Giving words new life - Language assessment and rehabilitation in Semantic Dementia

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Giving words new life –

Language assessment and rehabilitation in Semantic Dementia

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ABSTRACT

Language skills are central to our everyday living, but can be significantly impacted by neurological diseases, such as Semantic Dementia (SD). To date, very little has been offered to patients suffering this condition, despite their relatively preserved everyday memory, attention, and willingness to seek help. Effective assessment methods and approaches to restore vocabulary were investigated in this thesis, with a focus on the utility of word retraining to deliver meaningful and lasting benefits.

Chapter 3 showed that Semantic Dementia patients could clearly be distinguished from patients with other progressive language disorders, using a short battery of tests which assess single-word processing skills. **Chapter 4** demonstrated that, following an intensive word-retraining program, SD patients with mild, as well as severe, semantic impairments were able to improve their naming abilities using a simple, repetitive practice to relearn words. These investigations were expanded further in **Chapter 5**, where improvements in picture naming were shown to extend also to other tasks using these same words, including both expressive and comprehension based tasks. This transfer of skills was strongest for the milder patients, but could also occur to some extent when patients were more severely impaired. **Chapter 6** established that ongoing benefits could be observed if participants engaged in a less intense, revision practice, following the initial training period, despite the neurodegenerative nature of the disease. Thus, cognitive intervention could provide an effective, meaningful and lasting benefit to these patients.

Finally, **Chapter 7** demonstrated that SD patients were aware of having language problems, but not of specific deficiencies in language content. In particular, SD patients were prone to making errors regarding past knowledge for everyday words and in even being aware if specific object-related words existed.

The work within this thesis carries important clinical implications for the characterisation and management of patients with SD. In the absence of disease-modifying treatments, simple cognitive interventions provide a viable option to reduce the impact of language impairments.

PUBLICATIONS AND PRESENTATIONS

Results from the following chapters are based on publications, published abstracts and conference presentations as follows:

Peer reviewed articles

Chapter 3

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Chapter 4

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Chapter 5

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Savage, S.A., Piguet, O., & Hodges, J.R. Word retraining programs can provide meaningful benefits to patients with Semantic Dementia. In *Enabling Active Ageing, Conference proceedings of the 12th National Conference of Emerging Researchers in Ageing* (pp 98-102), 25-26th November, Sydney, Australia.

Chapter 6

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Chapter 7

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Published abstracts

Chapter 4

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Chapter 5

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Conference presentations

Chapter 3

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Chapter 4

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Chapter 5

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AWARDS

- CCD Excellence in Research Postgraduate Award (2012) – for the journal paper: Bringing words back to mind: Improving word production in semantic dementia. *Cortex,* 49(7), 1823-1832.

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- CCD Excellence in Research Student Award (2013) - for the journal paper: Distinguishing subtypes in primary progressive aphasia: Application of the Sydney Language Battery. *Dementia and Geriatric Cognitive Disorders*, 35(3-4), 208-218.

- 1st Place University of New South Wales Interfaculty 3 Minute Thesis Competition (September, 2013) and Semi-Finalist, Trans-Tasman 3 Minute Thesis Finals (October, 2013) for the presentation: "Giving words new life in dementia".

- Finalist, University of New South Wales, Faculty of Medicine 3 Minute Thesis Competition (July, 2013) – for the presentation: "Words lost to Dementia can be brought back to mind".

- Emerging Researchers in Ageing bursary (2013) – to present at the 12th Conference of the Emerging Researchers in Ageing Conference, Sydney, Australia.

- Emerging Researchers in Ageing Conference Best Poster Prize (2013) – for the poster presentation: "Word retraining programs provide meaningful benefits to patients with Semantic Dementia."

- APS Psychology in Ageing Student Travel Award (2013) to present at the 19th Annual College of Clinical Neuropsychology Conference, Brisbane, Australia.

LIST OF ABBREVIATIONS

ACE-R	Addenbrooke's Cognitive Examination – Revised
AD	Alzheimer's Disease
ANOVA	Analysis of variance
BNT-15	Boston Naming Test – 15 item version
bvFTD	Behavioural-variant Frontotemporal Dementia
CDR	Clinical Dementia Rating
COWAT	Controlled Oral Word Association Test
fMRI	Functional magnetic resonance imaging
FRS	Frontotemporal dementia Rating Scale
FTD	Frontotemporal Dementia
M	Mean
MRI	Magnetic resonance imaging
LLR	Look, Listen, Repeat
LPA	Logopenic Progressive Aphasia
PNFA	Progressive Non-fluent Aphasia
PPA	Primary Progressive Aphasia
PPT	Pyramids and Palm trees Test
RAVLT	Rey Auditory Verbal Learning Test
RCFT	Rey Complex Figure Test
SD	Semantic Dementia
SGE	Sentence Generation Exercise
StD	Standard Deviation
SYDBAT	Sydney Language Battery

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CHAPTER 1. Introduction

Our ability to understand and use words is central to many activities of our everyday lives, providing us opportunities to express ourselves and build and sustain relationships with others. Neurodegenerative conditions that progressively attack language skills have significant impact on the wellbeing of individuals and their families – with no current cures available. This thesis investigates the potential for positive change by exploring methