>Psychiatric</b></p> <ul style="list-style-type: none"> <li>• Depression</li> <li>• Substance abuse</li> <li>• Psychiatric disease</li> </ul>	<p><b>Motor</b></p> <ul style="list-style-type: none"> <li>• Hemiparesis</li> <li>• Limb weakness</li> </ul>

Cognitive impairments were the most commonly reported exclusion criteria (68%), followed by communication issues (62%), then endurance problems (42%), sensory loss (39%), psychiatric illness (38%) and motor limitations (27%). Only nine studies reported actual numbers and reasons for excluded patients, which precluded statistical analysis. In five of these studies, aphasia was the most frequent reason for exclusion (15% (23), 17% (24), 5% (25), 27% (26), 27% (27)). Overall, findings from these individual studies were in agreement with our identified categories; the most frequent reasons for excluding patients were due to communication and cognitive impairments.

Of the 28 (26%) articles reporting drop-outs, only 20 itemised the reasons. The reasons were primarily related to study logistics, such as “participant refusal” or “unable to be reached”. Another common reason for patient drop-outs was death. Computer and virtual reality studies reported drop-outs associated with technical difficulties, which were not applicable to the other modes of delivery.

Studies that itemised reasons for missing data were primarily reported from pen-and-paper based studies ( $n = 12$ , 10%). The reasons for missing data were mainly attributed to patients being unable to complete tasks due to communication and cognition deficits.

Six different modes for assessing cognition post-stroke were identified from the included studies. Pen-and-paper cognitive assessments were the most prevalent mode of delivery (73%), followed by virtual reality (11%), then computer (6%), observational functional performance (5%), assessment by informants (patient or carer informants) (3%) and telephone (3%). The frequency of the broad exclusion categories used by studies employing different modes of cognitive assessment is presented in [Table 2.2](#). Excluding patients based on cognition and communication was common, irrespective of the mode of cognitive assessment. The frequency of the sub-categories used by the different modes of cognitive assessments is outlined in [Appendix D](#). Each mode of cognitive assessment is considered separately below.

#### **2.4.1 Pen-and-Paper**

Eighty studies evaluated clinimetric properties for a variety of pen-and-paper cognitive assessments post-stroke. The most commonly used reference standard (as a comparison for validation) was an alternative pen-and-paper cognitive screen or neuropsychological battery ( $n = 50$ , 65%). Disability rating scales, such as the Functional Independence Measure and the Barthel Index, were commonly used for predictive validity.

**Table 2.2** Frequency of broad exclusion categories used by the different modes of cognitive assessments

<b>Eligibility Categories (%)</b>	<b>Pen-and-</b>	<b>Virtual</b>	<b>Computer</b>	<b>Functional*</b>	<b>Informant</b>	<b>Telephone</b>
	<b>paper</b>	<b>reality</b>				
	( <i>n</i> = 80)	( <i>n</i> = 12)	( <i>n</i> = 6)	( <i>n</i> = 5)	( <i>n</i> = 3)	( <i>n</i> = 3)
<b>Communication</b>	64	83	67	80	33	100
<b>Cognition</b>	63	58	50	80	100	33
<b>Endurance</b>	46	33	50	20	0	0
<b>Sensory</b>	35	58	50	40	33	33
<b>Psychiatric</b>	40	33	33	20	33	33
<b>Motor</b>	21	75	33	0	33	0

\*Observational functional performance

Many studies excluded specific disorders, such as aphasia and depression, of a certain severity. To illustrate, one study excluded patients with severe aphasia based on a score of less than three on the Boston Diagnostic Aphasia Examination (Leeds, Meara, Woods, & Hobson, 2001), and another study excluded severe aphasia with no reported quantitative measure (Hargrave, Nupp, & Erickson, 2012).

Of the 10 (13%) studies not reporting a criterion for communication or cognition, three used a neglect assessment (Chiba & Haga, 2008; Leibovitch, Vasquez, Ebert, Beresford, & Black, 2012; Mattingley et al., 2004), another employed a typical neglect task being evaluated as a measure for executive function (Woods & Mark, 2007), another used an aphasia screening tool (Thommessen, Thoresen, Bautz-Holter, & Laake, 2002), and one study targeted patients with dementia (Mast, MacNeill, & Lichtenberg, 2000). The remaining two studies' eligibility criteria were not categorised due to the criteria being unique to the individual studies. For example, one study required patients to "complete assessment within 30 minutes at a time" (McKinney et al., 2002), and the other study required "patients to be independent of another person at least indoors and living in ordinary housing" (Wendel, Risberg, Pessah-Rasmussen, Stahl, & Iwarsson, 2008).

### 2.4.2 Virtual Reality

Nine of the 12 studies using virtual reality technology used a pen-and-paper reference standard. Four of the nine studies also used real life observations to measure validity. Two studies used healthy controls to validate their cognitive assessment (Rand et al., 2007;

Weiss, Naveh, & Katz, 2003). Unlike the other modes of cognitive assessments, the frequency of excluding patients with motor limitations was high (75%). Only one study did not include criteria for communication or cognition (Weiss et al., 2003).

### **2.4.3 Computer**

Five of six studies using computer cognitive assessments employed pen-and-paper cognitive assessments as a reference standard. A reference standard was not applicable in one study that measured test-retest reliability (Mazer, Sofer, Korner-Bitensky, & Gelinas, 2001). Only one study did not incorporate exclusion criteria for communication or cognition (George, Clark, & Crotty, 2008). This study evaluated predictive validity of the Visual Recognition Slide Test for driving performance in a sample of patients whose goals were to return to driving.

### **2.4.4 Observational Functional Performance**

Five studies evaluating three individual observational functional cognitive assessments were identified. All assessments incorporated functional tasks involving executive skills. The Executive Performance Test (EFPT) was evaluated by three studies that primarily targeted mild stroke at six months post-onset (Baum et al., 2008) and the acute phase of stroke recovery (Cederfeldt et al., 2011; Wolf, Stift, Connor, Baum, & Cognitive Rehabilitation Research, 2010).

Only two of the five studies used pen-and-paper reference standards in their clinimetric evaluation (Baum et al., 2008; Wolf et al., 2010). The remaining studies used an alternative observational functional cognitive assessment (Cederfeldt, Gosman-Hedstrom, Savborg, & Tarkowski, 2009; Marom, Jarus, & Josman, 2006) or an informant rating scale (Cuberos-Urbano et al., 2013), in addition to disability and stroke severity rating scales. All studies incorporated exclusion criteria for communication or cognition. No studies reported exclusion criteria for motor or endurance deficits.

### **2.4.5 Informant**

Three studies used informant-based methods to assess cognitive skills, where patients (Aben et al., 2009; Barber & Stott, 2004) and family members (Maki et al., 2000) were used as informants. All studies used a pen-and-paper reference standard for validation

and excluded patients with aphasia. Endurance was the only exclusion criterion not used in the studies.

#### **2.4.6 Telephone**

Three studies evaluated clinimetric properties of cognitive assessments via a telephone mode of delivery. The aims for assessment differed in that one study evaluated cognitive performance using a functional telephone task (Hopkins Telephone Task) (Higginson, Johnson-Greene, & Langrall, 2010), while the other two studies applied a pen-and-paper cognitive assessment that was modified for telephone use (Gavett, Crane, & Dams-O'Connor, 2013; Pendlebury et al., 2013). All studies used a pen-and-paper reference standard. The study that aimed to validate the telephone version of the Montreal Cognitive Assessment (MoCA) only excluded patients with dementia, and targeted community dwelling participants (Pendlebury et al., 2013). The study validating the Brief Test of Adult Cognition by telephone also had minimal exclusion criteria, and used other neuropathological subgroups to compare results (Gavett et al., 2013). These telephone-based studies did not include criteria for motor or endurance.

### **2.5 Discussion**

In the present systematic review of studies measuring clinimetric properties of cognitive assessments post-stroke, we found that specific stroke subgroups are poorly represented. Common exclusion criteria emerged, with over 2/3 of studies excluding patients on the basis of cognition or communication issues, or both. Clinical guidelines for stroke management recommend that patients should be assessed for cognitive deficits using valid and reliable tools (National Stroke Foundation, 2010; Scottish Intercollegiate Guidelines Network, 2010; Stroke Foundation of New Zealand and New Zealand Guidelines Group, 2010). Given the high incidence of post-stroke cognitive impairments (Lindén et al., 2004) and communication deficits (Engelter et al., 2006), major barriers exist for meeting these guidelines in clinical practice. Properties of reliability, validity and feasibility for cognitive assessments need to be evaluated in all patient groups to guide the selection of appropriate tools (Dekker, Dallmeijer, & Lankhorst; Harrison, McArthur, & Quinn, 2013).

Pen-and-paper cognitive assessments were clinimetrically evaluated substantially more than any other mode of delivery. Other modes of cognitive assessment identified in the review did not appear to overcome the barriers present in traditional pen-and-paper assessments. This may be because many of the studies investigating alternative modes retained the use of pen-and-paper assessments as a reference standard, and were therefore restricted to narrow eligibility criteria.

Other methodological issues may have influenced the eligibility criteria used in the clinimetric studies. Many studies evaluated test accuracy, where cognitive assessments detecting cognitive impairments in individuals with a first-time, focal lesion is needed. Therefore, patients with a history of dementia, recurrent stroke or psychiatric condition may have been excluded to ensure cognitive performance was not confounded by other sources of cognitive decline (Knopman et al., 2009; Liu et al.; Saposnik et al.). These are substantial subgroups of stroke patients: the four-year stroke recurrence rate is 18% (Feng, Hendry, & Adams, 2010), and depression is experienced by 31% of stroke survivors (Hackett & Pickles, 2014). While their exclusion may be justifiable, these are additional subgroups that are poorly represented in clinimetric studies. Communication and cognition exclusion criteria were applied more frequently in virtual reality studies compared to any other mode of delivery. A reason for this could be that patients are required to learn how to navigate and interact with the virtual environment, which could present problems for patients who are unable to understand complex instructions (Albert & Gerard Jounghyun, 2005). Similarly, motor function criteria were used more frequently in virtual reality studies compared to the other modes of delivery. This may reflect the need for a functioning upper-limb to navigate the virtual environment. The results from the review confirm previous systematic reviews of stroke rehabilitation (Laver, George, Thomas, Deutsch, & Crotty, 2012; Saposnik & Levin, 2011) showing that patient eligibility criteria applied to virtual reality studies are highly selective. Virtual reality technology provides opportunities to combine simulated real-life scenarios, with the accuracy of computerised measures to assess cognitive performance. However, future developments in virtual reality need to look carefully at minimising the linguistic demands and motor skills needed to participate, which will better reflect the capabilities of older stroke survivors.

The search strategy used in the review was limited to studies published from 2000 onwards, as we aimed to identify contemporary methods used to measure clinimetric properties of cognitive assessments post-stroke. The identified studies were inclusive of non-English speaking studies, and authors were emailed for missing information to ensure comprehensive reporting.

The unique combination of systematically selecting quantitative studies, and using a theming method to synthesise the data, facilitated thorough analysis and reporting of the exclusion criteria used. Clinicians need to be aware of sampling methods used by clinimetric studies evaluating cognitive assessments post-stroke to ensure they select tools that are tailored to patient needs. While the challenges of assessing cognition are recognised for stroke survivors, particularly for patients with communication and more severe cognitive impairments, these patients need to be represented in clinimetric studies. Future research in cognitive assessment post-stroke needs to consider these subgroups to ensure all patients have access to valid and reliable measures of their cognitive performance.

While our review methods were comprehensive, our findings were necessarily reliant on reporting methods used in the original studies. The percentages associated with the reasons for patient exclusions, drop-outs and missing data were rarely reported. Thus, how many stroke survivors miss out on cognitive assessments, and the reasons why, remains unclear. Studies evaluating the clinimetric properties of cognitive assessments should report excluded patients, detailing the proportions and reasons for exclusion. This will clarify the generalisability of each study's findings, and will also provide clinicians with important information on the feasibility of each assessment across different stroke subgroups.

## Chapter 3: Determining the Association between Language and Cognitive Tests in Post-Stroke Aphasia

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The systematic review, reported in chapter 2, indicated that pen-and-paper cognitive tests were used considerably more than any other testing method in stroke. The most common exclusion criteria used in the reviewed studies were communication and cognition. Aphasia impairments meet both these exclusion criteria. In many studies, the linguistic and cognitive demands associated with standard pen-and-paper tests were considered sufficient reasons for excluding individuals with impairments in these areas.

Little is known about the association between language performance and non-linguistic cognitive performance in post-stroke aphasia. The purpose of chapter 3 is to report the findings of the association between language performance (in aphasia and controls) and pen-and-paper cognitive tests typically used in stroke. This chapter also reports the association between language performance and a standard real-life measure of cognition. The results of this study will inform existing practice and provide a foundation for research addressing the barriers posed by aphasic deficits in cognitive testing.

The content of this chapter has been published in “Determining the association between language and cognitive tests in post-stroke aphasia” in *Frontiers in Psychology* (Wall, Cumming & Copland, 2017; see [Appendix E](#) for a URL link to the published manuscript). The content included in this chapter is identical to the submitted manuscript, but the formatting was modified to match the style of this thesis.



### 3.1 Abstract

**Background:** Individuals with aphasia are often excluded from studies exploring post-stroke cognition because so many of the standard cognitive assessments rely on language ability. Our primary objective was to examine the association between performance on cognitive tests and performance on comprehension and naming tests in post-stroke aphasia. Second, we aimed to determine the association between language performance and a real-life measure of cognition (Kettle Test). Third, we explored the feasibility of administering cognitive tests in aphasia.

**Methods:** Thirty-six participants with post-stroke aphasia and 32 controls were assessed on a battery of pen-and-paper cognitive tests recommended in stroke. Auditory comprehension was measured using the Comprehensive Aphasia Test and naming was measured using the Boston Naming Test. Twenty-two community dwelling participants with aphasia and controls were also asked to complete the Kettle Test. Multiple linear regressions were used to explore the relationship between language performance and performance on the cognitive tests. Feasibility was determined by quantifying missing data.

**Results:** The cognitive tests with the highest variance accounted for by auditory comprehension and naming were animal fluency ( $R^2 = .67$ ,  $R^2 = .78$ ) and the Hopkins Verbal Learning Test (recognition discrimination Index) ( $R^2 = .65$ ,  $R^2 = .78$ ). All cognitive tests were significantly associated with auditory comprehension and naming, except for the Star Cancellation and the Kettle Test. Thirty-three per cent of participants with aphasia were unable to complete all the cognitive tests.

**Conclusion:** Language and non-linguistic cognitive processes are often interrelated. Most pen-and-paper cognitive tests were significantly associated with both auditory comprehension and naming, even in tests that do not require a verbal response. Language performance was not significantly associated with a real-life cognitive performance measure. Task instructions, stimuli and responses for completion need to be tailored for individuals with aphasia to minimise the influence of language deficits when testing non-linguistic cognitive performance.

**Keywords:** aphasia, cognition, cognitive impairments, stroke, neuropsychological tests, pen-and-paper tests

## 3.2 Introduction

Up to 30% of stroke survivors experience difficulty with receptive and expressive language – called aphasia (Engelter et al., 2006). There is an assumed relationship between language and non-linguistic cognitive performance in post-stroke aphasia, but the nature and management of this relationship is poorly understood. Studies show that impaired executive skills, working memory and attention can adversely influence aphasia rehabilitation outcomes (Harnish & Lundine, 2015; Lambon Ralph et al., 2010; Murray, 2012) and cognitive performance may predict aphasia recovery better than language performance (van de Sandt-Koenderman et al., 2008). El Hachioui et al. (2014) explored cognitive deficits in aphasia during the first-year post-stroke and the association with functional outcome. Participants with persisting aphasia had poorer cognitive performance, poorer functional outcome, and they were more depressed compared to participants with resolved aphasia. To optimise aphasia therapy, clinicians need to measure linguistic and non-linguistic performance to ensure all aspects of cognitive impairments are considered.

International guidelines recommend that all stroke survivors should be screened for cognitive impairments using valid and reliable tools, and comprehensive neuropsychological testing should be undertaken for those that fail screening (Dworzynski, Ritchie, Fenu, Macdermott, & Playford, 2013; National Stroke Foundation, 2010; Winstein et al., 2016). Pen-and-paper screening tools and assessments are used more frequently than alternative methods for assessing cognition post-stroke (Lees et al., 2012; Wall et al., 2015). Such tools are often linguistically-loaded, and aphasic deficits may confound non-linguistic cognitive performance (de Koning, 2009; Gorelick et al., 2011). Consequently, patients with aphasia are often excluded from studies validating cognitive assessments and exploring cognitive outcomes in stroke (Pendlebury et al., 2015; Sachdev et al., 2004; Wall et al., 2015).

A reliance on verbal response is an obvious barrier to obtaining accurate measures of non-linguistic cognitive performance in aphasia. For example, verbal fluency is a task often used in standard language assessments (Swinburn, Porter, & Howard, 2005), but it is also used to measure executive skills in stroke (Hachinski et al., 2006). This highly language-dependent task (Whiteside et al., 2016) is unlikely to accurately represent executive skills in aphasia. Yet, eliminating verbal responses may not resolve language deficits confounding non-linguistic cognitive performance in aphasia. Comprehension

deficits associated with aphasia may also confound results. Cognitive tests are often complex, with detailed instructions requiring sophisticated comprehension skills to understand the tasks (Keil & Kaszniak, 2002). Increased syntactical complexity negatively influences comprehension in aphasia (DeDe, 2013), and the linguistic complexity of instructions needs consideration in this stroke subgroup.

To quantify the association between language performance and cognitive tests without a verbal response, Fucetola et al. (2009) explored how much variance in the non-verbal subtests from the Wechsler Adult Intelligence Scale-III (block design, matrix reasoning, picture arrangement) and Wechsler Memory Scale-III (spatial span) was accounted for by auditory comprehension and oral expression in aphasia. Auditory comprehension accounted for 41% of the total variance ( $p < .001$ ), whereas no significant relationship was found with naming performance. This study suggests that non-verbal cognitive performance is related to auditory comprehension severity, but 59% of the variance remains unexplained.

Cognitive tests vary in the cognitive domain being tested, the task complexity, the delivery of instructions and the responses needed for completion. There has been no systematic analysis of the relationship between language performance in post-stroke aphasia (naming and comprehension) and performance on a broad range of widely used neuropsychological tasks. Exploring the potential variability in the association between language and scores on cognitive tests (including an everyday real-life measure of cognition, such as making a hot drink) in aphasia is necessary to better inform clinical practice.

Our primary objective was to examine the association between performance on cognitive tests and assessments of comprehension and naming in post-stroke aphasia. Our second aim was to determine the association between auditory comprehension and naming performance and a validated real-life cognitive performance assessment in aphasia and controls. Our last aim was to determine the feasibility of all cognitive tests used by quantifying missing data in patients with aphasia compared to controls.

### 3.3 Material and Methods

#### 3.3.1 Participants

Thirty-six participants with post-stroke aphasia and 32 controls were recruited from three Brisbane Hospitals, the Communication Registry at The University of Queensland, community posters, social groups and newsletters. Participants with aphasia had diagnostic imaging evidence of stroke (or a clinical diagnosis if imaging was unavailable) and a diagnosis of aphasia according to the Comprehensive Aphasia Test (CAT) (using auditory comprehension sub-tests' cut-off scores) (Swinburn et al., 2005) or the Language Screening Test (cut-off < 15) (Flamand-Roze et al., 2011). Patients were excluded if they: (1) had visual and hearing impairments that impeded testing; (2) needed an interpreter to participate if English was their second language; or (3) were too medically unwell. The included control participants passed a mood screen (The Patient Health Questionnaire; Kroenke, Spitzer, & Williams, 2001); to eliminate the potential influence of depression on cognitive performance (Thomas & O'Brien, 2008; S. Wang & Blazer, 2015). Controls were excluded if they had a history of neurological disease or acquired injury, or if they needed an interpreter to participate if English was their second language.

Ethical clearance was obtained through relevant Human Research Ethics Committees in Brisbane, Australia, including the Royal Brisbane and Women's Hospital. Written consent was sourced for all participants and a substitute decision maker was used for patients with cognitive deficits that precluded informed consent.

#### 3.3.2 Assessments

Demographic data collected included age, sex, education level, handedness, time post-stroke and clinical setting. We did not report localisation of stroke lesion(s) because detailed neurological data could not be sourced for all community participants.

Language performance and severity of aphasia were assessed using the CAT (Swinburn et al., 2005) (auditory comprehension total score) and the 15-item abbreviated Boston Naming Test (Kent & Luszcz, 2002). The Boston Naming Test is one of the most widely used standardised aphasia measures in clinical practice (Vogel, Maruff, & Morgan, 2010). The 15-item abbreviated Boston Naming Test strongly correlates with the full Boston Naming Test ( $r = .93$ ) (Franzen, Haut, Rankin, & Keefover, 1995), and it was recommended as part of neuropsychological testing for stroke survivors (Hachinski et al.,

2006). Fifty per cent of stroke survivors experience fatigue irrespective of time post stroke (Cumming, Packer, Kramer, & English, 2016). The practicality of testing individuals with fatigue was considered in selecting our battery.

Our battery of pen-and-paper neuropsychological tests has been validated in stroke. The battery included the following tests.

- **Star Cancellation** (Bailey, Riddoch, & Crome, 2004): A visual neglect test that includes small stars on an A4 sheet with visual distractors (large stars and letters). Participants are provided with a visual demonstration, along with brief verbal instruction, to cross out all the small stars using a pen.
- **The Brixton Spatial Anticipation Test** (Burgess, 1997): An executive function test with a 56-page stimulus booklet. It is a visuospatial sequencing task with rule changes where participants are required to detect rules in sequences of stimuli. Each page contains two rows of five circles, numbered from one to 10. On each page, a single circle is coloured blue, and the position of the blue circle changes from one page to the next, based on a series of patterns. Participants are provided with lengthy verbal instructions and a practice. The examiner clarifies understanding. Participants are required to point to where they predicted the filled circle will be on the following page, based on the pattern inferred from the previous page.
- **Trail Making Test** (parts A and B) (Reitan & Wolfson, 1985): Part A is often used to test attention. Participants are verbally instructed to connect circles numbered 1–25 in correct order as quickly as possible using a pen. Part B is an executive task where participants are verbally instructed to connect numbered and lettered circles in correct alternating order (i.e., 1-A-2-B, etc.) as quickly as possible. Both parts have practice trials for familiarisation.
- **Digit Span Test** (forwards and backwards) (Wechsler, 1997): The forwards test is used to measure verbal short-term memory. Participants are verbally instructed to repeat strings of numbers of increasing length. The backwards test is used to measure verbal working memory and executive skills. Participants are presented

with each number string and they are verbally instructed to recall each number string in reverse order.

- **Hopkins Verbal Learning Test (HVLТ)-Revised** (Brandt, 2001): Used to assess verbal memory. The examiner reads a list of 12 words (from 3 taxonomic categories). Participants are instructed to try to remember, and verbally repeat, as many words as possible from the list. The examiner then reads the same list twice more, with recall each time. The immediate recall score is the total number of words recalled over these three trials. Subsequently, the participants are asked to recall the word list 20–25 minutes later (delayed recall). A retention score is calculated to determine the percentage of words retained (delayed recall as a percentage of the best immediate recall from trial 2 or 3). This is followed by a forced-choice recognition test (RDI), where 12 target words from the learning trials are included with 12 distractor words (six semantically related and six semantically unrelated). Participants are instructed to provide a yes/no response.
- **Rey Complex Figure** (copy, immediate and delayed recall) (Osterrieth, 1944): Rey Complex Figure Copy (immediate, delayed and recall) is used to assess visuospatial, visual memory and executive skills. Participants are provided with a pen and paper and asked to reproduce the complex figure. The stimulus figure and reproduction are then removed. After a five minute delay, the participants are verbally instructed to reproduce the figure from memory. Then, after a 20–30 minute delay, the participants are instructed to reproduce the figure from memory again.
- **Animal fluency** (Rosen, 1980): A verbal fluency task where participants are verbally instructed to name as many different animals as possible within a minute. While fluency tasks (such as animal fluency) undoubtedly include facets of executive function in planning search and retrieval, they are predominantly a reflection of language skills (Whiteside et al., 2016).

- **Kettle Test** (Hartman-Maeir, Harel, & Katz, 2009): Kettle Test is a real-life everyday performance measure designed to detect cognitive processes needed for independent community living. Observations are rated on 13 distinct steps to complete the hot drink making task and guidelines for cueing are provided. The participants are scored according to the degree of cueing needed to complete the individual steps (0–4). Total scores range from 0 to 52, with higher scores indicating more assistance.

### **3.3.3 Statistical Analysis**

The relationships between auditory comprehension, naming and cognitive function were tested using separate multivariate linear regressions (controlling for age and education) for each cognitive test. To determine the distinct effects of auditory comprehension and naming, the independent variables were entered into different models. Demographic variables included in the models were years of education and age. If assumptions were not met to perform the multiple linear regressions, logistic regressions were used. To explore the feasibility of performing cognitive tests in aphasia compared to controls, we recorded reasons for missing data and the frequency for each individual test. All analyses were performed with Stata 14 software.

### 3.4 Results

The characteristics of the 36 participants with post-stroke aphasia and 32 controls are shown in [Table 3.1](#). Of the 36 participants with aphasia, 22 community dwelling participants and the controls were also asked to complete the Kettle Test. The Kettle Test was not performed in the acute phase of stroke due to practical restrictions on the ward.

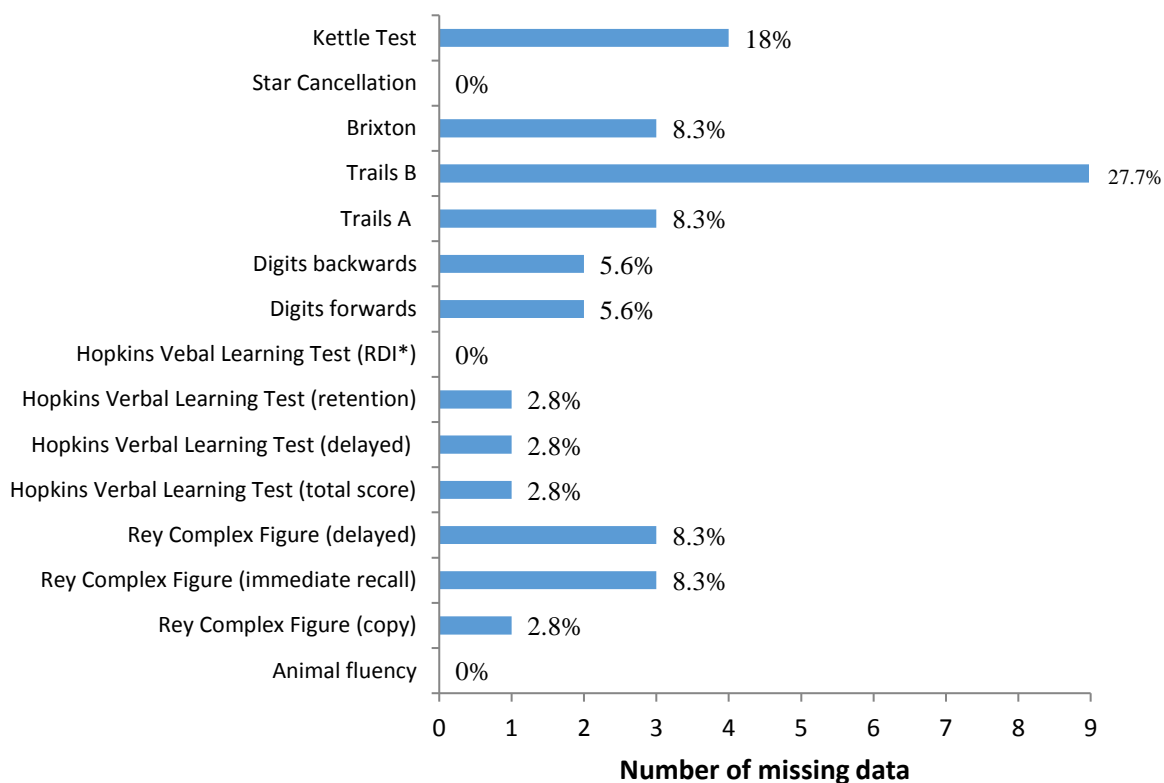
**Table 3.1** Characteristics of the aphasia and control groups

	<b>Aphasia</b>	<b>Controls</b>
Age in years, mean $\pm$ SD	70.1 $\pm$ 9.0	67.3 $\pm$ 12.3
Sex, <i>n</i> (%)		
Female	12 (33)	17 (53)
Male	24 (67)	15 (47)
Handedness, <i>n</i> (%)		
Right-handed	34 (94)	30 (85.7)
Left-handed	2 (5.5)	2 (6.3)
Ambidextrous	1 (2.7)	0
Education in years, mean $\pm$ SD	11.0 $\pm$ 2.6	15.1 $\pm$ 3.4
Pre-morbid neurological disease/injury ( <i>n</i> )	3	–
Time post-stroke, mean $\pm$ SD by clinical setting		
Acute setting ( <i>n</i> = 12)	9.2 $\pm$ 13.2 days	–
Inpatient rehabilitation ( <i>n</i> = 2)	23.5 $\pm$ 11.5 days	–
Community dwelling ( <i>n</i> = 22)	6.35 $\pm$ 5.2 years	–

The severity of auditory comprehension and naming impairments in the aphasia group ranged from very severe to mild language deficits. Total scores for auditory comprehension ranged from 5/66 to 63/66 (median = 53, interquartile range = 29–58) as measured by the CAT. The results from the Boston Naming Test ranged from 0/15 to 15/15 (median = 10, interquartile range = 1–12). Control participants completed all tests, while 33% (*n* = 12) of participants with aphasia had missing data. All participants completed the auditory comprehension and naming tasks. There was a total of 32 missed cognitive test scores.



Figure 3.1 shows the number and frequency of missing data for the cognitive tests. The Trail Making Test (part B) had more missing data than any other test (28%). The non-verbal cognitive tests had more missing data compared to the tests that required a verbal response. For example, verbal fluency (0%) and the HVLT (0%–2.8%) compared to the Brixton (8.3%) and the Rey immediate and delayed recall (8.3%). Reasons for missing data in the pen-and-paper tests were: (1) refusal to attempt test ( $n = 3$  participants), (2) incomplete due to task complexity ( $n = 3$  participants), (3) unable to understand instructions ( $n = 3$  participants), and (4) incomplete due to difficulty using a pen ( $n = 2$  participants). Four of the 22 community dwelling participants with aphasia (15%) had missing data for the Kettle Test due to upper and lower limb hemiparesis. Participants with missing data had more severe auditory comprehension deficits (median = 27.5, interquartile range = 25.0–49.0) and more severe naming deficits (median = 1, interquartile range = 0–7.5), compared to participants without missing data (auditory comprehension median = 53, interquartile range = 45.8–58.0, naming median = 10.5, interquartile range = 6.5–13.5). The clinical setting did not influence missing data, where there was an equal distribution of participants in the acute versus community setting.



\*RDI, recognition discrimination index

**Figure 3.1** Number and frequency of missing data by cognitive tests in aphasia

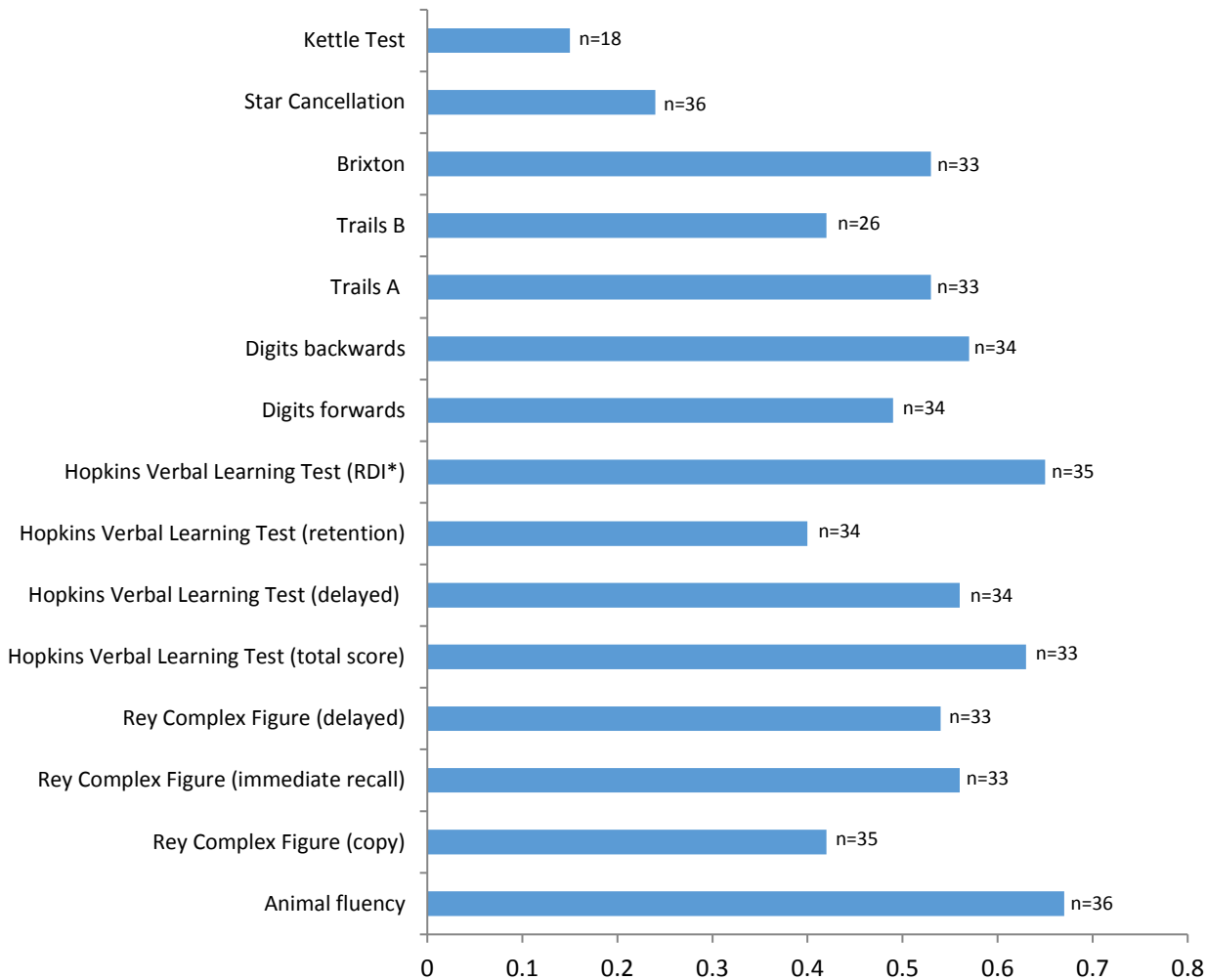
Table 3.2 shows the descriptive statistics for the language and cognitive tests. As expected, there was minimal variance in the auditory comprehension and the Boston Naming Test scores of the control group, and therefore no regressions associating language and cognitive performance were run in this group. The data for the regressions were sourced only from the participants with aphasia. We conducted a pairwise regression between the independent variables (auditory comprehension and naming), and confirmed that they were too closely related (pairwise correlation = .86) to be included in the same regression model.

**Table 3.2** Descriptive statistics of the language and cognitive tests

Test	Aphasia Group				Controls		
	Mean (SD)	Median	Range	Mean (SD)	Median	Range	
Auditory comprehension	46.1 (15.5)	52.0	5–63	61.4 (3.2)	62.0	55–66	
Boston Naming Test	8.2 (5.3)	9.5	0–15	13.8 (1.2)	14.0	11–15	
Kettle Test	4.6 (4.0)	4.0	0–15	1.5 (1.6)	1.0	0-5	
Star Cancellation	51.6 (6.3)	54.0	24–54	53.9 (0.4)	54.0	52–54	
Brixton	28.9 (12.4)	28.0	4–52	22.6 (8.8)	20.0	7– 40	
Trail B	181.9 (85.4)	178.0	44.2–300	87.4 (33.7)	83.8	33–160	
Trail A	91.9 (60.6)	75.0	20–300	36.6 (9.8)	35.6	17.5–63.7	
Digits backwards	3.3 (2.9)	4.0	0–11	7.4 (2.6)	7.0	2–14	
Digits forwards	5.8 (4.1)	6.0	0–14	10.2 (2.2)	10.0	6–14	
HVLT* (RDI**)	6.0 (3.9)	7.0	0–12	9.7 (1.8)	10.0	6–12	
HVLT* (delayed)	3.6 (2.9)	3.5	0–9	7.3 (2.8)	7.0	3–12	
HVLT* (total)	11.6 (7.8)	13.0	0–23	23.3 (4.9)	23.5	13–32	
Rey Figure (delay)	10.0 (9.2)	8.5	0–30	18.2 (6.6)	17.8	7–32	
Rey Figure (immediate)	11.2 (9.0)	9.0	0–29	19.5 (6.6)	19.3	7.5–32	
Rey Figure (copy)	23.9 (11.7)	26.0	0–36	34.5 (2)	35.0	28.5–38	
Animal fluency	10.2 (7.5)	10.5	0–25	24.7 (7)	24.0	16–44	

\*HVLT, Hopkins Verbal Learning Test; \*\*RDI, recognition discrimination index

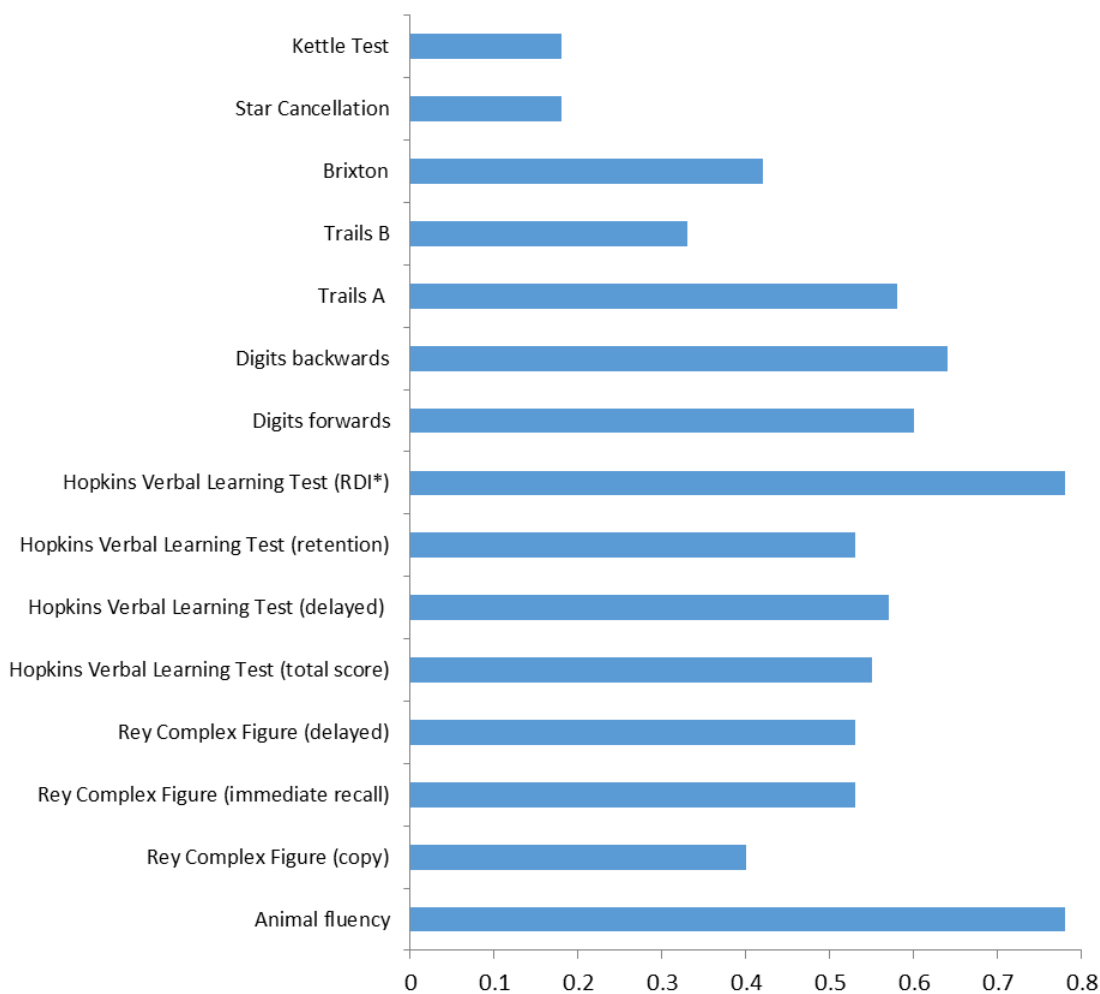
Figure 3.2 shows that all cognitive tests were significantly associated with auditory comprehension (all  $p < .01$ ) with a variance ranging from 40% to 67%, except for the Kettle Test ( $F(3,14)=.75, p = .54$ ) with a variance of 14%, and the Star Cancellation ( $F(3) = 4.9, p = .18$ ) with a variance of 24%. A multiple logistic regression was used for Star Cancellation due to a ceiling effect (refer to Table 3.2), and a pseudo  $R^2$  was reported. Animal fluency had the highest variance explained by auditory comprehension (67%), closely followed by HVLT RDI (65%) and immediate recall (63%).



\*RDI = recognition discrimination index

**Figure 3.2** Association between auditory comprehension and the cognitive tests ( $R^2$ ), with demographic factors included in the models

Figure 3.3 displays the results of the multiple linear regressions used to determine the relationship between the naming and the cognitive tests, with age and education included in the models. A multiple logistic regression was again used for the Star Cancellation Test. All cognitive tests were significantly associated with naming (all  $p < .01$ ) with a variance ranging from 33% to 78%, except for the Kettle Test ( $F(1,16) = 3.44, p = .08$ ) with a variance of 18%, and the Star Cancellation ( $F(3) = 3.8, p = .28$  with a variance of 18%). Animal fluency and the HVLRT RDI had the highest variance explained by naming (both 78%).



\*RDI, recognition discrimination index

**Figure 3.3** Association between naming and the cognitive tests ( $R^2$ ), with demographic factors included in the models

### 3.5 Discussion

Both auditory comprehension and naming performance in aphasia were significantly associated with all pen-and-paper cognitive tests, with the lone exception of Star Cancellation. The total variance explained by auditory comprehension performance differed between the cognitive tests. The cognitive tests requiring a verbal response showed more variance explained by naming compared to the non-verbal cognitive tests. We also confirmed that auditory comprehension and naming were not significantly associated with an everyday real-life measure of cognition (Kettle Test). Feasibility was an issue, with substantial missing data for the pen-and-paper cognitive tests, and missing data for the Kettle Test due to upper and lower limb hemiparesis, in aphasia. While non-linguistic cognitive impairments co-occur with aphasia (Harnish & Lundine, 2015; Lambon Ralph et al., 2010; Murray, 2012), non-verbal cognitive tests may not necessarily overcome the potential confounding influence of aphasia-related deficits. The Kettle Test shows that individuals with aphasia can undertake a real-life cognitive task without the confounding influence of language impairments.

Animal fluency and the HVLTRDI had the highest variance explained by both auditory comprehension and naming. Our animal fluency results are supported by Whiteside et al. (2016) where factor analysis was used to verify that animal fluency loaded exclusively to language, rather than executive functioning. Although executive skills may be impaired in aphasia (Fridriksson, Nettles, Davis, Morrow, & Montgomery, 2006) using the animal fluency task to determine executive skills in people with aphasia may mislead diagnoses.

The RDI component of the HVLTRDI requires a yes/no response to identify previously learned words. Eliciting a yes/no response from a person with aphasia is a suggested technique to overcome verbal barriers and facilitate communication (Stein & Brady Wagner, 2006), yet the variance was largely explained by auditory comprehension (65%) and naming (78%). These results may not be surprising given the HVLTRDI requires participants to remember linguistic targets, thus impaired language will influence recognition performance. Also, to identify a correct response, participants need to discriminate between semantically related distractors. The literature supports observed semantic deficits in both auditory comprehension and naming in aphasia (Butterworth, Howard, & McLoughlin, 1984). Thus, using semantically related distractors in a verbal

recognition task will likely be confounded in aphasia, even when the response is restricted to a yes/no response.

The total variance explained by auditory comprehension for the pen-and-paper cognitive tests without language stimuli or a verbal response (i.e., Star Cancellation, Rey Complex Figure, the Brixton), was variable (24% to 56%). This means a large amount of variance remains unexplained, which may be attributed to concomitant non-linguistic cognitive deficits. Auditory comprehension was not significantly associated with the Star Cancellation test. A weak association between neglect and language comprehension stroke is verified in the literature (Timpert, Weiss, Vossel, Dovern, & Fink, 2015), but the simplicity of the Star Cancellation's instructions, and the simplicity of the response (crossing out stars with a pen), will assist comprehension in aphasia. The Star Cancellation test was completed by all participants with aphasia and it is a reliable assessment to use post-stroke (Bailey et al., 2004) where visual spatial screening is recommended.

There was a significant association between all sub-tests of the Rey and auditory comprehension. Pyun, Yi, Hwang, Ha, and Yoo (2009) explored visuospatial skills in 23 participants with aphasia and found that the Rey copy scores were significantly correlated with the severity of the overall language performance ( $r = .654$ ,  $p < .05$ ). Visual perceptual deficits may be underestimated in aphasia. While the Rey copy is supported by simple verbal instructions, the complex copy task has been shown to involve planning and organization skills for successful completion (Schwarz, Penna, & Novack, 2009). Thus, the relationship with language performance and the Rey copy task could be partly explained by concomitant executive deficits in aphasia. The association between non-linguistic memory performance in the Rey immediate task can be compared with Lang and Quizt (2012), where 99 participants post-stroke (49 with aphasia and 50 without aphasia) were assessed using linguistic and non-linguistic memory tests. Participants with aphasia performed worse than participants without aphasia in the memory tests, even when participants had similar cerebral lesions, which the authors attributed to a common working memory impairment in aphasia.

The total variance explained by auditory comprehension for the Brixton was 53%. The aphasia group, and to a lesser degree the controls, experienced difficulty understanding the Brixton's lengthy verbal instructions. This was evidenced by the need to repeat instructions for clarity. However, as part of the Brixton assessment, direct feedback is provided for each response (e.g., participants are aware of a correct or incorrect response based on where the blue dot appears on the following sheet). This immediate visual feedback may have assisted with participants learning what is needed. Thus, executive tests that necessitate lengthy verbal instructions can incorporate non-linguistic prompts to facilitate understanding.

Fucetola et al. (2009) explored the association between auditory comprehension and non-verbal subtests of the WAIS-III and WMS-III [e.g., block design (constructional), Matrix Reasoning (reasoning by visual analogy), Picture Arrangement (sequencing), and Spatial Span (visual working memory)]. Auditory comprehension accounted for 41% of the total variance in the non-verbal cognitive tests. Naming was also significantly associated with the non-verbal cognitive tests in the present study, which contrasts with the findings of Fucetola et al. (2009). It is difficult to distinguish between a confounding language influence and a co-occurring non-linguistic cognitive impairment in cognitive tests that are not tailored for individuals with aphasia.

Auditory comprehension was not significantly associated with the Kettle Test. This everyday real-life cognitive test contains verbal instructions, but understanding is maximised by using a meaningful task with familiar everyday objects. The kitchen setting may further support understanding by incorporating a multisensory environment. Using multiple sensory modalities facilitates the ability to identify, discriminate, and recognise stimuli, and learning can be optimised (Johansson, 2012; Tinga et al., 2016). Our results demonstrate that using a familiar, real-life functional measure of cognitive performance may minimise the language skills needed to complete the task. The Kettle Test may be appropriate for individual with aphasia, but participants needed adequate motor skills to complete the task. Upper and lower limb hemiparesis was the sole reason for missing data associated with the Kettle Test. While the Kettle Test is regarded as an executive task (Hartman-Maeir et al., 2009), it may underestimate the potential association between language and cognitive skills needed for more complex community living activities. Further testing using functional cognitive performance measures in aphasia is needed.

Testing cognition in aphasia was not feasible in a number of participants, particularly those with more severe language impairments. There were no missing data for the language tests in both the aphasia and control group. Primary reasons for missing data in the pen-and-paper cognitive tests were participant refusal and an inability to understand the tasks. Chapman (2015) explored the association between semantic comprehension deficits and executive skills in aphasia and semantic dementia and reported that participants found many executive tests too difficult to understand. If an individual is unable to undertake task instructions, performance may reflect comprehension deficits rather than the target non-linguistic cognitive domain intended for testing. This may result in inaccurate information being used to guide cognitive therapy, inaccurate education given to stroke survivors and their families, and the potential for misinformed discharge planning. Missing data associated with the Kettle Test were due to upper and lower limb hemiparesis. Participants with aphasia were particularly resistant to participate in the Trail Making Test (part B). This executive task has linguistic stimuli and requires a more complex response (i.e., participants use a pen to sequentially track the alternate numbers and letters). In contrast to another executive task, the Brixton, a simple response is required (i.e., pointing to a coloured circle) and participants were more likely to attempt and complete it. It appears that feasibility of testing participants with aphasia not only relates to complexity of instructions, but it may also be influenced by the complexity of the response needed for completion.

To determine feasibility of cognitive testing, we minimised the exclusion criteria to be inclusive of participants that represent clinical practice. A limitation is that the high frequency of missing data for the cognitive tests may have biased the regression findings to exclude the association of participants with profound comprehension deficits and cognitive performance.

Assessing non-linguistic cognitive skills in aphasia is challenging, which results in people with aphasia being excluded from studies that have validated cognitive assessments in stroke (Wall et al., 2015). Using non-verbal cognitive tests may not ensure accurate results due to potentially confounding auditory comprehension impairments observed in aphasia. Difficulty understanding the tasks may also influence an individual's willingness to participate in testing, creating feasibility barriers for both clinical and



research practice. Clinical guidelines for post-stroke aphasia (Royal College Speech and Language Therapists, 2005; Simmons-Mackie et al., 2016) require further evidence of the association between linguistic and non-linguistic cognitive skills in aphasia, to warrant the inclusion of non-linguistic cognitive assessment in clinical recommendations. The Star Cancellation and the Kettle Test were the only cognitive assessments not significantly associated with auditory comprehension and naming performance in aphasia. To maximise the accuracy and feasibility of cognitive testing in aphasia, cognitive tests need to be tailored to enhance understanding of the tasks. Multidisciplinary expertise is needed to look beyond typical pen-and-paper methods and consider multisensory input for cognitive testing in aphasia.

## **Chapter 4: Using Technology to Overcome the Language Barrier: The Cognitive Assessment for Aphasia App (C3A)**

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The previous chapters outlined the barriers to assessing non-linguistic cognitive performance after stroke. Pen-and-paper tests are not feasible for many stroke survivors, and are potentially confounded by language impairments in aphasia. Individuals with post-stroke aphasia do not have access to clinimetrically sound cognitive assessments. The major undertaking of this thesis was the development and validation of a non-immersive virtual reality cognitive assessment, designed to be appropriate for stroke survivors with or without aphasia: the Cognitive Assessment for Aphasia App (C3A). The work detailed in Chapter 4 reports the development, feasibility and user acceptance of this cognitive assessment in stroke (both with and without aphasia) and controls.

The content of this chapter has been published in “Using technology to overcome the language barrier: the Cognitive Assessment for Aphasia App (C3A)” in *Disability and Rehabilitation* (Wall, Cumming, Koenig, Pelecanos & Copland, 2017; [Appendix F](#)). The content included in this chapter is identical to the submitted manuscript, but the formatting was modified to match the style of this thesis.

## 4.1 Abstract

**Purpose:** We developed and explored the feasibility and user acceptance of the Cognitive Assessment for Aphasia App: a non-immersive virtual reality cognitive assessment for stroke survivors, designed to be inclusive of individuals with aphasia.

**Methods:** Participants with stroke and controls were assessed on a battery of pen-and-paper cognitive tests and the Cognitive Assessment for Aphasia App. Feasibility was explored by quantifying missing data for test completion, determining user acceptance for the app by measuring participants' preferred testing method, enjoyment and perceived task difficulty and time-taken to complete the test.

**Results:** Sixty-four stroke participants (35 with aphasia, 29 without aphasia) and 32 controls were recruited. Only one participant with aphasia was unable to complete all the Cognitive Assessment for Aphasia App tasks, whereas 13 participants were unable to complete all pen-and-paper tasks. Only 14% of participants preferred the pen-and-paper tests, and preference did not significantly differ between groups. Ninety-five per cent of participants were neutral or enjoyed the app and 4% perceived it to be very difficult. Higher age was negatively associated with user acceptance measures.

**Conclusion:** The study shows preliminary evidence for the Cognitive Assessment for Aphasia App to be a feasible cognitive assessment for stroke survivors with and without aphasia. The app is currently being validated in stroke.

**Keywords:** virtual reality, technology, neuropsychological tests, language impairments, cognitive impairments, user acceptance

## 4.2 Introduction

Pen-and-paper tests are the most common method to assess cognition in stroke (Lees et al., 2012; Wall et al., 2015). This method has robust psychometric rigor (Lezak, Howieson, Loring, Hannay, & Fischer, 2004), but access barriers exist for specific stroke subgroups. A systematic review by Wall et al. (2015) reported that over two-thirds of studies validating cognitive assessments in stroke excluded participants based on communication and severe cognitive impairments. The eligibility criteria used in studies exploring post-stroke cognition creates a systematic research bias (Pendlebury et al., 2015), where included participants do not represent the broader stroke population (Wall et al., 2015). A study exploring the feasibility of cognitive screening tools in stroke found that only 27% of participants were able to complete the tests and 65% of participants needed direct assistance to participate (Lees et al., 2016). Post-stroke communication and motor deficits were the primary reasons impeding test completion. There is a pressing need to overcome access barriers to assessing cognitive skills for specific stroke subgroups.

Aphasia is a language disorder observed in approximately 30% of stroke survivors (Engelter et al., 2006), where individuals may experience difficulty with understanding spoken language, talking, reading and writing. Pen-and-paper cognitive tests are often dependent on language skills for completion, thus results will be confounded if individuals experience difficulty with expression or understanding instructions. Using pen-and-paper cognitive tests to assess non-linguistic cognitive performance in aphasia is often unfeasible and results may be misleading (Lees et al., 2016).

Non-linguistic cognitive impairments (i.e., executive functioning, attention, working memory) may co-occur in aphasia, which negatively impacts aphasia recovery (Harnish & Lundine, 2015; Lambon Ralph et al., 2010). Individuals with aphasia spend longer in hospital, require more rehabilitation services (Flowers et al., 2016), and experience more frequent depression and anxiety compared to other stroke survivors (Dickey et al., 2010). To optimise functional outcomes for individuals with aphasia, rehabilitation needs to extend beyond language-targeted therapy and consider all aspects of cognition. The limited availability of cognitive assessments that are tailored for aphasia constrains clinicians' ability to guide holistic cognitive rehabilitation.

Kalbe, Reinhold, Brand, Markowitsch, and Kessler (2005) validated the Aphasia Check List, which included non-verbal tasks to assess attention, memory, and abstract reasoning, in an aphasia group and a control group. Significant correlations were found between language skills and cognitive performance, but the potential influence of language impairments on cognitive performance (and vice versa) was not determined. Using non-verbal tasks to assess cognition in aphasia is essential to ensure cognitive performance is not confounded by expressive deficits. A more challenging consideration is the receptive language deficits observed in aphasia, where the instructions and stimuli of cognitive tests may influence performance. If an individual is unable to understand the tasks, results may reflect receptive language deficits rather than the target cognitive domain intended for testing. Aphasia Practice guidelines emphasise that information provided to individuals need to be in an “aphasia-friendly” format (Simmons-Mackie et al., 2016) to maximise understanding. This practice needs to be translated to cognitive assessments for individuals with aphasia.

Advances in technology may help overcome the barriers to assessing cognitive skills in aphasia. Virtual reality is an emerging technology that has been applied to cognitive assessments post-stroke using simulated real-life scenarios (Rand et al., 2007; Simona Raspelli et al., 2012; Weiss et al., 2003). The advantages of using virtual reality to assess cognition post-stroke include improved ecological validity, multisensory input and feedback to enhance learning (Johansson, 2012; Tinga et al., 2016), and the precision of computerised performance measures. Users may also draw upon intuition when undertaking familiar real-life simulated scenarios to aid understanding, thus potentially minimising the need for complex instructions to complete cognitive tasks. However, studies validating virtual reality cognitive assessments in stroke have been highly selective in their inclusion criteria (Wall et al., 2015). High functioning participants may be targeted due to the cognitive and motor skills needed to permit complex navigation skills (Rizzo & Kim, 2005). Existing virtual reality cognitive assessments are not tailored for individuals with aphasia.

In order to successfully transition the use of technology to the clinical setting, user acceptance is necessary. Existing theories for user acceptance have been integrated by a unified model – the Unified Theory of Acceptance and Use of Technology (UTAUT) (Morris, Davis, & Davis, 2003). This model proposes that technology use is influenced through intention by performance expectancy (perceived usefulness), effort expectancy

(ease of use), social influences, and facilitating conditions (e.g., matching technology with existing values, need and experience of targeted users). Past studies have identified perceived usefulness and perceived ease of use as the primary precursors for explaining older persons' intention to adopt information technology (Amma & Panicker, 2013).

Findings on the use of technology among healthy community-dwelling adults ranging from 18–91 years ( $n = 1,204$ ) demonstrated that older and less educated adults were less likely to use technology (Czaja et al., 2006). The association between age and use of technology was mediated by cognitive abilities, computer self-efficacy, and computer anxiety. Other studies on the adoption of technology confirm that technology use remains limited amongst older people, with higher education and support being associated with increased use (Heart & Kalderon, 2013). Clinical studies exploring the perceptions of people with aphasia using computers verify that support is an important factor for user satisfaction (Finch & Hill, 2014; Newton, Acres, & Bruce, 2013).

We developed a non-immersive virtual reality cognitive assessment that was tailored to be inclusive of post-stroke aphasia – the Cognitive Assessment for Aphasia App (C3A). Evaluating the clinimetric properties for cognitive assessments is necessary to determine validity, feasibility, including acceptability for users and examiners (Harrison et al., 2013). This paper will report on key feasibility factors associated with the C3A with respect to the selected hardware and design of the apparatus, time-taken to complete the C3A, missing data compared to pen-and-paper methods, and user acceptance.

We designed the C3A to be feasible for all stroke survivors, from those in the acute phase to those many years post-stroke living in the community. This paper will describe the cognitive tasks and the “aphasia-friendly” techniques that we applied to create the C3A. We explored the feasibility of the C3A in stroke survivors with aphasia, stroke survivors without aphasia, and controls in acute, rehabilitation, and community settings by comparing assessment completion time and proportion of missing data between the C3A and a battery of pen-and-paper cognitive tests. Other aspects of feasibility explored were user acceptance by determining the participants' preferred assessment method

(C3A vs. pen-and-paper), participants' self-reported enjoyment, and their perceived level of task difficulty of the C3A. The relationship between demographic variables (i.e., age, education, frequency of smartphone or tablet use, and computer use) and the ratings for user acceptance were examined.

## **4.2 Methods**

### **4.2.1 Planning Phase**

Co-design principles formed the basis for developing the cognitive assessment. This approach encourages input from key stakeholders and considers their varying perspectives equally during the development process (Craven, De Filippis, & Dening, 2014; Yan, Wu, Shao, & An, 2014). Key stakeholders included an interdisciplinary clinical and research team, which included stroke survivors, speech pathologists, neuropsychologists, occupational therapists, medical staff, nurses, and a human interface technology engineer. The purpose of the cognitive assessment was pre-determined, but the design of the tasks was iteratively adjusted through stakeholder input and trialling of tasks with stroke survivors.

The cognitive domains we targeted were attention, visual memory, executive functioning and visuoperceptual skills. Deficits in these cognitive domains often co-occur with aphasia, and influence aphasia recovery (Harnish & Lundine, 2015; Lambon Ralph et al., 2010; Murray, 2012). Neglect is not considered a common impairment in aphasia (Timpert et al., 2015), but we included a visuoperceptual task to identify impairments that may influence performance on other visual tasks in the assessment. Computerised visual search tasks also offer additional information on performance, including search patterns and response latency (Dalmaijer, Van der Stigchel, Nijboer, Cornelissen, & Husain, 2015).

### **4.2.2 Apparatus**

The C3A was designed to run on an Android Samsung Galaxy NotePro (12.2 in.) tablet. Unity game engine (version 4.6) was used to develop the application. During testing, anonymous data were saved to the cloud storage service Parse. The option for offline data

storage was available if an internet connection was unavailable. All user responses were saved, including redundant or random screen taps. Time stamps were saved with each user interaction.

The non-immersive virtual reality system, a tablet, was selected based on reduced costs and easier portability compared to immersive virtual reality systems. Discomfort with head-mounted displays, and difficulty using a mouse and joysticks in virtual reality are potential issues for users with stroke (Kang et al., 2008). Nausea is another potential barrier to employing an immersive virtual reality system in clinical practice (Viirre & Ellisman, 2003). Using a touch screen was considered easier for navigation and feasible for non-dominant hand use. Vision and dexterity decline in older people (Martin, Ramsay, Hughes, Peters, & Edwards, 2015; Muskens, Van Lent, Vijfvinkel, Van Cann, & Shahid, 2014) and upper-limb hemiparesis may constrain users to their non-dominant upper limb to complete tasks. A larger tablet size (12 in.) was selected to permit a larger visual display to make it easier to see and minimise dexterity errors.

#### **4.2.3 Outline of the C3A**

The C3A is divided into four distinct tasks: (1) simple reaction time task to assess psychomotor speed, (2) visual search task to assess neglect and attention, (3) sequence copy tasks to assess visual memory, and (4) kitchen task to assess executive functioning. Details of the individual tasks are described below.

The aims of the first three tasks were to capture domain specific measures, to acquaint the users with the tablet and to familiarise them with navigation. The fourth task was an interactive kitchen task, where participants demonstrated their learnt navigation skills to make a cup of tea and place a dessert on a plate. Measures to evaluate cognitive performance included commission and omission errors, sequencing errors and latency times.

Individuals with aphasia display varying abilities across language modalities. We capitalised on the computerised technology to ensure the instructions and tasks considered potential linguistic strengths and weaknesses in those with aphasia. A standardised script was developed to maintain scientific rigour, which included short,



simple verbal explanations. Understanding of tasks was further supported by a computerised visual demonstration and the users had practice opportunities prior to testing. A variety of auditory and visual feedback techniques were employed for each task to facilitate learning. Specifically, the sequence and kitchen tasks included simulated real-life multisensory inputs (e.g., participants heard and viewed the steam when the kettle was boiling, as well heard a “click” sound when an object was selected). If the participants were unable to understand the task within three practice trials, further testing would cease. Details of the individual tasks and the multisensory feedback are described below.

#### **4.2.4 Cognitive Tasks**

4.2.4.1 Simple Reaction Time Task. Reaction time tasks are used to assess processing speed (Gerritsen, Berg, Deelman, Visser-Keizer, & Jong, 2003) and attentional impairments in stroke survivors (Cumming et al., 2012). These very simple tasks may provide clinically meaningful information alone, but the purpose of this task in the current assessment was to familiarise users with a touch screen and reduce anxiety for individuals without tablet and/or computer experience (C. Lee & Coughlin, 2015).

Participants were instructed to touch the target stimulus in the centre of the screen – a milk carton – as quick as possible. A successful touch was reinforced by a “click” sound followed by the milk carton disappearing from the screen. If the milk carton was untouched, it remained on the screen for 12s before continuing to the next screen. Inter-stimulus interval rates varied between 1.03s and 3.70s. Intervals were identical for each participant. Five intervals were consecutively displayed for practice, followed by 15 trials for the actual task.

4.2.4.2 Visual Search Task. Visuoperceptual deficits are often related to visual memory deficits in stroke (Nys, Van Zandvoort, De Kort, Jansen, Van Der Worp, et al., 2005). This domain specific task was included to detect visuoperceptual impairments, which may influence performance on the remaining visual memory and executive functioning tasks. This will assist with differential diagnosis of cognitive impairments to guide appropriate therapy.

This task consisted of a four by four (16 item) grid containing four target items – milk cartons – with three semantically and visually related distractors (see [Figure 4.1](#)). The

target stimulus was consistent with the previous reaction time task to avoid added instructions and confusion.

Participants were instructed to touch all the milk cartons using one finger. Auditory and visual feedback to signal a correct response was consistent with the reaction time task. If a distractor item was touched (commission error), the item would remain on the screen without auditory feedback. If participants were unable to identify all the milk cartons within 12s (omission errors), a new grid would appear on the screen. Inter-stimulus interval rates varied between 1.42s and 3.19s. Intervals were identical for each participant. Five grids were consecutively displayed for practice, followed by 10 grids for testing.



**Figure 4.1** Visual search task

4.2.4.3 Sequence Copy Task. Visual working memory is central for sustaining attained information across saccades and other visual disruptions, to compare visual objects and scenarios, and to navigate the virtual and real world (Blacker, Curby, Klobusicky, & Chein, 2014). We assessed visual working memory using functional visual

sequences (i.e., open fridge door, get the milk out, close fridge door, finish sequence button) in an interactive 3D kitchen setting (see [Figure 4.2](#)).

Participants viewed a functional sequence, then they were asked to copy the sequence exactly how they viewed it. Participants were asked to complete as much of the sequence as they could remember. Up to three practice trials were offered using the same sequence. This was followed by five discrete sequences for testing, where complexity was increased by the number of steps needed to complete the sequence. The task instructions unavoidably required lengthier verbal explanation. If the participant was unable to exhibit understanding of the first practice trial, the examiner provided a visual demonstration. The participant was required to attempt the final practice independently to continue testing.



**Figure 4.2** Sequence copy task

The sequences are functional tasks, which we predicted would create an intuitive element to aid memory recall. To ensure users were not fully reliant on intuition, distractor items were incorporated (e.g., target item was a red mug; two mugs in different colours were included as distractors).

The sequential copy task was also included to teach users how to navigate the simulated kitchen. For example, participants copied “filling the kettle”, “turning the kettle on” and

“pouring the water into a mug”. More complex navigation skills were included multiple times across the five tested sequences to enhance learning.

4.2.4.4 Kitchen Task. The final task was designed to assess executive functioning, where users applied their learnt navigation skills to independently make a cup of tea with milk and put a dessert on a plate (see [Figure 4.3](#)). This task requires planning, sequencing and problem-solving skills for completion. Other kitchen tasks, such as the Therapeutic Virtual Kitchen, have been used to rehabilitate executive functioning in acquired brain injury (Fuchs, 2009). To augment the verbal instructions, a picture of the finished items was displayed on the screen and further supported by a written description of the items. Given that elements of the tea-making task were replicated from the previous sequencing task, we incorporated the “dessert on the plate” to ensure participants were required to problem solve how to apply their navigation skills in previously unseen kitchen items and functions.

Scoring of sequence errors differed in the kitchen task compared to the previous sequence copy task. Participants were not required to replicate previously seen sequences, but they needed to complete the task in an order that would be logical and safe in real-life. For example, to obtain a sequence error in the kitchen task a participant might stir an empty mug with the teaspoon; then put the tea and hot water in the mug. If the participant selected an item that was unrelated to the kitchen task, such as a random background selection, this was scored as a commission error. If the participant missed an item related to the task (e.g., they did not put the milk in the tea), this was scored as an omission error.



**Figure 4.3** Kitchen task

#### **4.2.6 Participants**

Post-stroke participants and controls were recruited from three Brisbane Hospitals, The Communication Registry at The University of Queensland, community posters, social groups and newsletters from February 2015 to October 2015. Stroke survivors without aphasia were sourced from inpatient hospital settings, whereas stroke survivors with aphasia were also sourced from the community to increase the aphasia sample size. Stroke was confirmed with brain imaging or with a clinical diagnosis if imaging was unavailable. Aphasia was diagnosed according to The Comprehensive Aphasia Test (CAT; Swinburn et al., 2005) (score > 1.5 SD below the mean). Individuals with stroke were excluded if they: (1) had visual and hearing impairments that impeded testing, (2) needed an interpreter to participate, (3) were too medically unwell, or (4) had bilateral upper limb issues that precluded tablet use. Controls were excluded if they: (1) had a history of neurological disease or acquired injury, (2) needed an interpreter to participate, (3) had visual and hearing impairments that impeded testing, (4) had bilateral upper limb issues that precluded tablet use, or (5) failed a mood (The Patient Health Questionnaire; Kroenke et al., 2001) so depression would not confound cognitive performance (Thomas & O'Brien, 2008; S. Wang & Blazer, 2015).

Ethical clearance was obtained through local Human Research Ethics Committees in Brisbane, Australia. Written consent was obtained from all participants, or from a carer or family member of individuals with cognitive deficits that precluded informed consent.

#### **4.2.7 Assessments**

Demographic and descriptive measures were collected included age, sex, education, handedness, time post-stroke, and clinical setting. Missing data were also recorded. Either smartphone or tablet, and computer experience, was ascertained using a questionnaire based on frequency of use. Due to polarity in results, the ratings were collapsed into two categories (rarely used and frequently used) for analysis. If participants were unable to self-report prior experience, information was sourced from a carer or family member. Descriptive details regarding the kind of computer uses would have been interesting, but extending testing time and increasing the complexity of the questionnaire were beyond the scope of this study.

All participants attempted the C3A prior to the pen-and-paper cognitive tests. Immediately following completion of the C3A, participants' task enjoyment and perceived level of difficulty were explored using five-point Likert scales. Administering the C3A and completing the Likert scales before the pen-and-paper tests controlled for the potential confusion and confounding influences of the pen-and-paper cognitive tests on responses. The C3A enjoyment and perceived difficulty were not compared to pen-and-paper testing methods.

Left hemisphere participants with stroke were screened for aphasia using the Language Assessment Screening Test (Flamand-Roze et al., 2011) and those who failed undertook the CAT (Swinburn et al., 2005) (auditory comprehension total score) to determine a diagnosis and severity of aphasia. The 15-item abbreviated Boston Naming Test (Kent & Luszcz, 2002) was also used to determine aphasia severity, and all participants completed both the Boston Naming Test and an animal fluency test (Rosen, 1980).

The pen-and-paper neuropsychological tests we selected were recommended and validated in stroke (Hachinski et al., 2006). To develop a uniform practices for vascular cognitive impairment, the National Institute for Neurological Disorders and Stroke (NINDS) and the Canadian Stroke Network (CSN) assembled research expertise in clinical diagnosis, epidemiology, neuropsychology, brain imaging, neuropathology, experimental models, biomarkers, genetics, and clinical trials to recommend minimum, common, clinical and research standards for the description and study of vascular cognitive impairment (Hachinski et al., 2006). Our tests were selected based on these recommendations. We also included the Brixton Spatial Anticipation Test (Burgess, 1997) as this was a non-verbal executive function measure to consider participants with aphasia.

The cognitive tests were: Star Cancellation (Bailey et al., 2004) to assess visual neglect, Brixton Spatial Anticipation Test (Burgess, 1997) to assess executive function; Trail Making Test (Reitan & Wolfson, 1985) to assess attention and executive function; Digit Span Test (Wechsler, 1997) to assess attention, working memory, and executive function; Hopkins Verbal Learning Test-Revised (Brandt, 2001) to assess verbal memory; and Rey-Osterrieth Complex Figure (Osterrieth, 1944) to assess visuospatial skills, visual memory, and executive skills. A rest period was provided for all participants between completing the C3A and commencing the cognitive tests and additional rest periods were offered upon participant request or examiner's observations to control for fatigue. The pen-and-paper battery was administered in a fix order. All testing aimed to be completed within a day, but four participants completed testing within two consecutive days due to clinical scheduling.

To determine user preference of testing method, participants were asked "Did you prefer to have your thinking assessed using the C3A, the pen-and-paper methods or no preference?" The C3A and paper-and-paper tests were displayed during questioning to support clarity of the question. Participants completed the C3A in approximately 20 minutes, then the preference questionnaire was asked following 20 minutes of pen-and-paper testing to eliminate testing time bias. User preference was ascertained in a single session for all participants.

Reporting missing data was another feasibility comparison between the C3A and the pen-and-paper assessments.

#### 4.2.8 Statistical analysis

To compare the feasibility of the C3A with the pen-and-paper tests we documented the frequency of missing data and reported associated reasons.

Frequencies (percent), means (standard deviation [SD]) or medians (interquartile range [IQR]) were used to describe participant characteristics, time-taken, and measured outcomes. Differences in user preference between participant groups (aphasia, stroke non-aphasia, control) were explored using a Kruskal-Wallis test. For each participant group, we used the nonparametric trend test (Cuzick, 1985) to examine trends between user preferences and age, education, smartphone or tablet use and computer use. Tests were declared statistically significant at  $\alpha < .05$  (two-sided).

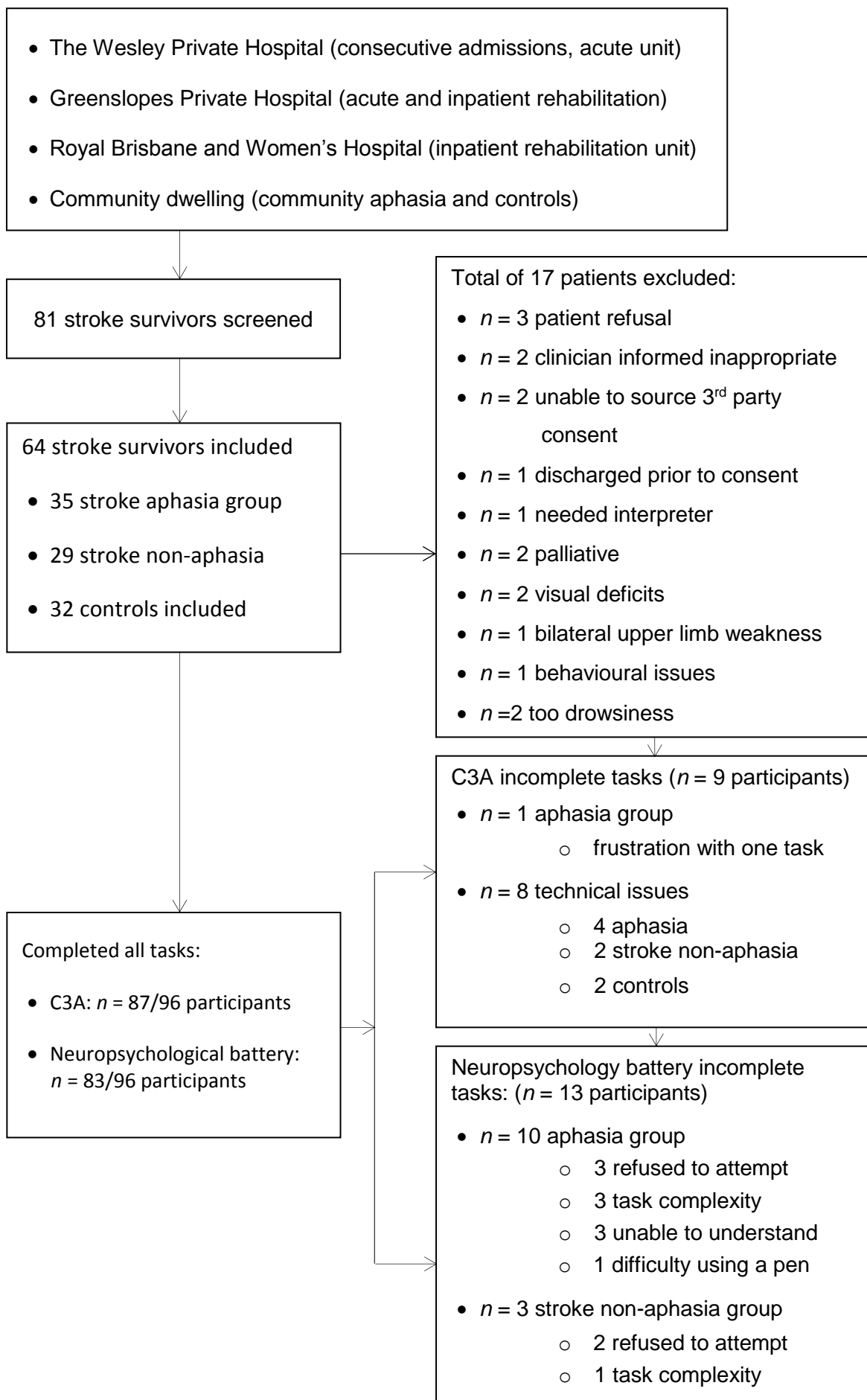
General linear models were used to determine if demographic variables were associated with participants' enjoyment and perceived task difficulty for the C3A, with adjustment for participant group. The base model consisted of participant group where demographic variables were sequentially added using forward selection. Demographics with a  $p$ -value less than .05 were retained in the model.

All analyses were performed using Stata 14.0 (StataCorp, 2015).

### 4.3 Results

During the 31-week recruitment period, 113 participants were screened against the eligibility criteria. A total of 96 participants were included (35 aphasia, 29 stroke non-aphasia, 32 controls). [Figure 4.4](#) displays the recruitment and feasibility data, with reasons for excluding patients and missing data. [Table 4.1](#) details the included participant characteristics by group.





**Figure 4.4** Recruitment and feasibility data

**Table 4.1** Included participant characteristics

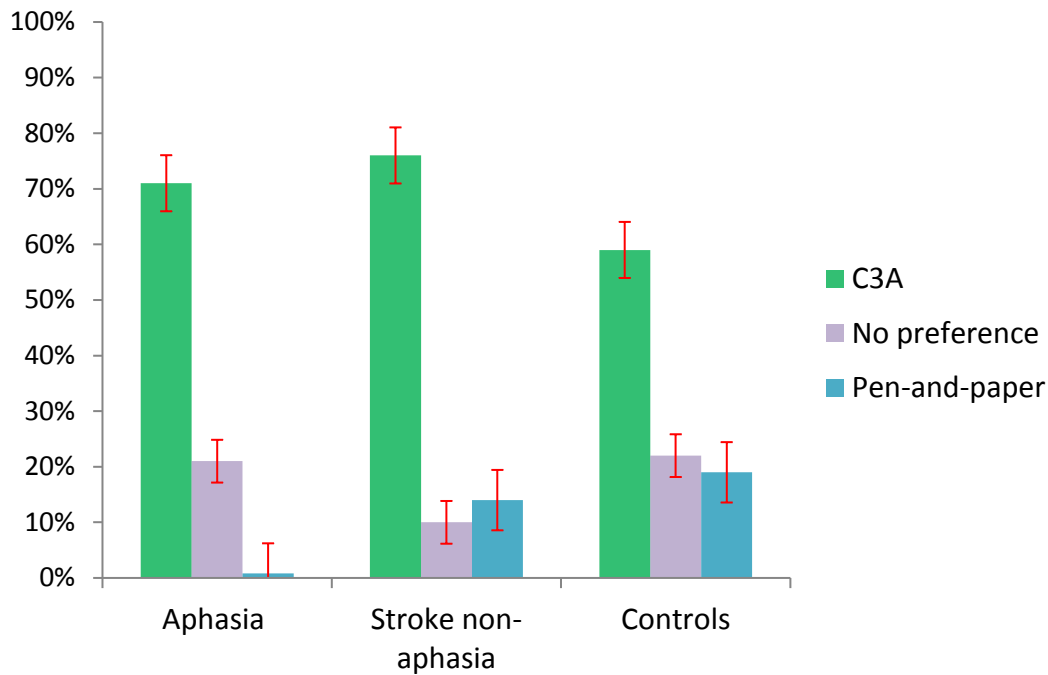
<b>Variable</b>	<b>Aphasia (<i>n</i> = 35)</b>	<b>Stroke non- aphasia (<i>n</i> = 29)</b>	<b>Controls (<i>n</i> = 32)</b>
Age in years, mean (SD)	69.8 (8.9)	69.5 (13.0)	67.4 (12.3)
Sex, <i>n</i> (%)			
Female	11 (31.4)	9 (31.0)	17 (53.1)
Male	24 (68.6)	20 (69.0)	15 (46.9)
Education in years, mean (SD)	10.8 (3.1)	11.8 (3.5)	15.1 (3.4)
Handedness, <i>n</i> (%)			
Right	31 (88.6)	27 (93.1)	29 (90.6)
Left	3 (8.6)	2 (6.9)	3 (9.4)
Ambidextrous	1 (2.9)	0	0
Pre-morbid neurological disease/injury <i>n</i> (%)	2 (5.7)	8 (27.6)	N/A
Time post-stroke, <i>n</i> (median, IQR*) by clinical setting			
Acute setting (days)	11 (5.0, 2.0–13)	17 (4.0, 2.0–5.0)	N/A
Inpatient rehabilitation (days)	2 (23.5, 12–35)	12 (26.5, 14.0–52.0)	N/A
Community dwelling (years)	22 (4.5, 2.9–11.3)	N/A	N/A
Uses a smartphone or tablet, <i>n</i> (%)	23 (65.7)	20 (70.0)	27 (84.4)
Uses a computer, <i>n</i> (%)	22 (62.9)	16 (55.2)	30 (93.8)

N/A: not applicable; \*IQR, interquartile range

The severity of the participants with aphasia ranged from very severe to mild language deficits. Total scores for auditory comprehension in the aphasia group ranged from 5/66 to 63/66 (median = 53, interquartile range = 29–58) as measured by the CAT. The results from the Boston Naming Test ranged from 0/15 to 15/15 (median = 10, interquartile range = 1–12). Only one participant with aphasia was unable to complete all C3A tasks (they missed one out of five trials in the visual memory task), whereas 13 participants were unable to complete all tasks in the neuropsychological battery. Eight participants had missing data for elements of the C3A due to technical difficulties with saving data on the Android tablet. In the battery, the Trail Making Test part B had the highest frequency of missing data ( $n = 9$ ), followed by the Brixton ( $n = 5$ ), the Rey immediate recall ( $n = 4$ ) and the Rey delayed recall ( $n = 4$ ). Other missing data included the Trail Making Test part A ( $n = 2$ ), Hopkins Verbal Learning Test ( $n = 2$  recall,  $n = 2$  delayed recall,  $n = 2$  retention, and  $n = 2$  recognition discrimination index, and Digit Span test ( $n = 3$ ). Participants with missing data had more severe auditory comprehension deficits (median = 27.5, interquartile range = 25.0–49.0) and more severe naming deficits (median = 1, interquartile range = 0–7.5), compared to participants without missing data (auditory comprehension median = 53, interquartile range = 45.8–58.0, naming median = 10.5, interquartile range = 6.5–13.5).

The overall time-taken to administer the C3A was approximately 20 minutes. The median time participants spent touching the screen to complete tasks was 5.8 minutes (interquartile range = 4.6–7.0), with a median time of 6.4 (interquartile range = 5.2–7.6), 6.0 (interquartile range = 4.5–7.6) and 5.1 minutes (interquartile range = 4.5–5.9) in the aphasia, stroke non-aphasia and control groups respectively. Time spent touching the screen significantly differed between participant groups ( $p = .024$ ).

Only 13 of 95 participants (14%) preferred pen-and-paper cognitive tests over the C3A. One participant with aphasia was unable to provide an answer due to difficulty understanding the question. The frequency for participants preferring the C3A was much higher across all participant groups (see [Figure 5.1](#)). There was no statistical difference in participant preferences between the aphasia, stroke non-aphasia and control groups ( $p = .38$ ) with 71%, 76% and 59% preferring C3A respectively.



**Figure 5.1** Participants preferred testing method with standard error bars

There was a significant participant preference for the C3A with decreasing age ( $p = .001$ ). When comparing this analysis by the participant groups, the association with age was shown in the stroke non-aphasia group ( $p = .044$ ) and control group ( $p = .047$ ). There was no significant user preference with education and smartphone or tablet use in the individual groups, but there was a significant participant preference for the C3A in those who frequently used a computer in the stroke non-aphasia group ( $p = .011$ ). [Table 4.2](#) details the demographic relationships to participant preferences for each participant group.

**Table 4.2** Demographic relationship to participant preference for assessment method for participant groups

<b>Variable</b>	<b>C3A <i>n</i> (%)</b>	<b>No preference <i>n</i> (%)</b>	<b>Pen-and- paper <i>n</i> (%)</b>	<b><i>p</i>- value</b>
<b>Aphasia Group</b>				
Age <60 years	5 (100.0)	0 (0)	0 (0)	.09
60–79 years	18 (66.8)	7 (25.9)	2 (7.4)	
80+ years	1 (50.0)	0 (0)	1 (50.0)	
Education				.51
<12 years	16 (66.8)	6 (25.0)	2 (8.3)	
12+ years	8 (80.0)	1 (10.0)	1 (10.0)	
Smartphone use				.59
Rarely	10 (66.8)	3 (20.0)	2 (13.3)	
Often	14 (73.7)	4 (21.1)	1 (5.3)	
Computer use				.31
Rarely	7 (58.3)	4 (33.3)	1 (8.3)	
Often	17 (77.3)	3 (13.6)	2 (9.1)	
<b>Stroke non-aphasia</b>				
Age <60 years	6 (100.0)	0 (0)	0 (0)	.044
60–79 years	13 (76.5)	2 (11.8)	2 (11.8)	
80+ years	3 (50.0)	1 (16.8)	2 (33.3)	
Education				.32
<12 years	11 (68.8)	2 (12.5)	3 (18.8)	
12+ years	11 (84.6)	1 (7.7)	1 (7.7)	
Smartphone use				.43
Rarely	11 (68.8)	3 (18.8)	2 (12.5)	
Often	11 (84.6)	0 (0)	2 (15.4)	
Computer use				.011
Rarely	7 (53.9)	2 (15.4)	4 (30.8)	
Often	15 (93.8)	1 (6.3)	0 (0)	
<b>Controls</b>				
Age <60 years	6 (75.0)	2 (25.0)	0 (0)	.047
60–79 years	12 (63.2)	3 (15.8)	4 (21.1)	
80+ years	1 (20.0)	2 (40.0)	2 (40.0)	
Education				.25
<12 years	4 (80.0)	1 (20.0)	0 (0)	
12+ years	15 (55.6)	6 (22.2)	6 (22.2)	
Smartphone use				.75
Rarely	5 (62.5)	2 (25.0)	1 (12.5)	
Often	14 (58.3)	5 (20.8)	5 (20.8)	
Computer use				1.00
Rarely	1 (50.0)	1 (50.0)	0 (0.0)	
Often	18 (60.0)	6 (20.0)	6 (20.0)	

Two participants had missing data for the enjoyment and task difficulty results. One participant with aphasia was unable to respond due to difficulty understanding the questions, and there was a technical issue with the computerised recording for a control participant. Eighty nine of 94 participants (95%) were neutral or enjoyed the C3A, with Likert scores of three and above. Only four of 94 participants (4%) perceived the C3A to be very difficult and 11 (12%) perceived the C3A to be very easy. [Table 4.3](#) details the frequencies of enjoyment and difficulty by participant groups.

[Table 4.4](#) shows the final multivariable models for enjoyment and perceived task difficulty. Enjoyment did not significantly differ between groups. The only significant demographic variable associated with enjoyment was age ( $p = .004$ ) when adjusted for participant groups. Age was also the sole variable significantly associated with perceived task difficulty ( $p = .020$ ) when adjusted for participant groups.

**Table 4.3** Self-reported enjoyment and perceived task difficulty with the C3A

<b>How much did you enjoy the task?</b>					
	<b>Dislike very much (1)</b>	<b>(2)</b>	<b>Neutral (3)</b>	<b>(4)</b>	<b>Like very much (5)</b>
Aphasia, <i>n</i> (%)	0 (0)	1 (2.9)	5 (14.7)	15 (44.1)	13 (38.2)
Stroke non-aphasia, <i>n</i> (%)	1 (3.4)	2 (6.9)	7 (24.1)	7 (24.1)	12 (41.4)
Controls, <i>n</i> (%)	0 (0)	1 (3.2)	4 (12.9)	6 (19.4)	20 (64.5)
<b>TOTAL, <i>N</i> (%)</b>	<b>1 (1.1)</b>	<b>4 (4.3)</b>	<b>16 (17.0)</b>	<b>28 (29.8)</b>	<b>45 (47.9)</b>

<b>How difficult was the task?</b>					
	<b>Very difficult (1)</b>	<b>(2)</b>	<b>Neutral (3)</b>	<b>(4)</b>	<b>Easy (5)</b>
Aphasia, <i>n</i> (%)	2 (5.9)	10 (29.4)	11 (32.4)	9 (26.5)	2 (5.9)
Stroke non-aphasia, <i>n</i> (%)	2 (6.9)	3 (10.3)	13 (44.8)	6 (20.7)	5 (17.2)
Controls, <i>n</i> (%)	0 (0)	6 (19.4)	12 (38.7)	9 (29.0)	4 (12.9)
<b>TOTAL, <i>N</i> (%)</b>	<b>4 (4.3)</b>	<b>19 (20.2)</b>	<b>36 (38.3)</b>	<b>24 (25.5)</b>	<b>11 (11.7)</b>

**Table 4.4** Predictor variables' estimated marginal means for enjoyment and perceived difficulty of the C3A

<b>Multivariable model</b>	<b>Enjoyment</b>		<b>Perceived difficulty</b>	
	<b>Marginal mean (95% CI)</b>	<b><i>p</i>-value</b>	<b>Marginal mean (95% CI)</b>	<b><i>p</i>-value</b>
Groups		.10		.38
Aphasia	4.2 (3.9–4.5)		3.0 (2.7–3.4)	
Non-aphasia	4.0 (3.6–4.3)		3.3 (2.9–3.7)	
Controls	4.4 (4.1–4.8)		3.3 (3.0–3.7)	
Age		.004		.020
< 60 years	4.8 (4.4–5.2)		3.8 (3.3–4.3)	
60-79 years	4.1 (3.9–4.4)		3.1 (2.8–3.3)	
80+ years	3.7 (3.2–4.2)		3.1 (2.8–3.3)	

Enjoyment model  $R^2_{adj} = .12$ , perceived difficulty model  $R^2_{adj} = .07$

### 4.3 Discussion

We demonstrated that using non-immersive virtual reality technology can be tailored to overcome feasibility barriers when assessing cognition in post-stroke aphasia. The C3A was completed within 20 minutes, permitting a practicable assessment to administer throughout the continuum of stroke recovery. Only one participant with aphasia was unable to complete all aspects of the C3A, which indicates that the C3A may be more feasible than the pen-and-paper cognitive tests. Positive user acceptance was evidenced by the majority of participants enjoying and preferring the C3A compared to pen-and-paper cognitive tests.

Our minimal exclusion criteria, and consenting procedures that involved family or carers, were designed to be inclusive of stroke subgroups typically excluded from studies exploring cognition post-stroke. The C3A employs “aphasia-friendly” tasks and instructions (e.g., short, simple phrases, use of graphics rather than language) (Rose, Worrall, Hickson, & Hoffmann, 2011), and capitalises on computerised multisensory input (i.e., immediate auditory and visual feedback and a real-life simulated setting), to maximise learning and understanding of the tasks (Johansson, 2012; Tinga et al., 2016). We also included practice opportunities to further understanding and reduce potential anxiety associated with technology use for older people (C. Lee & Coughlin, 2015). The assessment was designed to be undertaken with an examiner present, which aligns with the needs of older people (Heart & Kalderon, 2013), and is desired by individuals with aphasia (Finch & Hill, 2014; Newton et al., 2013). Examiner support, task instructions, stimuli and response methods all need consideration to maximise feasibility and user satisfaction for individuals with aphasia.

The benefits of using simulated real-life scenarios, and the precision and accuracy of computerised tasks have major advantages over traditional neuropsychology testing methods (Parsons & Rizzo, 2008). Unlike neuropsychological testing, missing data associated with technical difficulties in the C3A needs resolution. Missing data due to technical difficulties is consistent with other studies using computerised measures of cognitive performance (Buxbaum et al., 2012; Cumming et al., 2012; Hansen, Haferstrom, Brunner, Lehn, & Håberg, 2015). While the frequency of missing data associated with technical difficulties is infrequent compared to participant related missing data, comprehensive feasibility testing is needed to solve any technical issues prior to clinical



use. The reliability of technology is essential to foster acceptance and trust amongst users (Montague, Winchester, & Kleiner, 2010).

User acceptance measures (preferred assessment method, enjoyment and perceived task difficulty) for the C3A were negatively associated with increasing age. Previous research confirms the association between age and user acceptance in older people (Czaja et al., 2006; Heart & Kalderon, 2013). The stroke non-aphasia group was the only group where frequent computer use was significantly associated with preferring the C3A. Smartphone or tablet use and education were not significantly associated with any user acceptance measures.

Newton et al. (2013) investigated preferences between traditional pen-and-paper language assessments and a computerised version of the assessments (with and without support by a clinician) in individuals with aphasia ( $n = 15$ ). Most participants preferred pen-and-paper testing methods and the computer-only method was least preferred. Participants rated their ease of responses much higher (easier) for the pen-and-paper method compared to the computer method, even though the same instructions and responses were required. This study used language tests as opposed to cognitive tests in aphasia. Language tests are designed for individuals with language deficits, thus our positive results for the C3A may reflect the incompatibility when using pen-and-paper cognitive tests in individuals with aphasia. It should also be noted that the pen-and-paper tests were administered following the C3A, thereby fatigue influencing participant preferences. However, controlling for fatigue was minimised by providing a rest period after completing the C3A and the preference questionnaire was administered following the same amount of testing time it took to complete the C3A. Also, 33 out of 34 participants with aphasia scored three and above on the Likert scale for enjoyment, confirming positive user satisfaction with the C3A. Positive ratings for enjoyment were consistent across all participant groups. Positive virtual reality user experience to assess cognition in stroke has been previously demonstrated, where 90% ( $n = 12$ ) of the participants reported a desire to experience other simulated scenarios (Kang et al., 2008).

Twenty-four percent of participants rated their perceived difficulty as one and two on the Likert scale. While ease of use is recommended for the successful adoption of technology in older people (Heart & Kalderon, 2013; Ogata, Ueda, Suto, Kumada, & Ifukube, 2012), the C3A was designed to detect cognitive impairments. Varying levels of

task complexity were needed to avoid floor and ceiling effects. We aimed to design tasks that are feasible to complete in individuals with severe cognitive impairments, as well as incorporating complex elements to detect mild cognitive impairments. Much attention was paid to familiarising participants with the tablet, training for navigation and examiner support to facilitate ease of tablet use, while creating variability in complexity in the cognitive tasks for assessment purposes.

A disadvantage of using a non-immersive virtual reality application is that the users were not fully immersed in the real-life task to permit strong verisimilitude validity. Verisimilitude is a form of ecological validity that refers to the similarity between the stimuli and cognitive processing in the simulated task and the stimuli and cognitive processing in real life (Franzen & Wilhelm, 1996). We aimed to establish veridicality ecological validity, where the creation of an everyday cognitive task permits inferences between performance on the simulated task and an individual's likely ability to perform tasks in daily life (Franzen & Wilhelm, 1996).

It should be acknowledged that the frequency of missing data associated with pen-and-paper tests compared to the C3A may be influenced by the fixed order and higher number of pen-and-paper tests administered, creating more potential for missing data and fatigue. Resting periods were provided to minimise the influence of fatigue. The highest frequency of missing data was associated with the executive tasks from the Trail Making Test part B and the Brixton. The frequency of missing data associated with these tests may be better explained by the complexity of the task construct and the difficulty participants may experience when understanding what is required. Also, participant preferences may have been influenced by the differing level of difficulty between the tests. Another potential confounding factor is the number and fixed order of pen-and-paper tests that were completed within the 20-minute period, rather than having the opportunity to complete all the pen-and-paper tests. However, controlling for time-taken to complete testing and fatigue were considered a priority over completing all tests when aiming to minimise confounding factors. Another limitation is the small sample size within each participant group, possibly leading to type II errors. It should be noted that these results are exploratory and further studies are needed to strengthen the evidence base in this area.

User acceptance of technology in older people is likely to change as younger people age (Fazeli, Ross, Vance, & Ball, 2013). Nevertheless, the current stroke population requires innovative approaches to permit the inclusion of aphasia in both research and clinical practice when exploring cognition. The simplicity of using a tablet, employing techniques to optimize understanding and applying meaningful simulated scenarios to assess cognition in stroke was feasible, and preferred, over pen-and-paper testing methods. Validating the C3A in the stroke population has commenced. Future research should explore clinicians' user acceptance and investigate the differing clinical demands and resource implications of this assessment in varying clinical settings.

## **Chapter 5: Validating a Non-Immersive Virtual Reality**

### **Cognitive Assessment in Stroke:**

#### **The Cognitive Assessment for Aphasia App (C3A)**

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Findings from the previous chapter indicated that the C3A was not only more feasible than standard pen-and-paper tests; it was also the preferred mode of assessment in all three groups (stroke survivors with and without aphasia, controls). The next step was to determine the validity of the C3A in the target population.

Chapter 5 reports validation results of the C3A in stroke and controls. First, we established if C3A performance could differentiate between individuals with post-stroke aphasia, post-stroke non-aphasia and controls. Second, construct validity was determined by comparing the C3A with non-verbal pen-and-paper tests (in the absence of a criterion standard non-immersive virtual reality cognitive assessment) in stroke survivors with and without aphasia. Third, ecological validity was investigated by comparing C3A performance with a functional cognition measure (FIM-cog) in stroke survivors with and without aphasia. We examined the influence of demographic variables on C3A performance, and adjusted for these in statistical analyses where necessary.

## 5.1 Abstract

**Background:** Pen-and-paper cognitive tests often rely on language skills for completion, creating barriers for individuals with aphasia. We developed the Cognitive Assessment for Aphasia App (C3A) – a non-immersive virtual reality cognitive assessment designed to be inclusive of individuals with post-stroke aphasia.

**Aims:** To: (1) determine if the C3A can differentiate between stroke participants, with and without aphasia, and controls, (2) investigate construct validity by comparing the C3A with neuropsychological tests, (3) determine ecological validity by comparing the C3A with a functional cognitive outcome measure.

**Methods:** Participants with stroke were recruited from the acute, rehabilitation and community settings. Performance on the C3A was compared between groups and was examined in relation to performance on pen-and-paper tests validated in stroke and the Functional Independence Measure – cognition (FIM-cog).

**Results:** Sixty-four participants with stroke (35 with aphasia, 29 without aphasia) and 32 controls were recruited. C3A performance significantly differed between participants with stroke and the controls, but not between the aphasia and the stroke non-aphasia group. Number of errors made on the C3A kitchen task was closely associated with performance on pen-and-paper tests and had strong correlations with the FIM-cog in both the aphasia ( $r = .84, p = .001$ ) and stroke non-aphasia ( $r = .79, p = .001$ ) groups.

**Conclusion** C3A performance differed between stroke and control participants, while not disadvantaging those with aphasia. Associations with standard pen-and-paper tests and with the FIM-cog demonstrate good construct and ecological validity.

## 5.2 Introduction

Up to 70% of stroke survivors experience cognitive impairment (Lindén et al., 2004), which negatively impacts activities of daily living (Kihun & Wanhee, 2012), quality of life (Grenthe Olsson & Sunnerhagen, 2007) and independence (Narasimhalu et al., 2011). Detecting cognitive impairments early after stroke onset, and throughout the continuum of stroke recovery, is needed to diagnose, educate and guide rehabilitation.

Neuropsychological tests aim to characterise performance based on cognitive domains, which typically include language, attention, memory, processing speed, visuospatial and executive skills (Barker-Collo & Feigin, 2006). Measuring domain-specific performance is challenging, particularly for individuals with post-stroke aphasia. Traditional pen-and-paper tests are often dependent on language skills for completion and results will be confounded if individuals experienced difficulty responding to questions and understanding instructions.

Virtual reality is a developing field that has been used to assess cognitive skills post-stroke (Simona Raspelli et al., 2012). Simulated real-life scenarios provide users with functional and meaningful tasks to measure cognitive performance, permitting options that are unavailable using traditional pen-and-paper testing methods (Parsons & Rizzo, 2008). However, the restrictive inclusion criteria of many studies evaluating virtual reality cognitive assessments in stroke means that participants are often high functioning (Wall et al., 2015). This may be due to the cognitive and motor skills required for navigation (Rizzo & Kim, 2005).

We developed a non-immersive virtual reality cognitive assessment, the Cognitive Assessment for Aphasia App (C3A), for stroke survivors with and without aphasia (Wall, Cumming, Koenig, Pelecanos, & Copland, 2017). The C3A consists of four distinct cognitive tasks that aim to measure attention, visuoperceptual ability, visual memory and executive skills. The delivery of instructions and execution of the C3A tasks used “aphasia-friendly” techniques. This included simulated real-life auditory and visual feedback to aid learning (Tinga et al., 2016), and simple instructions that were augmented with practice opportunities to verify that participants understood instructions.

The aims of this study were to: (1) determine if the C3A can differentiate between stroke participants, with and without aphasia, and controls, (2) investigate construct validity by comparing the C3A with traditional neuropsychological tests that have been validated in stroke, (3) determine ecological validity by comparing the C3A with a functional cognitive outcome in stroke, and (4) investigate the association between C3A performance and age, education, computer experience and non-dominant hand use in stroke participants, with and without aphasia, and controls.

## **5.3 Methods**

### **5.3.1 Participants**

Stroke survivors were recruited from three hospitals in Brisbane, Australia, and those with aphasia were also recruited from the community via The Communication Registry at The University of Queensland. Controls living in the community in Queensland were sourced from posters, social groups and newsletters. Recruitment occurred from February 2015 to October 2015. Stroke was confirmed with neuroimaging or with a clinical diagnosis if imaging was unavailable. Aphasia was diagnosed according to The Comprehensive Aphasia Test (CAT; Swinburn et al., 2005) (score > 1.5 SD below the mean). Individuals with stroke were excluded if they: (1) had visual or hearing impairments that impeded testing, (2) needed an interpreter to participate, (3) were too medically unwell, (4) had bilateral upper limb issues that precluded tablet use. Controls were excluded if they: (1) had a history of neurological disease or acquired brain injury, (2) needed an interpreter to participate, (3) had visual or hearing impairments that impeded testing, (4) had bilateral upper limb issues that precluded tablet use, or (5) failed a mood screen (The Patient Health Questionnaire; Kroenke et al., 2001), to ensure depression would not confound cognitive performance (S. Wang & Blazer, 2015).

Ethical clearance was obtained through local Human Research Ethics Committees in Brisbane, Australia. Written consent was obtained from all participants or from a family member if cognitive deficits impeded informed consent.

### 5.3.2 Assessments

Demographic data collected included age, sex, education, time post-stroke, handedness and clinical setting. Computer experience was ascertained using a questionnaire based on frequency of use. Due to clear polarity in the computer frequency questionnaire responses, the ratings were collapsed into two categories (rarely used and frequently used) for analysis. If participants were unable to self-report computer experience, information was sourced from a carer or family member.

Participants with a left hemisphere stroke were screened for aphasia using the Language Assessment Screening Test (Flamand-Roze et al., 2011), and those who failed undertook the CAT (Swinburn et al., 2005) (auditory comprehension sub-tests) and the 15-item abbreviated Boston Naming Test (Kent & Luszcz, 2002), to determine a diagnosis and severity of aphasia. All participants completed a measure of manual dexterity using the Peg Test (Y.-C. Wang et al., 2011) and the hand with the faster time was selected to complete the C3A. All participants attempted the C3A prior to the pen-and-paper cognitive tests.

An Android Samsung Galaxy NotePro (12.2 inch) tablet was used to run the C3A. A standardised script was developed. Measures to evaluate cognitive performance included latency times and errors (commission, omission and sequencing errors). The C3A is divided into four distinct tasks: (1) simple reaction time task to assess psychomotor speed, (2) visual search task to assess neglect and attention, (3) sequence copy tasks to assess visual memory, and (4) kitchen task to assess executive functioning. [Figure 5.2](#) displays the C3A's kitchen. A full description of the C3A can be viewed in [Appendix G](#) (see also Wall, Cumming, Koenig, et al., 2017).





**Figure 5.2** The C3A interactive kitchen

### **5.3.3 Cognitive Tests**

While limitations to neuropsychological testing are apparent, this method of assessment is recommended in clinical stroke guidelines (National Stroke Foundation, 2010). Without access to a comparable gold standard virtual reality cognitive assessment in stroke, we used neuropsychological tests that have been validated in stroke that do not require a verbal response to compare with the C3A. The cognitive tests were: Trail Making Test (Reitan & Wolfson, 1985) to assess attention and executive function, Brixton Spatial Anticipation Test (Burgess, 1997) to assess executive function, Rey-Osterrieth Complex Figure (Osterrieth, 1944) to assess visuospatial, visual memory and executive skills. The Functional Independence Measure total cognition score (FIM-cog) (Keith, Granger, Hamilton, & Sherwin, 1987) was used to measure functional cognition.

### **5.3.4 Statistical Analysis**

All analyses were performed using Stata 14.0 (StataCorp, 2015) and tests with an  $\alpha < .05$  were declared statistically significant. Data were summarised using descriptive statistics. To compare measured outcomes between stroke participants, with and without aphasia, and controls a Kruskal Wallis test was used (Bonferroni corrected for multiple testing). Pairwise differences were explored post-hoc using a Dunn's test.

To investigate the association between the C3A and demographic variables Pearson's correlations were used for continuous data and *t*-tests were used for the categorical variables (Bonferroni corrected for multiple testing), as the transformed data met parametric assumptions.

To explore the strength of the relationship between the C3A and the pen-and-paper cognitive tests and FIM-cog in the stroke groups, a partial Pearson's correlation was used to permit adjustment for the statistically significant demographic variables. A post-hoc pairwise correlation was also used to explore if the C3A latency times were associated with C3A errors.

## 5.4 Results

A total of 113 participants were screened against the eligibility criteria. Ninety-six participants were included (35 aphasia, 29 stroke non-aphasia, 32 controls). Reasons for exclusion were patient refusal ( $n = 3$ ), clinician informed that the participant was not appropriate ( $n = 2$ ), unable to source third party consent ( $n = 2$ ), palliative ( $n = 2$ ), visual deficits ( $n = 2$ ), discharged prior to consent ( $n = 1$ ), needed an interpreter ( $n = 1$ ), and bilateral upper limb weakness ( $n = 1$ ). There was no significant difference between the groups for age ( $p = .69$ ), but the control group had completed more years of education and had more computer experience compared to the aphasia group and the stroke non-aphasia group (all  $p < .05$ ). Refer to [Table 5.1](#) for details of the included participant characteristics.

Participants with aphasia had language deficits that ranged from mild to severe. Total auditory comprehension scores in the aphasia group ranged from 5/66 to 63/66 (median = 53, interquartile range = 29–58) as measured by the CAT. The Boston Naming Test results ranged from 0/15 to 15/15 (median = 10, interquartile range = 1–12). Only one participant with aphasia was unable to complete all C3A tasks, and six participants (all with aphasia) were unable to complete all pen-and-paper tests. Eight participants had missing data for components of the C3A (4 aphasia, 2 stroke non-aphasia and 2 controls), due to technical problems with saving data. Participants took approximately 20 minutes to complete the C3A.

**Table 5.1** Included participant characteristics

<b>Variable</b>	<b>Aphasia (<i>n</i> = 35)</b>	<b>Stroke non- aphasia (<i>n</i> = 29)</b>	<b>Controls (<i>n</i> = 32)</b>
Age in years, mean (SD)	69.8 (8.9)	69.5 (13.0)	67.4 (12.3)
Sex, <i>n</i> (%)			
Female	11 (31.4)	9 (31.0)	17 (53.1)
Male	24 (68.6)	20 (69.0)	15 (46.9)
Education in years, mean (SD)	10.8 (3.1)	11.8 (3.5)	15.1 (3.4)
Handedness, <i>n</i> (%)			
Right	31 (88.6)	27 (93.1)	29 (90.6)
Left	3 (8.6)	2 (6.9)	3 (9.4)
Ambidextrous	1 (2.9)	0	0
Pre-morbid neurological disease/injury <i>n</i> (%)	2 (5.7)	8 (27.6)	N/A
Time post-stroke, <i>n</i> (median, IQR*) by clinical setting			
Acute setting (days)	11 (5.0, 2.0–13)	17 (4.0, 2.0–5.0)	N/A
Inpatient rehabilitation (days)	2 (23.5, 12–35)	12 (26.5, 14.0–52.0)	N/A
Community dwelling (years)	22 (4.5, 2.9–11.3)	N/A	N/A
Uses a smartphone or tablet, <i>n</i> (%)	23 (65.7)	20 (70.0)	27 (84.4)
Uses a computer, <i>n</i> (%)	22 (62.9)	16 (55.2)	30 (93.8)

N/A: not applicable; \*IQR, interquartile range

The C3A raw data can be viewed in [Appendix H](#). This includes a breakdown of errors with itemised commission, omission, and latency errors. In the visual search task, only three of 98 participants made errors; no statistical analysis of visual search errors was conducted.

#### 5.4.1 Between Group Comparisons for all Measured Outcomes

Performance on all C3A tasks differed significantly between the stroke groups and controls, except for the sequence copy latency times where the stroke non-aphasia group did not significantly differ from the controls ( $p = 1.0$ ). Performance between the aphasia group and the stroke non-aphasia group did not differ, except for the sequence copy latency times ( $p = .002$ ), where the aphasia group was slower (median = 6.87, IQR = 4.94–8.62); than the stroke non-aphasia group (median = 5.50, IQR = 3.85–6.63), and controls were the quickest (median 5.50, IQR 5.09–6.08). There were no significant

differences between the aphasia group and the stroke non-aphasia group for all pen-and-paper tests. The FIM-cog significantly differed between all three groups, with the aphasia group exhibiting more functional impairment (median = 24, IQR = 11–27) compared to the stroke non-aphasia group (median = 27, IQR = 24–32) and controls (median = 36, IQR = 33.5–35).

#### **5.4.2 C3A Association with Demographic Variables**

In all participant groups, computer experience, education and handedness were not significantly associated with any C3A tasks. In the stroke non-aphasia group, increasing age was significantly associated with slower latency times for the reaction time task ( $r = 0.54$ ,  $p = .034$ ), and the kitchen task ( $r = .44$ ,  $p = .019$ ).

#### **5.4.3 C3A Association with Pen-and-Paper Cognitive Tests**

While the C3A performance did not significantly differ between the aphasia group and stroke non-aphasia group, there were differences between the two groups in the strength of association between the C3A and the pen-and-paper tests. [Table 5.2](#) details the correlations between the C3A tasks and the reference standards, adjusted for age.

#### **5.4.4 Reaction Time Task**

In the aphasia group, no significant associations between the reaction time task and the pen-and-paper tests were identified. In the stroke non-aphasia group, latency times were moderately correlated with the Rey copy, Rey delayed, and Trails B (see [Table 5.2](#)).

#### **5.4.5. Sequence Copy Task**

In the aphasia group, latency times for the sequence copy task were moderately associated with the Rey immediate, Rey delayed, Brixton and Trails A, but the errors were only associated with Trails B. In the stroke non-aphasia group, there was no significant association between sequence copy latency times and the pen-and-paper tests, but the errors were moderately associated with Rey copy and Trails A (see [Table 5.2](#)).

#### **5.4.6 C3A Kitchen Task**

In the aphasia group, all pen-and-paper tests were significantly related to the kitchen task errors. In the stroke non-aphasia group, kitchen task errors were significantly associated with the Rey copy, Trails B and Brixton. Kitchen task latency was not significantly associated with any of the pen-and-paper tests in either group (see [Table 5.2](#)).

#### **5.4.7 C3A Association to the FIM-cog**

The FIM-cog was more closely associated with the error measures than the latency measures from the C3A; it was strongly correlated with kitchen task errors in both the aphasia and stroke non-aphasia groups (see [Table 5.2](#)).

**Table 5.2** Comparison of C3A task outcomes with reference standards using partial Pearson's correlations; adjusted for age

Reference standards	Simple Reaction Task		Sequence Task latency		Sequence Task errors		Kitchen Task latency		Kitchen Task errors	
	Stroke non-Aphasia <i>r</i>	non-aphasia <i>r</i>	Stroke non-Aphasia <i>r</i>	non-aphasia <i>r</i>	Stroke non-Aphasia <i>r</i>	non-aphasia <i>r</i>	Stroke non-Aphasia <i>r</i>	non-aphasia <i>r</i>	Stroke non-Aphasia <i>r</i>	non-aphasia <i>r</i>
Rey copy	.28	.49*	-.34	.01	-.06	-.37	.04	-.04	-.54**	-.56**
Rey immediate	.17	.34	-.50*	.01	-.25	-.42	-.24	.02	-.74**	-.20
Rey delayed	.17	.40*	-.51*	-.07	-.33	-.34	-.16	-.04	-.69**	-.29
Trails A	-.17	-.17	0.51*	.12	.43*	.43*	-.21	-.05	.73**	.32
Trails B	-.15	-.40*	0.25	.23	.38	.39	.18	-.12	.59**	.45*
Brixton	-.31	-.25	0.50*	-.09	.14	.32	.07	.18	.54**	.76**
FIM-cog	.31	.43*	-.54*	-.13	-.36*	.52*	-.10	-.12	-.84**	-.79**

\**p* value < .05; \*\**p* value < .01

## 5.5 Discussion

Our findings demonstrate that the C3A can distinguish between participants with stroke (with and without aphasia) and controls. The aphasia group C3A performance did not differ to the stroke non-aphasia group. Of all the C3A metrics, errors on the kitchen task were most strongly associated with the cognitive assessment reference standards. The C3A kitchen task errors were also strongly correlated with FIM-cog in both the aphasia and stroke non-aphasia groups, demonstrating robust ecological validity.

Increasing age was significantly associated with poorer C3A performance. Historically, computer use has been lower in older adults (Czaja et al., 2006). Seventy-one per cent of the participants in the current study frequently used a computer, which reflects the changing demographics of computer users. Importantly, computer experience and was not significantly associated with C3A performance. Equally important, handedness was not significantly correlated with C3A performance.

Almost half of the participants with aphasia used their non-dominant hand to complete the C3A tasks. Upper limb motor impairments are present in more than 80% of all individuals with stroke, with 30% to 40% regaining some dexterity after six months (Buma, Lindeman, Ramsey, & Kwakkel, 2010). The option to complete the C3A tasks using a non-dominant upper limb without negatively influencing performance extends testing to another stroke subgroup often excluded from pen-and-paper cognitive testing (Wall et al., 2015).

A bias occurred in the aphasia group, where individuals with more severe language deficits were unable to complete, or refused, many pen-and-paper tests. This bias likely influenced the between group comparisons in the pen-and-paper tests, where a difference in pen-and-paper performance between the aphasia group and the stroke non-aphasia may have been more apparent. The limitations of the pen-and-paper tests in aphasia were overcome in the C3A, where all except one participant with aphasia completed all C3A tasks. The between group comparisons in the C3A performance, which included individuals with severe aphasia, yielded no differences (except for sequence copy latency), suggesting that individuals with mild to severe language impairments were not disadvantaged when undertaking the C3A.

Evaluating the clinimetric properties for cognitive assessments is necessary to determine validity and feasibility, including user experience (Harrison et al., 2013). C3A performance differed between stroke and controls, and notably, individuals with aphasia performed no differently than stroke participants without aphasia. The association between C3A performance and FIM-cog also highlighted strong ecological validity. The encouraging discriminant, construct, and ecological validity results of the C3A, combined with our previous findings of feasibility and user acceptance (Wall, Cumming, Koenig, et al., 2017), suggest that non-immersive virtual reality technology can be used to measure cognitive performance in a way that reduces reliance on linguistic skills. The C3A provides clinicians and researchers with an alternative option for assessing cognitive skills in stroke survivors with or without aphasia.



## **Chapter 6: Determining the Association between Language Performance and a Non-Immersive Virtual Reality Cognitive Assessment: The Cognitive Assessment for Aphasia App (C3A)**

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The data in chapters 4 and 5 provide evidence for the feasibility, user acceptance and validity of the C3A. We have not yet established, however, the direct relationship between language impairments and C3A performance. In chapter 3, we identified a strong association between language status and performance on many pen-and-paper cognitive tests in post-stroke aphasia. The purpose of this chapter was to explore the association between language performance and C3A performance in post-stroke aphasia.

## 6.1 Abstract

**Objectives:** Language impairments in aphasia may confound non-linguistic cognitive performance, particularly when using pen-and-paper tests. We developed and validated a non-immersive virtual reality cognitive assessment designed to be inclusive of individuals with post-stroke aphasia. The primary objective of this study was to determine the association between language performance in aphasia and the Cognitive Assessment for Aphasia App (C3A).

**Methods:** We recruited individuals with post-stroke aphasia from inpatient hospital and community settings. The C3A tasks include a simple reaction time task, visual search task, sequence copy task, and a kitchen task. Errors and latency times were recorded. Auditory comprehension was measured using the Comprehensive Assessment for Aphasia and naming was measured using the Boston Naming Test. General linear regressions were used to explore the association between language performance and C3A performance.

**Results:** A total of 35 participants with aphasia were recruited. The severity of auditory comprehension and naming deficits ranged from mild to severe. Neither language measures were significantly associated with C3A simple reaction time, errors on sequence copy, or latency on the kitchen task (all  $p > .05$ ). Both auditory comprehension and naming were significantly associated with sequence copy latency, and with errors on the kitchen task (all  $p < .01$ ).

**Conclusions:** The C3A is a valid, “aphasia-friendly” assessment for assessing non-linguistic cognitive performance in post-stroke aphasia. The association with language differed depending on the task. We argue that this finding is more consistent with concomitant visual memory and executive function deficits in aphasia rather than language confounding non-linguistic cognitive performance.

**Keywords:** stroke; virtual reality; cognitive impairments; language impairments

Introduction

## 6.2 Introduction

Aphasia occurs in up to 30% of stroke survivors (Engelter et al., 2006). This language disorder may involve impairments in spoken language and comprehension, reading and writing. Individuals with aphasia experience increased anxiety and depression (Dickey et al., 2010) are less likely to return to work (Graham, Pereira, & Teasell, 2011), and have more difficulty maintaining social networks (Northcott, Marshall, & Hilari, 2016) compared to stroke survivors without aphasia. Interventions to improve aphasia typically focus on compensating and resolving the language impairments (Brady, Godwin, Enderby, Kelly, & Campbell, 2016), and often neglect the non-linguistic cognitive impairments that may be present. Executive functioning, attention and memory deficits that may co-occur with aphasia negatively influence aphasia recovery (Harnish & Lundine, 2015; Lambon Ralph et al., 2010). Nicholas, Hunsaker, and Guarino (2015) explored linguistic and non-verbal cognitive measures as predictors of quality of life in 28 individuals with aphasia. Non-verbal cognitive measures explained more than three times the variance in quality of life compared to the language measures. Cognition needs to be considered when assessing and planning interventions for individuals with aphasia.

Assessing non-linguistic cognitive performance in aphasia is complex. Many pen-and-paper cognitive tests are linguistically-loaded and aphasia deficits may confound the results. Wall et al. (2015) conducted a systematic review and identified studies evaluating the clinimetric properties of cognitive assessments in stroke. Of the 109 included studies, approximately two-thirds excluded participants based on communication and cognitive deficits. As such, the findings from these studies are unlikely to be generalisable to individuals with aphasia. A study exploring the feasibility of cognitive screening tools in stroke survivors found that only 27% of participants completed the tests and 65% of participants needed direct assistance to participate (Lees et al., 2016). Communication deficits were identified as one of the primary barriers for test completion. Testing cognitive skills in individuals with aphasia is often not feasible (Wall, Cumming, & Copland, 2017) and may yield results that measure language impairments rather than the cognitive domain intended for testing.

To independently measure non-linguistic cognitive performance in individuals with aphasia, cognitive domains require isolation (to the extent that this is possible) from linguistic performance during testing. Eliminating a verbal response does not necessarily ensure language-free performance. Wall, Cumming, and Copland (2017) explored the association between auditory comprehension and naming performance in individuals with aphasia ( $n = 36$ ) and performance on a neuropsychological battery typically used in stroke. All pen-and-paper tests, excluding Star Cancellation, were significantly associated with naming and auditory comprehension, even the non-verbal tests. Unless cognitive assessments accommodate the needs of individuals with aphasia, the validity and reliability of results remain uncertain, and individuals with aphasia will continue to be excluded from studies exploring post-stroke cognition (Wall et al., 2015).

We developed a non-immersive virtual reality cognitive assessment, the Cognitive Assessment for Aphasia App (C3A), that used “aphasia friendly” techniques in the design and administration to meet the needs of individuals with post-stroke aphasia (Wall, Cumming, Koenig, et al., 2017). The C3A incorporates the familiarity of an everyday task, with computerised auditory and visual feedback, to create tasks that minimise the dependency on language skills for completion. The tasks also include practice opportunities to maximise understanding and to demonstrate to examiners that the tasks are understood, rather than users guessing or not completing tasks. The C3A includes four distinct tasks (reaction time, visual search, sequence copy and kitchen task) to measure psychomotor skills attention, visuospatial skills, visual memory and executive skills respectively.

A previous study evaluating feasibility and user acceptance of the C3A showed that the non-immersive virtual reality cognitive assessments were preferred and were more feasible compared to pen-and-paper testing in stroke survivors (with and without aphasia) and controls (Wall, Cumming, Koenig, et al., 2017). The validation study in chapter 5 demonstrated strong ecological and construct validity in stroke survivors (with and without aphasia), and showed that the C3A differentiated between participants with stroke and controls. Importantly, C3A performance between stroke survivors with aphasia and those without aphasia was not significantly different.

The association between auditory comprehension and naming performance and performance on this virtual reality cognitive assessment, designed to be “aphasia-friendly”,

is yet to be determined. The primary objective of the current study was to examine this association in post-stroke aphasia. We hypothesised that language performance would not be associated with performance on the simple reaction time task or the visual search task. Based on research reporting co-occurring memory impairments (Lang & Quitz, 2012) and executive impairments (Mayer, Mitchinson, & Murray, 2016) in aphasia, we hypothesised that the sequence copy task (measuring visual memory) and the kitchen task (measuring executive function) would be significantly associated with language performance.

## **6.3 Materials and Methods**

### **6.3.1 Participants**

Participants with aphasia following stroke were recruited from three hospitals in Brisbane and the community from February 2015 to October 2015. Stroke was diagnosed with diagnostic imaging or a clinical diagnosis if imaging was unavailable. Aphasia was diagnosed according to The Comprehensive Aphasia Test (CAT) (Swinburn et al., 2005) (score >1.5 SD below the mean on sub-tests) or the Language Screening Test (cut-off <15) (Flamand-Roze et al., 2011). Individuals were excluded if they: (1) had visual and hearing impairments that impeded testing, (2) needed an interpreter to participate, or (3) were too medically unwell, or (4) had bilateral upper limb issues that precluded tablet use.

Ethical clearance was obtained through local Human Research Ethics Committees in Brisbane, Australia. Written consent was sourced for all participants and a substitute decision maker was used for patients with cognitive deficits that precluded informed consent.

### **6.3.2 Assessments**

Demographic data collected included age, sex, education, time post-stroke, clinical setting, handedness, and if participants used their dominant hand for C3A tasks. All participants completed a measure of hand dexterity using the Peg Test (Y.-C. Wang et al., 2011) to determine what hand to use to complete the C3A tasks. The hand with the faster time was selected to complete all the C3A tasks. Computer experience was ascertained using a questionnaire based on frequency of use. Smartphones and tablets are regarded as computers (Li, 2014), thus either smartphone or tablet use were regarded as computer experience. Due to polarity in the questionnaire results, the ratings were collapsed into

rarely used and frequently used for analyses. If participants were unable to report computer experience, information was sourced from a carer or family member.

Language performance was assessed using the CAT (Swinburn et al., 2005) (auditory comprehension total score, which includes single word, sentence and paragraph comprehension sub-tests) and the 15-item abbreviated Boston Naming Test (Kent & Luszcz, 2002).

### **6.3.3 C3A**

The C3A was designed to run on an Android Samsung Galaxy NotePro (12.2 inch) tablet. All participants undertook the C3A. All user responses were saved and time stamps were saved with each user response.

A detailed description of the C3A can be seen in [Appendix G](#) (see also Wall, Cumming, Koenig, et al., 2017). Standardised instructions using short, simple verbal explanations were provided. Up to three practice opportunities were allowed prior to each task, except for the kitchen task. In the kitchen task, participants applied their navigation skills to make a cup of tea with milk and place a dessert from the fridge onto a plate. Measures to evaluate cognitive performance included latency times and errors (commission, omission and sequencing errors).

### **6.3.4 Statistical Analysis**

All analyses were performed with Stata 14 software (StataCorp, 2015). The association between language (auditory comprehension and naming) and the C3A outcomes were examined using general linear regressions. To examine the distinct effects of auditory comprehension and naming, the independent variables were entered separately into the regression models (Wall, Cumming, & Copland, 2017). The base model consisted of auditory comprehension or naming, and the demographic variables (age, education, computer experience and hand used during C3A testing), were sequentially added using forward selection. Demographics with a *p*-value less than .05 were retained in the model.

## 6.4 Results

A total of 35 participants with post-stroke aphasia were included in the study. Participant characteristics are shown in [Table 6.1](#). Notably, 57% participants used their non-dominant hand to navigate the C3A tasks.

**Table 6.1** Characteristics of the participants with post-stroke aphasia ( $n = 35$ )

Age in years, mean $\pm$ SD	69.8 (8.9)
Sex, $n$ (%)	
Female	11 (31.4)
Male	24 (68.6)
Education in years, mean $\pm$ SD	10.8 (3.1)
Handedness, $n$ (%)	
Right-handed	31 (88.6)
Left-handed	3 (8.6)
Ambidextrous	1 (2.9)
Used non-dominant hand, $n$ (%)	20 (57.1)
Pre-morbid neurological disease or injury, $n$ (%)	2 (5.7)
Time post-stroke, $n$ (median, IQR*) by clinical setting	
Acute setting (days)	11 (5.0, 2.0–13)
Inpatient rehabilitation (days)	2 (23.5, 12–35)
Community dwelling (years)	22 (4.5, 2.9–11.3)
Frequent computer use, $n$ (%)	22 (62.9)

\*IQR = interquartile range

The severity of language impairments ranged from mild to severe. Total scores for auditory comprehension ranged from 5/66 to 63/66 (median = 53, IQR = 29–58) as measured by the CAT. The Boston Naming Test results ranged from 0/15 to 15/15 (median = 10, IQR = 1–12). Only one participant was unable to complete a single element of the most challenging sequence copy task in the C3A. There were a further three incomplete C3A outcomes due to technical difficulties associated with saving data.

We note that in chapter 6, a pairwise correlation between auditory comprehension and naming confirmed that they were too closely related ( $r = .87$ ) to be included in the same regression model. [Table 6.2](#) shows the final models for auditory comprehension and naming against each of the C3A outcomes. Age, education, computer experience and whether the participants used their dominant hand were not significantly associated with any C3A task outcomes in these multivariable models. In the visual search task, only two of 35 participants made errors; no statistical analysis of visual search errors was conducted.

**Table 6.2** Association between language and the C3A outcomes in aphasia ( $R^2$ )

C3A Tasks	Auditory Comprehension		Naming	
	$R^2$	$p$ -value	$R^2$	$p$ -value
Simple Reaction Time, $n = 35$	.12	$p = .15$	.05	$p = .18$
Sequence Copy Task, $n = 31$				
Latency	.36	$p = .001$	.37	$p = .001$
Errors	.06	$p = .20$	.09	$p = .10$
Kitchen Task, $n = 34$				
Latency	.01	$p = .61$	.01	$p = .59$
Errors	.61	$p = .001$	.56	$p = .001$

Auditory comprehension and naming were not significantly associated with the simple reaction time task, the sequence copy errors or the kitchen task latency times. Auditory comprehension was significantly associated with two of five C3A outcome measures. Auditory comprehension explained 61% of the variance in the kitchen task errors [ $F(1, 32) = 49.01, p = .001$ ] and 36% of the variance in the sequence copy latency [ $F(1, 33) = 18.69, p = .001$ ]. Similarly, naming explained 56% of the variance in the kitchen task errors [ $F(1, 32) = 49.01, p = .001$ ] and 37% of the variance in the sequence copy latency [ $F(1, 33) = 19.24, p = .001$ ].



## 6.4 Discussion

The C3A is a non-immersive virtual reality cognitive assessment, which was designed to overcome the confounding influence of language impairments when assessing non-linguistic cognitive skills in post-stroke aphasia (Wall, Cumming, Koenig, et al., 2017). Our hypotheses were confirmed, in part, by an observed association between auditory comprehension and naming and the sequence copy latency and with kitchen task errors. Neither language measure was significantly associated with simple reaction time, errors on sequence copy, or kitchen task latency. Age, education, prior computer experience, and non-dominant hand use were not associated with C3A performance when auditory comprehension or naming were in the regression models.

The C3A's kitchen task was designed to measure executive skills in stroke. In chapter 5 of the thesis, the kitchen task errors correlated strongly with the FIM-cog and the non-verbal reference standard. The association observed between kitchen task errors and auditory comprehension and naming likely reflects co-occurring executive dysfunction in the participants with aphasia, consistent with previous research demonstrating executive impairments in this population (Fridriksson et al., 2006; Mayer et al., 2016). While we cannot discount the potential influence of language impairments on kitchen task errors, the task was specifically designed to minimise language requirements. Instructions, practice opportunities and feedback were all designed to be "aphasia-friendly".

The sequence copy latency task was designed to measure visual memory. Interestingly, the sequence copy task latency was associated with auditory comprehension and naming in aphasia, but the sequence copy errors were not associated with the language measures. In chapter 5, it was demonstrated that latency and errors were not correlated in all C3A tasks, negating the notion that participants may have performed tasks slower to gain accuracy (and vice versa). Another finding from chapter 5 was that sequence copy latency was the only C3A performance measure to show a significant difference between the aphasia and non-aphasia stroke groups. While visual memory impairments are thought to co-occur in aphasia (Lang & Quitz, 2012) the reason for a relationship between language function and sequence latency but not errors, is unclear. It could be suggested that the sequence copy task errors reflect a visual memory task that may not be confounded by auditory comprehension and naming in aphasia.

The simple reaction time task was not associated with auditory comprehension or naming performance. While the reaction time task can distinguish between stroke survivors and controls (see chapter 5), the primary purpose of this task was to familiarise users with the tablet and reduce potential anxiety (Wall, Cumming, Koenig, et al., 2017).

The “aphasia-friendly” techniques used in the development and administration of the C3A minimises the linguistic skills needed for completion. Thus, the association between auditory comprehension and naming errors observed in some C3A measures are more likely to reflect co-occurring cognitive deficits observed in aphasia rather than the C3A tasks being confounded by language impairments observed in aphasia.

## Chapter 7: Conclusion

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Up to 70 per cent of stroke survivors live with cognitive impairments (Lindén et al., 2004), which can adversely impact activities of daily living (Kihun & Wanhee, 2012), the ability to return to work (van Es et al., 2011) and even survival (Melkas et al., 2009). Cognitive impairments commonly comprise multiple interconnected processes, including attention, memory, language, visuospatial and executive skills (Frankel et al., 2007; Fucetola et al., 2009). Measuring cognitive processes and generating cognitive profiles to understand functional cognitive behaviour are needed to guide rehabilitation. The interconnection between these cognitive processes makes this task challenging. Specifically, language skills are often involved in understanding and responding to non-linguistic cognitive tasks. This makes it difficult to measure non-linguistic cognitive performance in individuals with language impairments following stroke (aphasia).

In Phase 1 of the thesis, the aims were to (1) determine if stroke samples used in studies evaluating the clinimetric properties of cognitive assessments are representative of the wider stroke population, and (2) explore the association between language performance and standard cognitive tests in individuals with post-stroke aphasia and controls. The aims of Phase 2 were to (1) develop a non-immersive virtual reality cognitive assessment for stroke survivors, designed to be inclusive of individuals with aphasia, (2) examine the clinimetric properties of the cognitive assessment, and (3) explore the association between language performance and the virtual reality cognitive assessment in individuals with post-stroke aphasia.

## **7.1 Phase 1 Findings**

### **7.1.1 Samples used in Stroke Studies of Cognitive Assessments were Unrepresentative**

The first key undertaking in Phase 1 of this work was a systematic review to determine if post-stroke cognition is assessed in representative samples. After extracting and synthesising the eligibility criteria from 109 articles, communication problems and cognitive impairment were identified as the most common exclusion criteria, used in approximately two-thirds of the studies. Individuals with aphasia could be excluded based on either of these exclusion criteria, but the frequency of excluding individuals with aphasia could only be assumed given that numbers and precise reason for exclusion were rarely reported. Up to 30% of stroke survivors experience aphasia (Engelter et al., 2006), meaning that a large proportion of stroke survivors do not have access to clinimetrically sound measures of their cognitive performance.

Pen-and-paper cognitive tests were used in 73% of the included studies. This assessment method is often linguistically-loaded, thus non-linguistic cognitive performance may be confounded by language impairments observed in aphasia. The findings from the systematic review demonstrated that the samples used in studies evaluating the clinimetric properties of cognitive tests in stroke did not represent the broader stroke population, with aphasia meeting the description of the most commonly used exclusion criteria.

### **7.1.2 All Pen-and-Paper Tests, Except Star Cancellation, were Significantly Associated with Language Performance in Aphasia**

In view of individuals with aphasia being excluded from studies evaluating cognitive tests in stroke, exploring the association between language performance in aphasia and performance on standard cognitive tests was undertaken to complete Phase 1 of this thesis. All pen-and-paper cognitive tests (verbal and non-verbal), except Star Cancellation, were significantly associated with auditory comprehension and naming performance in aphasia. Most participants scored within normal limits on Star Cancellation, which supports previous research that neglect is rarely observed in aphasia (Timpert et al., 2015).

A real-life measure of cognitive performance, the Kettle Test, was not significantly associated with the language measures. The advantage of using the Kettle Test is that it incorporates a familiar everyday task (making hot drinks) and multisensory cues (e.g., kitchen setting, noise of boiling kettle) to aid understanding of the task. Multiple sensory cues facilitate the ability to identify, discriminate and recognise stimuli (Johansson, 2012; Tinga et al., 2016). A disadvantage of the Kettle Test was that not all participants could complete the task due to post-stroke motor impairments. Furthermore, the test may underestimate the association between language and cognitive skills needed for instrumental activities of daily living.

Feasibility was clearly an issue with completing pen-and-paper cognitive tests, with 37% of participants unable to complete all tests in the battery. Interestingly, a non-verbal cognitive test (Trails B) had the highest frequency of missing data and there were no missing data for any of the language measures. The primary reason for missing data was difficulty understanding the cognitive task. These results demonstrated that pen-and-paper tests were not feasible for many individuals with aphasia, and thus provide an explanation for why studies evaluating cognitive tests in stroke often use criteria to exclude individuals with aphasia. There is a pressing need for a cognitive assessment in stroke that is appropriate for individuals with post-stroke aphasia.

## **7.2 Phase 2 Findings**

### **7.2.1 Development of the C3A: The C3A is More Feasible than Pen-and-Paper Tests and Preferred in Stroke Survivors, With and Without Aphasia**

The first major undertaking of Phase 2 was the development of the C3A – a non-immersive virtual reality cognitive assessment for stroke survivors – designed to overcome the barriers to assessing non-linguistic cognitive performance in aphasia. Selecting virtual reality evolved from the work detailed in chapter 3, where no significant association between language performance and the Kettle Test (a real-life cognitive assessment) was found in aphasia. However, some participants with post-stroke motor impairments were unable to safely undertake the Kettle Test. Virtual reality technology was used to create a simulated real-life kitchen to replicate the familiarity of everyday tasks, enabling participants to draw upon their intuition, thus minimising the need for complex instructions. Using a touch screen enabled individuals with hemiparesis to safely complete the cognitive assessment with their dominant or non-dominant hand. The C3A was not created to replicate a fully immersed simulated kitchen experience, but the non-immersive 3D kitchen

setting was selected to minimise dependency on language and maximise ecological validity of the cognitive performance. The assessment was trialled with stroke survivors throughout the development process and modifications were made based on their feedback.

Other advantages of virtual reality technology are the precision of computerised performance measures (e.g., latency, errors) potential for multisensory input and availability of feedback to enhance learning (Johansson, 2012; Tinga et al., 2016). The C3A incorporated practice opportunities to reduce technology anxiety and to augment understanding of cognitive tasks. The practice opportunities also enabled participants to demonstrate comprehension to the examiner. Collectively, these techniques aimed to improve access to cognitive testing for people with mild to severe post-stroke cognitive impairments, including aphasia.

The C3A tasks included: (1) a simple reaction time task to assess psychomotor skills and attention; (2) a visual search task to assess visuospatial skills; (3) sequence copy tasks to assess visual memory; and (4) a kitchen task to assess executive functioning. These cognitive processes can co-occur with aphasia and negatively influence aphasia recovery (Harnish & Lundine, 2015; Lambon Ralph et al., 2010; Murray, 2012).

Feasibility was ascertained from missing data and user acceptance measures. The C3A was completed in approximately 20-minutes, thus, is appropriate to undertake in all phases of stroke recovery. Only one of 64 stroke survivors (with and without aphasia) and 32 controls did not complete all C3A tasks, whereas 13 participants were unable to complete all tests in the pen-and-paper battery. The inability to understand the cognitive tasks was the primary reason for missing data. Ten of the 13 participants who were unable to complete the battery of pen-and-paper tests had aphasia. User acceptance measures for the C3A were positive, with the majority in all participant groups preferring it to the pen-and-paper tests. Ninety-five per cent of participants were either neutral or enjoyed the C3A. Positive user acceptance for the C3A is important if it is to be implemented successfully in the clinical setting. This study provides preliminary evidence that the C3A is a feasible cognitive assessment for stroke survivors with and without aphasia.

### **7.2.3 The C3A is a Valid Cognitive Assessment in Stroke Survivors with and without Aphasia**

The next major undertaking in Phase 2 was validating the C3A. Three levels of evidence were reported. First, performance on the C3A could distinguish between participants with stroke and controls, whereas the assessment did not distinguish between two stroke groups (with and without aphasia). This suggests that the C3A is sensitive to the cognitive deficits experienced by stroke survivors, but is not overly influenced by the language impairments that manifest in post-stroke aphasia. Second, the C3A outcome that was most strongly correlated to the reference standards was number of errors on the kitchen task. This executive task detects high level impairments, which are often overlooked post-stroke (Jaillard, Naegele, Trabucco-Miguel, LeBas, & Hommel, 2009). Third, the C3A kitchen task was strongly correlated to the FIM-cog. Using simulated real-life cognitive tests supports the notion that virtual reality improves ecological validity of cognitive testing. Ecological validity is a critical clinimetric property to measure in cognitive tests, to facilitate safe discharge planning and enhance person-centred rehabilitation.

Increasing age was the only demographic feature that was significantly associated with C3A tasks. Handedness did not influence C3A performance. Handedness is an important consideration in the field of stroke, with upper limb motor impairments present in more than 60% of stroke survivors (Broeks et al., 1999). Over half the participants with aphasia used their non-dominant hand to complete C3A tasks. The systematic review, detailed in chapter 2, identified motor limitations as a common exclusion criterion in studies exploring post-stroke cognition. This is thought to be due to a participant's inability to use their upper limb to write and draw in pen-and-paper tests. The findings in chapter 3 indicate that a number of stroke survivors with motor impairments were unable to safely undertake the Kettle Test and were unable to complete several pen-and-paper tasks. The C3A allows stroke survivors to use their non-dominant hand without being disadvantaged.

The C3A is a clinimetrically sound cognitive assessment for stroke survivors, with and without aphasia. C3A performance successfully differentiated between stroke survivors and controls. There was no difference C3A performance between stroke survivors with and without aphasia, demonstrating that language impairments did not confound non-linguistic cognitive performance. The significant association with the FIM-cog confirmed that using functional tasks to assess cognitive skills facilitates strong ecological validity in a cognitive assessment.

#### **7.2.4 The Association Between Language and C3A Performance was Task-dependent**

In chapter 3, all pen-and-paper tests (excluding Star Cancellation) were significantly associated with auditory comprehension and naming in aphasia. To finalise Phase 2 of this research, the methods used in chapter 3 were applied in chapter 6 to determine the association between C3A performance and auditory comprehension and naming in post-stroke aphasia. The relationship with language was more variable across C3A tasks than it was across the pen-and-paper tests. The reaction time task and the sequence copy task errors were not significantly associated with the language measures in aphasia. This suggests that even individuals with severe aphasia are able to complete a psychomotor and visual memory task without their language impairments confounding non-linguistic performance. The kitchen task errors were significantly associated with auditory comprehension and naming performance in aphasia. The design and administration of the C3A was developed to maximise understanding for individuals with poor comprehension. Thus, the association between kitchen task errors and language performance in aphasia may reflect concomitant executive dysfunction observed in aphasia (Harnish & Lundine, 2015; Lambon Ralph et al., 2010) rather than language impairments confounding C3A performance.

### **7.3 Limitations**

The main limitation of the work presented in this thesis was the inability to evaluate criterion validity for the C3A, where ideally, a gold standard non-immersive virtual reality cognitive assessment would be used for comparison. The work in chapter 3 applied alternative validation approaches to evaluate the C3A's validity in stroke. First, a between group comparison was used (stroke aphasia, stroke non-aphasia and controls), which demonstrated that C3A performance was sensitive to detecting cognitive impairment in stroke without language impairments confounding C3A performance. Second, non-verbal pen-and-paper tests were used to evaluate construct validity. These tests are not validated in aphasia and the cognitive results may be confounded by language impairments. Third, ecological validity was explored, where C3A performance was significantly associated with the FIM-cog. Multiple validation approaches were used in this work to ensure the C3A is a valid cognitive assessment for stroke survivors.



A potential bias of this project was that only stroke survivors with aphasia and controls were recruited from the community setting. The primary undertaking of this research was to create a cognitive assessment designed to be inclusive of individuals with post-stroke aphasia, representing up to 30% of the stroke population (Engelter et al., 2006). As the number of participants with aphasia recruited from inpatient hospital settings was insufficient, recruiting was expanded to the community setting to increase the sample size of stroke survivors with aphasia.

All tests were administered in fixed order and the higher number of pen-and-paper tests may have created more potential for missing data and fatigue. During testing, resting periods were provided to minimise the influence of fatigue and the missing data was associated with the more complex executive tasks (e.g., Brixton, Trail Making Test part B). Participant preferences (pen-and-paper vs. C3A) were evaluated and the preference questions was asked following 20 minutes (the time-taken to complete the C3A) to ensure time-taken did not influence responses. Future studies could randomise the testing order to eliminate the potential bias of fixed order testing.

The C3A included a visual search task that was designed to detect visual neglect. Statistical analysis of the visual search task was not possible because only three of the 98 participants made errors. Therefore, the sensitivity of the C3A's visual search task remains undetermined and requires evaluation. Post-stroke visual neglect is likely to negatively influence performance on the remaining C3A tasks that are designed to detect other cognitive processes. Future research that administers the C3A to a group of stroke participants with varying degrees of neglect is needed to address these questions.

#### **7.4 Future Directions**

The work reported in this thesis demonstrated that not all stroke survivors have access to clinimetrically sound assessments to measure their cognitive performance; particularly for individuals with aphasia. The commonly used pen-and-paper cognitive tests are often linguistically-loaded and are not feasible for individuals with aphasia. We used non-immersive virtual reality technology and “aphasia-friendly” techniques to create a cognitive assessment that minimises the language skills needed to complete the tasks – called the C3A.

Evaluating the clinimetric properties of a cognitive assessment is necessary to successfully translate an assessment into clinical practice. Clinimetrics includes the evaluation of psychometric properties and promotes the importance of feasibility and user acceptance in the evaluation of assessments. In chapter 3, feasibility and participant user acceptance of the C3A was explored. Clinical staff feedback was sourced during the development of the C3A, but exploring examiner acceptance following clinical application is now needed. This would include seeking feedback from consumers and clinical examiners. Validation of the C3A was determined in chapter 5, and now test-retest reliability of the C3A requires exploring.

The C3A has the potential to be used in other clinical populations. For example, individuals with traumatic brain injury may experience both motor and language impairments, and the C3A has been tailored to overcome these barriers to testing non-linguistic cognitive performance. Dementia is another disease where individuals may benefit from cognitive testing using the C3A. Individuals with dementia may not experience aphasia, but the deterioration of other cognitive processes (e.g., attention, memory) may prevent individuals' understanding complex instructions. Younger people with neurological injury are a population that may require different needs than older individuals. For example, a cognitive assessment to guide return to work goals may be needed for younger individuals. The C3A tasks are focused in a simulated kitchen setting, but the performance measures may be sensitive to return to work needs. Alternatively, using different simulated scenarios (e.g., work related tasks) can be created, and the "aphasia-friendly" techniques used in the C3A can be applied to different simulated scenarios. Validating the C3A in other clinical populations that are known to experience cognitive impairments is an important future consideration.

The C3A assesses non-linguistic cognitive processes, but expanding the assessment to target other cognitive processes would create a more comprehensive cognitive assessment. For example, the C3A can be expanded to include the assessment of linguistic processes. Developing simulated scenarios to target specific language processes (e.g., auditory phonological analysis, semantic processing), as well as measuring functional communication that requires multiple language and cognitive processes, is possible using virtual reality technology. Creating simulated functional communication scenarios to measure language performance (e.g., ordering a coffee at a café), would be a novel approach that may be more ecologically valid than current pen-

and-paper assessment methods. Using technology to adjust the level of complexity, and manipulate the tasks to assess specific language processes, is something pen-and-paper language tests are unable to offer. Task complexity can be easily manipulated, such as incorporating simulated auditory distractions in a controlled environment (e.g., radio playing in the background) or incorporating scenarios that require dual tasking (e.g., making a cup of tea while responding to questions). This flexibility in assessments aligns with adaptive assessment methods, which have been used for naming in aphasia (Hula, Kellough, & Fergadiotis, 2015). All manipulations can be employed while maintaining scientific rigor when virtual reality technology is used.

Technology will continue developing and health professionals need to be technologically savvy and transition to novel service delivery models to meet the needs of the online patient community. There is increasing emphasis on improving patient centricity, which includes developing “direct-to-patient” models of service delivery. For example, the C3A has the potential to be remotely applied to improve access for hard to reach populations. This may include individuals living in rural and remote areas, or those who live in metropolitan areas but rely on others to attend outpatient therapy. Creating an online option of the C3A to remotely assess cognition may improve health outcomes and satisfaction for individuals living in the community. Validation of a remote version of the C3A would need to be validated; using the face-to-face version of the C3A as a comparison.

The C3A capitalised on virtual reality technology to develop a cognitive assessment for stroke survivors, which overcomes the barriers to assessing non-linguistic cognitive performance in aphasia. The C3A was not designed to be the sole assessment of cognition post-stroke, but it provides clinicians with a clinimetrically sound tool to augment their evaluations and provide an unmet need for assessing cognitive skills in aphasia. The future clinical success of this technology will be driven by the creativity of healthcare professionals in applying it across a range of areas in need and harnessing its potential.

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## Appendix A

Link to URL published manuscript incorporated as chapter 3.

Wall, K. J., Isaacs, M. L., Copland, D.A., & Cumming, T. B. (2015). Assessing cognition after stroke. Who misses out? A systematic review. *International Journal of Stroke*, 46(8), 2206-2211. doi:10.1161/STROKEAHA.113.009522

## Appendix B

### Example of the full search strategy using Ovid Medline

The following example displays MeSH, Boolean operators, keywords, truncations, the explode and focus function used in Ovid Medline. This strategy was applied and modified where necessary to all databases.

```
1      exp *Stroke/
2      exp *Cerebrovascular Disorders
3      1 or 2
4      exp *cognition/
5      exp *Executive Function/
6      exp *Problem Solving/
7      exp *Memory/
8      exp *Attention/
9      exp *Language/
10     exp *Visual Perception/
11     4 or 5 or 6 or 7 or 8 or 9 or 10
12     3 and 11
13     (assess* or screen* or test*).mp
14     (therap* or intervention or rehabilitat*).mp
15     computer simulation/ or computer systems/ or
      computers/ or exp microcomputers/ or software/
16     (Virtual reality or virtual-reality or VR).mp
17     13 or 14
18     15 or 16
19     17 or 18
20     12 and 19
21     limit 20 to year = "2000–Current"
```

## Appendix C

### Characteristics of included studies (ordered by the mode of delivery of assessment, then alphabetically by author)

#### Pen-and-paper (*n* = 80 articles included)

Source	Title	Place	Stroke ( <i>n</i> )	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Akbari et al., 2011)	The correlation of independency in activities of daily living performance with cognitive status and the intensity of neurological impairment in right-handed stroke patients	Iran	27	57.7 ± 8.05	left = 37; right = 37	3.85 ± 1.48	Lowenstein Occupational Therapy Cognitive Assessment (LOCTA)
(Appelros, Karlsson, Tham, Nydevik, & Thorwalls, 2004 )	Unilateral neglect: Further validation of the Baking Tray Task	Sweden	330	76.6 group 1; 74 group 2	left = 200; right = 162 bilateral/ unknown = 15	2–4 weeks, 6 months, then 1 year	Baking Tray Task (BTT)
(Bailey, Riddoch, & Crome, 2000)	Evaluation of a test battery for hemineglect in elderly stroke patients for use by therapists in clinical practice	United Kingdom	107	75.2 ± 7.1	left = 46; right = 61	22.3 ± 11.9 days	The Star Cancellation Test, Line Bisection, Copy-a-Daisy, The Baking Tray Task, Draw-a-Clock
(Blake, McKinney, Treece, Lee, & Lincoln, 2002)	An evaluation of screening measures for cognitive impairment after stroke	United Kingdom	102	70.8 ± 12.2	left weakness = 50; right weakness = 56; bilateral weakness = 1; no signs = 2; unknown = 2	< 4 weeks from hospital admission	Mini-Mental State Examination, Sheffield Screening Test for Acquired Language Disorders, Raven's Coloured Progressive Matrices

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Bocti et al., 2013)	Vascular cognitive impairment: most useful subtests of the Montreal Cognitive Assessment in minor stroke and transient ischemic attack	Canada	285	69.6 ± 14	non-lacunar = 50; lacune = 144; stroke (total) = 172	3 months	Montreal Cognitive Assessment (MoCA)
(Boosman, Visser-Meily, Post, Duits, & van Heugten, 2013)	Validity of the Barrow Neurological Institute (BNI) screen for higher cerebral functions in stroke patients with good functional outcome	Netherlands	54	53.8 ± 12.3	left ischaemic = 44%; left haemorrhage = 50%; right ischaemic = 44%; right haemorrhage = 33.3%; bilateral ischaemic = 8%; bilateral haemorrhage = 16.7; SAH = 42%	15 ± 12.8 weeks	Barrow Neurological Institute Screen (BNI)
(Bour, Rasquin, Boreas, Limburg, & Verhey, 2010)	How predictive is the MMSE for cognitive performance after stroke?	Netherlands	194	68.3 ± 12.5	left = 41.1%; right = 58.9%; cortical = 37.6%	< 48 hours	Mini-Mental State Examination (MMSE)
(Brookes, Hannesdottir, Lawrence, Morris, & Markus, 2012)	Brief Memory and Executive Test: evaluation of a new screening test for cognitive impairment due to small vessel disease	United Kingdom	45	69.7 ± 8.3	small vessel disease defined by clinical lacunar stroke syndrome	>3 months	Brief Memory and Executive Test (BMET)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Brown, Mapleston, Nairn, & Molloy, 2013)	Relationship of cognitive and perceptual abilities to functional independence in adults who have had a stroke	Australia	32	73 ± 4.5	left = 14; right = 18	-	Neurobehavioural Cognitive Status Exam (Cognistat); Developmental Test of Visual Perception Adolescents and Adults (DTVP-A)
(Brown, Mapleston, & Nairn, 2012)	Can cognitive and perceptual standardized test scores predict functional performance in adults diagnosed with stroke: A pilot study	Australia	27	73 (46-91)	left = 44.4%; right = 56.6%; first stroke = 74.1%	subacute	Neurobehavioural Status Examination (Cognistat), Occupational Therapy Adult Perceptual Screening Test, Developmental Test of Visual Perception- Adolescent and Adult
(Brown, Mapleston, & Nairn, 2011)	Convergent validity of the Occupational Therapy Adult Perceptual Screening Test (OT-APST) with two other cognitive-perceptual tests	Australia	32	73 ± 4.5	left = 14; right = 18; first stroke = 24	subacute	Occupational Therapy Adult Perceptual Screening Test (OT-APST)
(Brunila, Jalas, Lindell, Tenovuo, & Hamalainen, 2003)	The Two Part picture in detection of visuospatial neglect	Finland	34	58.6 ± 8.02	right only	16.8 ± 8.9 days	Two Part Picture
(Chan et al., 2008)	The development of a Chinese equivalence version of letter-number span test	China	9	41.89 ± 14	left; more than 1 stroke	5.2 ± 2.21 years	Letter Number (LN) Span Test - Chinese version
(Chen, Koh, Hsieh, & Hsueh, 2009)	Test-retest reliability of two sustained attention tests in persons with chronic stroke	Taiwan	76	58.9 complete d all tests 39	left = 22; right = 17	712.6 (14-2626) days	Conners' Continuous Performance Test (CCPT); Digit Vigilance Test (DVT)



Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Chen, Koh, Hsieh, & Hsueh, 2013)	Test of Everyday Attention in patients with chronic stroke: test-retest reliability and practice effects	Taiwan	90	58.1 ± 12.4	left = 56; right = 34	30.0 ± 25.2 months	Test of Everyday Attention (TEA)
(Chiba & Haga, 2008)	Analysing non-motor bias in unilateral neglect with a new variant of the line bisection task	Japan	9	71 (58-85)	right only	–	Exactly Bisected Line Selection Task (EBLST)
(Cooke, Gustafsson, & Tardiani, 2010)	Clock drawing from the occupational therapy adult perceptual screening test: its correlation with demographic and clinical factors in the stroke population	Australia	179	70.6 ± 13.8	left = 90; right = 107; undetermined = 28	45.4 ± 67.6 days	Clock Drawing (from the occupational therapy adult perceptual screening test)
(Cooke, McKenna, Fleming, & Darnell, 2005)	The reliability of the Occupational Therapy Adult Perceptual Screening Test (OT-APST)	Australia	15	70.5 ± 17.6	left = 4; right = 10	15 ± 13.5 days	The Occupational Therapy Adult Perceptual Screening Test (OT-APST)
(Cooke, McKenna, Fleming, & Darnell, 2006a)	Construct and ecological validity of the Occupational Therapy Adult Perceptual Screening Test (OT-APST)	Australia	208	70.4 ± 14.1	left = 90; right = 107; SDH, ICH or non-specified lateralisation = 5	45.3 ± 66.4 days	The Occupational Therapy Adult Perceptual Screening Test (OT-APST)
(Cooke, McKenna, Fleming, & Darnell, 2006b)	Criterion validity of the Occupational Therapy Adult Perceptual Screening Test (OT-APST)	Australia	208	70.4 ± 14.1	left = 90; right = 107; SDH, ICH or non-specified lateralisation = 5	45.3 ± 66.4 days	Occupational Therapy Adult Perceptual Screening Test (OT-APST)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Cumming, Churilov, Linden, & Bernhardt, 2013)	Montreal Cognitive Assessment and Mini-Mental State Examination are both valid cognitive tools in stroke	Australia	60	72.1 ± 13.9	left = 20; right = 31; bilateral = 2; not visible on scan = 7	98.3 ± 12.0 days, then 8.1 ± 2.4 days after initial testing	Montreal Cognitive Assessment (MoCA); Mini-Mental State Examination (MMSE)
(Cumming, Bernhardt, & Linden, 2011)	The Montreal Cognitive Assessment: short cognitive evaluation in a large stroke trial	Australia	294	70.6 ± 12.8	mild stroke = 131, moderate stroke = 95, severe stroke = 68 (measured by NIHSS*)	3 months	Montreal Cognitive Assessment (MoCA)
(de Koning, Dippel, van Kooten, & Koudstaal, 2000)	A short screening instrument for poststroke dementia: the R-CAMCOG	Netherlands	238	69.2 ± 8.1	left = 116; right = 133; Infratentorial = 35	3-9 months	Rotterdam-CAMCOG (the cognitive and self-contained part of the Cambridge Examination for Mental Disorders of the Elderly)
(El Hachoui, Sandt-Koerрман, Dippel, Koudstaal, & Visch-Brink, 2012)	The ScreeLing: Occurrence of linguistic deficits in acute aphasia post-stroke	Netherlands	141	66.1 ± 14.9	left = 139; right = 2	acute 2–14 days chronic > 6 months	ScreeLing
(Flamand-Roze et al., 2011)	Validation of a New Language Screening Tool for Patients With Acute Stroke: The Language Screening Test (LAST)	France	300	62.6 ± 5.1	–	acute (< 24 hrs) and chronic	Language Screening Test (LAST)
(Gaber, Parsons, & Gautam, 2011)	Validation of the language component of the Addenbrooke's Cognitive Examination-Revised (ACE-R) as a screening tool for aphasia in stroke patients	United Kingdom	39	72 ± 11.9	left = 34; right = 11; bilateral = 14	(most admitted 3–7 days)	Addenbrooke's Cognitive Examination-revised (ACE-R, language component only)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Godefroy et al., 2011)	Is the Montreal Cognitive Assessment superior to the Mini-Mental State Examination to detect poststroke cognitive impairment	France	95	68.2 ± 13.7	left = 39; right = 44; bilateral = 12	< 3 weeks	Montreal Cognitive Assessment (MoCA); Mini-Mental State Examination (MMSE)
(Greve, Lindberg, Bianchini, & Adams, 2000)	Construct validity and predictive value of the Hooper Visual Organization Test in stroke rehabilitation	United States	101	70.7 ± 9.69	left = 29; right = 55; bilateral = 17	–	Hooper Visual Organisation Test (HVOT)
(Halper & Cherney, 2007)	Right hemisphere stroke and the California Verbal Learning Test: a preliminary study	United States	52	66.85 ± 12.12	single right	35.4 ± 28.33	California Verbal Learning Test (CVLT)
(Hargrave et al., 2012)	Two brief measures of executive function in the prediction of driving ability after acquired brain injury	United States	48	58.4 ± 15 median = 58	–	–	Frontal Assessment Battery (FAB); Trail Making Test - part B (TMT-B)
(Hoffmann, Schmitt, & Bromley, 2009)	Comprehensive cognitive neurological assessment in stroke	United States	1796	62.4 ± 16.38	left = 646; right = 275; hippocampal limbic = 397; frontal = 908; occipito-temporal = 107; miscellaneous = 481	–	Comprehensive cognitive neurological test in stroke (Coconuts)
(Hoffmann & Schmitt, 2006)	Metacognition in stroke: Bedside assessment and relation to location, size, and stroke severity	United States	132	45.7 (95% CI: 43.4, 48.1)	TOAST classification provided in article	< 4 weeks	Frontal Network Syndrome Score (FNSS)
(Jodzio & Biechowska, 2010)	Wisconsin Card Sorting Test as a measure of executive function impairments in stroke patients	Poland	44	56 ± 15	left = 22; right = 22; single	10 ± 5 days	Wisconsin Card Sorting Test (WCST)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Johnson-Greene, Touradji, & Emmerson, 2009)	The Three Cities Test: Preliminary validation of a short bedside memory test in persons with acute stroke	United States	60	70.4 ± 2.1	left = 15; right = 34, subcortical = 9; brainstem = 2	11.7 ± 5.1 days	Three Cities Test (TCT)
(Kato et al., 2012)	The relationship between visuospatial ability and cognitive function in patients with right-hemisphere infarction	Japan	54	69.3 ± 11.1	right only	–	Behavioural Inattention Test (BIT); Mini-Mental State Examination (MSSE)
(Katz, Averbuch, & Bar-Haim Erez, 2012)	Dynamic Lowenstein Occupational Therapy Cognitive Assessment–Geriatric Version (DLOTCA-G): Assessing change in cognitive performance	Israel	61	77.6 ± 6.18	first stroke	–	Dynamic Lowenstein Occupational Therapy Cognitive Assessment–Geriatric Version (DLOTCA-G)
Katz, Hartman-Maeir, Ring, and Soroker (2000)	Relationships of cognitive performance and daily function of clients following right hemisphere stroke: Predictive and ecological validity of the LOTCA battery	Israel	40	54.4 ± 10.1 neglect; 58.6 ± 8 no neglect	single right	< 12 months (admission to rehabilitation); discharge from rehabilitation; then 6 months post discharge	Lowenstein Occupational Therapy Cognitive Assessment (LOTCA)
Kessels, Nys, Brands, van den Berg, and Van Zandvoort (2006)	The modified Location Learning Test: Norms for the assessment of spatial memory function in neuropsychological patients	Netherlands	105	59.5 ± 14	left = 39; right = 34; bilateral = 3	7.5 ± 1.3 months	modified Location Learning Test (mLLT)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Kim, Kim, Kim, & Heo, 2011)	Differentiating between aphasic and nonaphasic stroke patients using semantic verbal fluency measures with administration time of 30s	Korea	53	67.13 ± 13.09 aphasic; 64.04 ± 12.30 non-aphasic	Infarction	–	semantic verbal fluency (30s)
(Kizony & Katz, 2002)	Relationships between cognitive abilities and the process scale and skills of the Assessment of Motor and Process Skills (AMPS) in patients with stroke	Israel	3	71.33 ± 8.39	right = 23; left = 7	4.8 ± 2.89 weeks	Assessment of Motor and Process Skills (AMPS)
(Korner-Bitensky et al., 2000)	Visual testing for readiness to drive after stroke: A multicenter study	United States; Canada	269	63.6 ± 12.5	–	6.9 ± 11 months	Motor-Free Visual Perception Test (MVPT)
(Larson, Kirschner, Bode, Heinemann, & Goodman, 2005)	Construct and predictive validity of the repeatable battery for the assessment of neuropsychological status in the evaluation of stroke patients	United States	158; 36 follow-up	study 1: 64.27 ± 14.45; study 2: 63.21 ± 16.19	study 1: left = 44%; right = 49%; bilateral = 7% study 2: left = 25%; right = 67%; bilateral = 8%	20 ± 19.4 days	Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)
(Larson et al., 2003)	Brief cognitive assessment and prediction of functional outcome in stroke	United States	34	65 (31–85)	left = 32.4%; right = 61.7%; bilateral = 5.9%	15 (4–44) days	Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)
(B. H. Lee et al., 2004)	The Character-line Bisection Task: A new test for hemispatial neglect	Korea	80	60.9 ± 11.3	right only	8.9 ± 10.5 days	Character-line Bisection Task (CLBT)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Leeds et al., 2001)	A comparison of the new executive functioning domains of the CAMCOG-R with existing tests of executive function in elderly stroke survivors	United Kingdom	83	75.4 ± 8.1	–	1 and 3 months	Cambridge Cognitive Examination–Revised (CAMCOG-R)
(Leibovitch et al., 2012)	A short bedside battery for visuoconstructive hemispatial neglect: Sunnybrook Neglect Assessment Procedure (SNAP)	Canada	224	72	left = 99; right = 125	7 ± 4 days	Sunnybrook Neglect Assessment Procedure (SNAP)
(Maeshima et al., 2001)	Factor analysis of the components of 12 standard test batteries, for unilateral spatial neglect, reveals that they contain a number of discrete and important clinical variables	Japan	94	63.0 ± 12.1	right with unilateral spatial neglect	22.3 ± 37.3 months	12 standard test batteries for unilateral neglect
(D. W. Man & Li, 2002)	Assessing Chinese adults' memory abilities: Validation of the Chinese Version of the Rivermead Behavioral Memory Test	Hong Kong	86	44 ± 17	single unilateral cortical lesion	< 6 months	Rivermead Behavioral Memory Test-Chinese Version (RBMT-CV)
(D. W. Man, Tam, & Hui-Chan, 2006)	Prediction of functional rehabilitation outcomes in clients with stroke	Hong Kong	148	70.4 ± 10.06	Right hemiparesis = 49%, left hemiparesis = 49.7; bilateral = 0.6%	< 4 weeks	Neurological Cognitive Status (NCS)
(Mark, Woods, Mennemeier, Abbas, & Taub, 2006)	Cognitive assessment for CI therapy in the outpatient clinic	United States	29	Upper extremity = 59.6 ± 20.6, lower extremity = 62.8 ± 14.2	equal proportions of left and right hemisphere lesion lateralisation	> 6 months	Mini Mental State Examination; Sustained Attention to Response Task (SART), Logical Memory and Visual Reproduction subtests from the Wechsler Memory Scale, Trail Making Test - B (TMT-B)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Mast et al., 2000)	Clinical utility of the Normative Studies Research Project Test Battery among Vascular Dementia patients	United States	65	76.57 ± 8.36	–	–	Normative Studies Research Project Test Battery among Vascular Dementia
(Mattingley et al., 2004)	The Greyscales Task: A perceptual measure of attentional bias following unilateral hemispheric damage	Australia	98	left = 64.4 ± 15.6; right = 60.7 ± 13.9	left = 20; right = 78	1–26 weeks	The Greyscale Task
(McKinney et al., 2002)	Evaluation of cognitive assessment in stroke rehabilitation	United Kingdom	228	71 ± 12.2	previous stroke = 41	< 4 weeks	Combination of assessments
(Messinis, Lyros, Georgiou, & Papathanasopoulos, 2009)	Benton Visual Retention Test performance in normal adults and acute stroke patients: Demographic considerations, discriminant validity, and test-retest reliability	Greece	28	67.43 ± 6.73	left = 12; right = 16	6.14 ± 2.16	Benton Visual Retention Test (BVRT)
(Mirena, Boyko, & Dora, 2012)	Screening for poststroke cognitive impairment via Mini Mental State Examination and Montreal Cognitive Assessment scale	Bulgaria	54	63.17 ± .96	first stroke	90 days	Mini Mental State Examination (MMSE); Montreal Cognitive Assessment (MoCA)
(Mok et al., 2004)	The validity and reliability of Chinese Frontal Assessment Battery in evaluating executive dysfunction among Chinese patients with small subcortical infarct	Hong Kong	30	73.5 ± 4.6	subcortical infarct = 6; cerebral white matter = 10; thalamus = 7; multiple = 7	> 3 months	Chinese Frontal Assessment Battery (CFAB)
(Nys, Van Zandvoort, De Kort, Jansen, Kappelle, et al., 2005)	Restrictions of the Mini-Mental State Examination in acute stroke	Netherlands	34	64.7 ± 11.5	left = 17; right = 17	4.2 ± 2.4 days	Mini Mental State Examination (MMSE)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Ojala-Oksala et al., 2012)	Educational history is an independent predictor of cognitive deficits and long-term survival in postacute patients with mild to moderate ischemic stroke	Finland	486	median = 72 ± 11	ischemic, previous stroke = 22%	3 months; then 12 month follow-up	unspecified comprehensive neuropsychological assessments
(Oneş et al., 2009)	Effects of age, gender, and cognitive, functional and motor status on functional outcomes of stroke rehabilitation	Istanbul	88	63.14 ± 10.14	left = 53; right = 35	9.3 ± 2.4 months	Mini Mental State Examination (MMSE)
(Ownsworth & Shum, 2008)	Relationship between executive functions and productivity outcomes following stroke	Australia	27	47.3 ± 10.7	left = 12; right = 11	2.1 ± 1.6 years	Multiple executive function tests
(Pendlebury, Cuthbertson, Welch, Mehta, & Rothwell, 2010)	Underestimation of cognitive impairment by Mini-Mental State Examination versus the Montreal Cognitive Assessment in patients with transient ischemic attack and stroke: A population-based study	United Kingdom	413	69.9 ± 12.4	–	6 month or 5 year follow-up	Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA)
(Pendlebury, Mariz, Bull, Mehta, & Rothwell, 2012)	MoCA, ACE-R, and MMSE versus the National Institute of Neurological Disorders and Stroke-Canadian Stroke Network Vascular Cognitive Impairment Harmonization Standards Neuropsychological Battery after TIA and stroke	United Kingdom	55	73.4 ± 11.6	–	1 or 5 year follow-up	Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Addenbrooke's Cognitive Examination-Revised (ACE-R)
(Pulsipher, Stricker, Sadek, & Haaland, 2013)	Clinical utility of the Neuropsychological Assessment Battery (NAB) after unilateral stroke	Mexico	69	left = 65.1 ± 11.4; right = 60.8 ± 10.2	left = 36; right = 33	5.9 ± 6.2 years	Neuropsychological Assessment Battery (NAB)



Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Salvadori et al., 2013)	Predictive value of MoCA in the acute phase of stroke on the diagnosis of mid-term cognitive impairment	Italy	137	68.2 ± 14.6 (follow-up); 71.8 ± 11.9 (no follow-up)	left no cognitive impairment = 55%; left cognitive impairment = 51%	5th and 9th day post-stroke; then 8.4 ± 2.2 months for follow-up	The Montreal Cognitive Assessment (MoCA)
(Shopin et al., 2013)	Cognitive assessment in proximity to acute ischemic stroke/transient ischemic attack: Comparison of the Montreal Cognitive Assessment test and MindStreams Computerized Cognitive Assessment Battery	Israel	316	68 ± 10.1	first ever mild to moderate stroke	< 3 days	Montreal Cognitive Assessment (MoCA); MindStreams Computerized Cognitive Battery
(Srikanth et al., 2006)	The validity of brief screening cognitive instruments in the diagnosis of cognitive impairment and dementia after first-ever stroke	Australia	99	69 ± 14.4	left = 29; right = 39; bilateral = 15	3 months (381.6 ± 45.6 days); 1 year (438.3 ± 83.9 days)	standardized Mini Mental State Examination(s-MMSE)
(Soyuer, Erdogan, & Ozturk, 2007)	Is there any relation between cognitive function and functional state in stroke patients?	Turkey	69	-	first stroke	-	Mini Mental State Examination (MMSE)
(Su, Lin, Kwan, & Guo, 2008)	Construct validity of the Wisconsin card sorting test-64 in patients with stroke	Taiwan	112	56.42 ± 8.7	left = 45; right = 63; bilateral = 4	90.84 ± 61.5	Wisconsin Card Sorting Test (WCST)
Tamez et al 2011 (120) (Tamez et al., 2011)	Assessing executive abilities following acute stroke with the Trail Making Test and Digit Span	United states	689	frontal = 63.5 ± 12.8; non-frontal = 62.5 ± 11.6	frontal and non-frontal groups	< 72 hours	Trail Making Test (TMT) and Digit Span

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(Tesio, Longo, & Rota, 2011)	The Subjective Visual Vertical: Validation of a simple test	Italy	3	69-87	left = 2; right = 1	4–10 weeks	Subject Visual Vertical
(Thommessen et al., 2002)	Validity of the aphasia item from the Scandinavian Stroke Scale	Norway	33	75.5 (45–96)	–	3-8 days	Aphasia item from the Scandinavian Stroke Scale
(Toglia, Fitzgerald, O'Dell, Mastrogiovanni, & Lin, 2011)	The Mini-Mental State Examination and Montreal Cognitive Assessment in persons with mild subacute stroke: Relationship to functional outcome	United States	72	70 ± 17	left = 27; right = 56; bilateral = 5	median = 8.5 days	Mini-Mental State Examination (MMSE); Montreal Cognitive Assessment (MoCA)
(van den Berg et al., 2009)	The Brixton Spatial Anticipation Test as a test for executive function: Validity in patient groups and norms for older adults	Netherlands	106	59.5 ± 14.2	left = 42; right = 37; bilateral = 3; brainstem or cerebellum = 15; unclear = 9	7.5 ± 1.3 months	Brixton Spatial Anticipation Test
(van der Zwaluw, Valentijn, Nieuwenhuis-Mark, Rasquin, & Van Heugten, 2011)	Cognitive functioning in the acute phase poststroke: A predictor of discharge destination?	Netherlands	188	71.3 ± 11.7	left = 48; right = 92	Acute phase	Mini-Mental State Examination (MMSE); Clock Drawing Test (CDT); Cognitive Screening Test (CST)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke subtype	Post-stroke onset (mean)	Name of pen-and-paper cognitive assessment
(van Zandvoort, Kessels, Nys, De Haan, & Kappelle, 2005)	Early neuropsychological evaluation in patients with ischaemic stroke provides valid information	Netherlands	57	56 ± 16	first ever; left = 21; right = 27; bilateral = 4; infratentorial ischaemic = 5	11.2 ± 6.7 days and 12–24 months	sub test of the Wechsler Adult Intelligence Scale (WAIS), 12-item short form of the Raven Advanced Progressive Matricesk, Boston Naming Test, Verbal Fluency, Digit Span, Rey Auditory Verbal Learning Task (RAVLT, Corsi Block Tapping Task and more)
(Verhoeven, Schepers, Post, & M., 2011)	The predictive value of cognitive impairments measured at the start of clinical rehabilitation for health status 1 year and 3 years poststroke	Netherlands	134	56.5 ± 11.3	right = 59.7%	1 and 3 years	Cambridge Cognitive Examination (CAMCOG)
(Wendel et al., 2008)	Long-term cognitive functional limitations post stroke: Objective assessment compared with self-evaluations and spouse reports	Swedish	84	median = 74 (31–94)	left = 51%; right = 39%; bilateral 5%; unknown = 5%	18–36 months	Cognistat
(Woods & Mark, 2007)	Convergent validity of executive organization measures on cancellation	Netherlands	29	69.6 ± 10	left = 8; right = 21	–	Star Cancellation Test (modified version)
(Zuverza-Chavarria & Tsanadis, 2011)	Measurement properties of the CLOX Executive Clock Drawing Task in an inpatient stroke rehabilitation setting	United States	112	58.8 ± 13.3	left = 30%; right = 52%; bilateral = 8%; could not be lateralized = 11%	–	CLOX Executive Clock Drawing Test
(Zwecker et al., 2002)	Mini-Mental State Examination, cognitive FIM instrument, and the Loewenstein Occupational Therapy Cognitive Assessment: Relation to functional outcome of stroke patients	Israel	66	72 ± 8.9	left = 34; right = 26; other = 6; previous stroke = 10	4 (1–56) days	Mini-Mental State Examination; Loewenstein Occupational Therapy Cognitive Assessment (LOCTA)

**Virtual reality (n = 12 articles)**

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke sub-type	Post-stroke onset (mean)	Name of virtual reality cognitive assessment
(Broeren, Samuelsson, Stibrant-sunnerhagen, Blomstrand, & Rydmark, 2007)	Neglect assessment as an application of virtual reality	Sweden	8	54 (44–63)	right	7–39 weeks	Star Cancellation Task (virtual reality version)
(Brooks, Rose, Potter, Jayawardena, & Morling, 2004)	Assessing stroke patients' prospective memory using virtual reality	United Kingdom	42	–	Left = 20; right = 21; bilateral = 1	1 week to 2 months	Virtual reality based prospective memory task
(Buxbaum et al., 2012)	Reliability and validity of the Virtual Reality Lateralized Attention Test in assessing hemispatial neglect in right-hemisphere stroke	United States	70	59.5 (21–29)	single right	29 months (5–87)	Virtual Reality Lateralized Attention Test (VRLAT)
(Buxbaum et al., 2008)	Assessment of spatial attention and neglect with a Virtual Wheelchair Navigation Task	United States	9	57.3 ± 14.6	single right	31.9 ± 23.1 months	Virtual Reality Wheelchair Navigation Test
(Jannink et al., 2009)	Assessment of visuospatial neglect in stroke patients using virtual reality: A pilot study	Netherlands	12	sub-acute = 51.2 ± 10.6; chronic = 61.8 ± 13.6	unilateral right	sub-acute = 69.4 ± 25.0 months; chronic = 276.2 ± 91.1 months	3D neglect test by means of virtual reality

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke sub-type	Post-stroke onset (mean)	Name of virtual reality cognitive assessment
(Kang et al., 2008)	Development and clinical trial of virtual reality-based cognitive assessment in people with stroke: Preliminary study	Korea	20	54.8 ± 8.9	Left = 6; right = 14	12.2 ± 12.5 months	Virtual Shopping Stimulator
(Rand, et al. Rand, Basha-Abu Rukan, Weiss, & Katz, 2009)	Validation of the Virtual MET as an assessment tool for executive functions	Israel	9	64.2 ± 7.7	left = 3; right = 6	n = 4 27–72 months; n = 5 4–9 months	Virtual Multiple Errands Test (MET)
(Rand et al., 2007)	Evaluation of virtual shopping in the VMall: Comparison of post-stroke participants to healthy control groups	Israel	14	65.4 (39-75)	left = 4; right = 10	n = 11 1–5 months; n=3 9, 27 and 96 months	Vmall
(S. Raspelli et al., 2011)	Validation of a Neuro Virtual Reality-based version of the Multiple Errands Test for the assessment of executive functions	Italy	5	59.6 ± 9.24	selected based on severity of impairment	–	Neuro Virtual Reality - Multiple Errands Test (MET)
(Weiss et al., 2003)	Design and testing of a virtual environment to train stroke patients with unilateral spatial neglect to cross a street safely	Israel	6	55-75	Right only	> 6 weeks	Virtual crossing a street
(Yip & Man, 2009)	Validation of a computerized cognitive assessment system for persons with stroke: A pilot study	Hong Kong	14	67 ± 7.5	left and right	> 2 weeks	Intelligent Cognitive Assessment System (ICAS)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke sub-type	Post-stroke onset (mean)	Name of virtual reality cognitive assessment
(Yip, 2010)	Validation of the Intelligent Cognitive Assessment System (ICAS) for stroke survivors	Hong Kong	66	72.8 ± 8.8	left = 33; right = 33	sub-acute (> 2weeks); rehabilitation (2-8weeks); community (>8weeks)	Intelligent Cognitive Assessment System (ICAS)

### Computer (n = 6 articles)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke sub-type	Post-stroke onset (mean)	Name of computer-based cognitive assessment
(Chen et al., 2009)	Test-retest reliability of two sustained attention tests in persons with chronic stroke	Taiwan	39	58.9 (32.5–82.6)	left = 22; right = 17	712.6 days (14-2626 days)	Conners' Continuous Performance Test (CCPT); Digit Vigilance Test (DVT)
(Cumming et al., 2012)	Cutting a long story short: Reaction times in acute stroke are associated with longer term cognitive outcomes	Australia	33	75.5 ± 11.9	left = 16; right = 15	5.4 ± 2.9 days (baseline), then 3 months	CogState
(George et al., 2008)	Validation of the Visual Recognition Slide Test with stroke: A component of the New South Wales occupational therapy off-road driver rehabilitation program	Australia	26	65.6 ± 13.2	left = 7; right = 15; other = 4	median = 83.5 days	Visual Recognition Slide Test (VRST)
(D. W. K. Man, Chung, & Mak, 2009)	Development and validation of the Online Rivermead Behavioral Memory Test (OL-RBMT) for people with stroke	Hong Kong	30	-	single, cortical lesion	-	Online Rivermead Behavioral Memory Test (OL-RBMT)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke sub-type	Post-stroke onset (mean)	Name of computer-based cognitive assessment
Mazer et al. (2001)	Use of the UFOV to evaluate and retrain visual attention skills in clients with stroke: A pilot study	Canada	52	65.2 ± 11.3	left = 26; right = 26	69 days (35–194)	Useful Field of View (UFOV)
(Shopin et al., 2013)	Cognitive assessment in proximity to acute ischemic stroke/transient ischemic attack: comparison of the Montreal Cognitive Assessment Test and MindStreams Computerized Cognitive Assessment Battery	Israel	316	68 ± 10.1	first ever mild to moderate stroke	< 3 days	MindStreams Computerized Cognitive Assessment Battery; Montreal Cognitive Assessment (MoCA)

#### Functional observational performance (n = 5 articles)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke sub-type	Post-stroke onset (mean)	Name of functional observational performance cognitive assessment
(Baum et al., 2008)	Reliability, validity, and clinical utility of the Executive Function Performance Test: A measure of executive function in a sample of people with stroke	United States	73	64.49 ± 14.28	mild n = 59; moderate n = 14	approximately 6 months	Executive Function Performance Test (EFPT)
(Cederfeldt et al., 2011)	Concurrent validity of the Executive Function Performance Test in people with mild stroke	Sweden	31	72 ± 10.9	left = 9; right = 14	median = 4 days of first assessment	Executive Function Performance Test (EFPT)
(Hartman-Maeir et al., 2009)	Kettle Test – A brief measure of cognitive functional performance: Reliability and validity in stroke rehabilitation	Israel	reliability 21; validity 36	reliability 79.3 ± 5.8; validity 74.8 ± 7.32	Validity left = 18; right = 18	Validity 63.1 ± 29.2	Kettle Test

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke sub-type	Post-stroke onset (mean)	Name of functional observational performance cognitive assessment
(Marom et al., 2006)	The relationship between the Assessment of Motor and Process Skills (AMPS) and the Large Allen Cognitive Level (LACL) test in clients with stroke	Israel	30	65.9 ± 7.34	left = 17; right = 11; unknown = 2	15 ± 16.5 months	Assessment of Motor and Process Scales (AMPS); Large Allen Cognitive Levels (LACL)
(Wolf et al., 2010)	Feasibility of using the EFPT to detect executive function deficits at the acute stage of stroke	United States	20	58.8 ± 13.2	mild to moderate	1 week	Executive Function Performance Test (EFPT)

#### Informant (n = 3 articles included)

Source	Title	Place	Stroke (n)	Age (mean years)	Stroke sub-type	Post-stroke onset (mean)	Name of informant-based cognitive assessment
(Aben et al., 2009)	Metamemory and memory test performance in stroke patients	Netherlands	57	55.04 ± 11.6	left = 17; right = 35; brainstem = 5	highly variable	Memory Self-Efficacy (MSE)
(Barber & Stott, 2004)	Validity of the Telephone Interview for Cognitive Status (TICS) in post-stroke subjects	–	64	median = 72 (IQR 63–80)	left = 33; right = 31	median = 118 days (IQR 84–142)	Telephone Interview for Cognitive Status (TICS)
(Maki et al., 2000)	Validity of the Short-Memory Questionnaire in vascular dementia	Japan	26	79.3 ± 6.1	single or multiple infarct	–	Short-term memory Questionnaire (SMQ)



**Telephone (n = 3 articles included)**

<b>Source</b>	<b>Title</b>	<b>Place</b>	<b>Stroke (n=)</b>	<b>Age (mean years)</b>	<b>Stroke sub-type</b>	<b>Post-stroke onset (mean)</b>	<b>Name of telephone-based cognitive assessment</b>
(Gavett et al., 2013)	Bi-factor analyses of the Brief Test of Adult Cognition by telephone	United States	117	55.8 ± 12.3	–	12 months to lifetime	Brief Test of Adult Cognition
(Higginson et al., 2010)	Neurocognitive predictors of performance on a telephone task following stroke	United States	51	69.4 ± 10.5	left = 10; right = 39; bilateral = 2; brainstem and cerebellar excluded	Post-acute	Hopkins Telephone Task
(Pendlebury et al., 2013)	Telephone assessment of cognition after transient ischemic attack and stroke: Modified telephone interview of cognitive status and telephone Montreal Cognitive Assessment versus face-to-face Montreal Cognitive Assessment and neuropsychological battery	United Kingdom	91	73.4 ± 7	–	1 year; then 5 year follow-up	Telephone Montreal Cognitive Assessment

## Appendix D

### Frequency of exclusion sub-categories used by the different modes of cognitive assessments

Mode of cognitive assessments (*n* = articles)

Exclusion sub-categories (% = frequency of sub-categories used)		Pen-and-paper ( <i>n</i> = 80)	Virtual reality ( <i>n</i> = 12)	Computer ( <i>n</i> = 6)	Functional* ( <i>n</i> = 5)	Informant ( <i>n</i> = 3)	Telephone ( <i>n</i> = 3)
COGNITION	Dementia	32	36	33	40	0	67
	General cognition	13	27	17	0	0	0
	Visual perception	12	54	33	0	33	0
	Re-current stroke / other neuropathology	37	27	17	40	0	67
COMMUNICATION	Aphasia	29	9	0	40	100	33
	Non-native language	31	0	33	20	0	0
	General language	29	54	33	20	33	0
	Motor speech	3	0	0	20	0	0
ENDURANCE	Attention	4	18	7	0	0	0
	Fatigue / endurance	9	0	17	0	0	0
	Reduced consciousness	26	0	0	20	0	0
	Medically unstable	22	18	50	0	0	33
SENSORY	Hearing	19	27	17	20	50	33
	Visual	32	46	50	40	0	33
PSYCHIATRIC	Psychiatric Disease	32	18	33	20	0	0
	Depression	14	18	17	0	33	0
	Substance abuse	13	18	0	0	0	0
MOTOR	Limb weakness	19	73	33	0	0	0
	Hemiparesis	4	0	0	0	50	0

\*Functional observational performance

## Appendix E

Link to URL published manuscript incorporated as chapter 3.

[Wall, K. J., Cumming, T. B., Copland, D. A. \(2017\). Determining the association between language and cognitive tests in post-stroke aphasia, 8\(149\) Frontiers in Neurology, doi: 10.3389/fneur.2017.00149](#)

## Appendix F

Link to URL published manuscript incorporated as chapter 4.

[Wall, K. J., Cumming, T. B., Koenig, S. T., Pelecanos, A. M., & Copland, D. A. \(2017\). Using technology to overcome the language barrier: The Cognitive Assessment for Aphasia App. \*Disability and Rehabilitation\*, 19\(1\), 1-12. doi:10.1080/09638288.2017.1294210](#)

## Appendix G

### Description of the Cognitive Assessment for Aphasia App (C3A)

#### Apparatus

An Android Samsung Galaxy NotePro (12.2 inch) tablet was used to run the C3A. Anonymous data were saved to a cloud storage service Parse during testing. Offline data storage was available if an internet connection was unavailable. Time stamps were saved with each user interaction.

A standardised script was developed, which included short, simple verbal explanations. Measures to evaluate cognitive performance included latency times and errors (commission, omission and sequencing errors). The C3A was divided into four distinct tasks:

#### Simple reaction time task

Participants were instructed to touch the target stimulus – a milk carton displayed in the centre of the screen – as quickly as possible. A correct response was verified by a “click” sound followed by the milk carton disappearing from the screen. If the milk carton was untouched, it remained on the screen for 12s before continuing to the next screen. Inter-stimulus intervals were variable, but they were identical across participants. Five practice trials were provided, followed by 15 test trials.

One trial was defined as one stimuli displayed on the screen. Five practice trials were provided, followed by 15 test trials. Scoring included recording the latency mean (for a normal distribution), or latency median (for a non-normal distribution), for correct responses over the 15 test trials. Thus, a single outcome measure was used in the data analyses.

#### Visual search task

This task consisted of a four by four grid containing four target items – milk cartons – with three semantically and visually related distractors (e.g., glass of milk, juice carton). The target stimulus was consistent with the reaction time task to minimise added instructions.

Participants were asked to touch all the milk cartons using one finger. Feedback for a correct and incorrect response was consistent with the reaction time task. If participants were unable to identify all the milk cartons within 12s a new grid would be displayed. Five trials were displayed for practice, followed by 10 test trials.

One trial was defined as the completion of a single grid. There were two separate scores for this task; number of errors and latency. The mean (for a normal distribution), or median (for a non-normal distribution), for the errors and latencies over the 10 test trials were obtained.

### **Sequence copy tasks**

An interactive 3D kitchen setting (see Figure 1) was used to display functional sequences (e.g., open cupboard door, get the mug out, close cupboard door, finish sequence button). Participants were asked to view the sequence, then copy the sequence exactly how they viewed it. They were encouraged to complete as much of the sequence as they could remember. Up to three practice trials were offered using the same sequence, followed by five different sequences for testing. If the participant was unable to demonstrate understanding in the first practice trial, a second practice trial could be modelled by the examiner. The participant was required to attempt the final practice independently to continue testing. Each sequence increased in complexity by increasing the number of steps in the sequence.

The total errors and latency over the five separate test trials were obtained. The mean (for a normal distribution), or median (for a non-normal distribution), for the errors and latencies were used in the data analyses.

### **Kitchen task**

Participants were asked to make a cup of tea with milk and place the dessert on the plate in the interactive 3D kitchen. To augment the verbal instructions, a picture and written description of the finished items were displayed on the screen. Kitchen items were not displayed on the kitchen bench (e.g., mugs were in the cupboard, milk was in the fridge), thus participants were required to access the items accordingly. Practice trials were not offered for this task. Elements of the final kitchen task were replicated from the previous sequencing task. The inclusion of novel elements (e.g., locating the dessert and placing it

on a plate) was to ensure that participants used problem solving skills, rather than being fully reliant on their memory.

Scoring of sequencing errors differed in the kitchen task compared to the previous sequence copy task. Participants were asked to complete the kitchen task in an order that would be logical and safe in real-life, rather than copying the sequences that were previously seen in the sequence copy task. In the kitchen task, three different kind of errors were recorded (sequencing, commission and omission) and latency. An example of a sequence error would be if the participant stirred an empty mug with the teaspoon prior to pouring the hot water in the mug. If the participant selected an item that was unrelated to the required task (e.g., a random background selection or selecting a piece of fruit), this was recorded as a commission error. If the participant missed an item related to the task (e.g., they did not pour the hot water into the mug), this was scored as an omission error. In the final regressions, the median of the total errors (e.g., combined sequencing, commission and omission errors) were used for the data analyses. The median latency was also used for data analyses.

## Appendix H

**C3A raw data: latency times, commission errors, omission errors and sequencing errors**

<b>Task</b>	<b>Aphasia <i>n</i>, median (interquartile range)</b>	<b>Stroke non-aphasia <i>n</i>, median (interquartile range)</b>	<b>Controls <i>n</i>, median (interquartile range)</b>
<b>Simple Reaction Time, <i>n</i></b>	35	29	32
Latency (s)	0.69 (0.60–0.77)	0.71 (0.60–0.86)	0.55 (0.52–0.62)
<b>Visual Search task, <i>n</i></b>	35	29	31
Latency (s)	0.88 (0.71–1.22)	0.90 (0.784–1.03)	0.60 (0.54–0.78)
Commission errors	0 (0–1.0)	1.0 (0–2.0)	0 (0–0)
Omission errors	0 (0–0)	0 (0–0)	0 (0–0)
<b>Sequence Copy task 1, <i>n</i></b>	35	28	32
Latency (s)	5.77 (4.76–6.18)	5.08 (4.24–6.46)	5.39 (5.01–6.03)
Commission errors	0 (0–3.0)	1.0 (0–2.0)	0 (0–1.0)
Omission errors	0 (0–1.0)	0 (0–0)	0 (0–0)
<b>Sequence Copy task 2, <i>n</i></b>	35	27	32
Latency (s)	5.77 (4.76–6.18)	5.08 (4.24–6.46)	5.39 (5.01–6.03)
Commission errors	0 (0–3.0)	1.0 (0–3.0)	0 (0–1.5)
Omission errors	0 (0–1.0)	0 (0–0)	0 (0–0)
Sequencing errors	0 (0–0)	0 (0–0)	0 (0–0)



<b>Task</b>	<b>Aphasia <i>n</i>, median (interquartile range)</b>	<b>Stroke non-aphasia <i>n</i>, median (interquartile range)</b>	<b>Controls <i>n</i>, median (interquartile range)</b>
<b>Sequence Copy task 3, <i>n</i></b>	34	26	31
Latency (s)	5.55 (4.61–7.14)	5.02 (3.86–6.98)	5.09 (3.39–5.48)
Commission errors	2.0 (1.0–5.0)	2.0 (0–4.0)	1.0 (0–2.0)
Omission errors	1.0 (0–2.0)	1.0 (0–2.0)	0 (0–1.0)
Sequencing errors	0 (0–1.0)	1.0 (0–1.0)	0 (0–1.0)
<b>Sequence Copy task 4, <i>n</i></b>	33	27	31
Latency (s)	5.62 (4.19–7.26)	4.97 (3.44–6.96)	5.10 (4.52–5.62)
Commission errors	3.0 (1.0–5.0)	1.0 (0–5.0)	0 (0–1.0)
Omission errors	0 (0–1.0)	1.0 (0–2.0)	0 (0–0)
Sequencing errors	0 (0–0)	1.0 (0–1.0)	0 (0–0)
<b>Sequence Copy task 5, <i>n</i></b>	33	28	31
Latency (s)	8.33 (6.71–11.30)	6.10 (4.41–8.00)	6.24 (5.09–8.09)
Commission errors	5.0 (1.0–10.0)	3.0 (0–8.0)	2.0 (0–5.0)
Omission errors	1.0 (0–2.0)	2.0 (0–2.0)	0 (0–1.0)
Sequencing errors	1.0 (0–2.0)	1.0 (0.5–2.0)	1.0 (0–1.0)
<b>Kitchen task, <i>n</i></b>	34	28	31
Latency (s)	5.97 (3.74–9.56)	4.42 (2.98–5.64)	4.29 (4.29–5.83)
Commission errors	9.0 (6.0–18.0)	9.0 (6.5–12.0)	2.0 (1.0–5.0)
Omission errors	3.0 (2.0–7.0)	2.5 (1.0–5.5)	1.0 (0–2.0)
Sequencing errors	0 (0–1.0)	0 (0–1.0)	1.0 (0–1.0)

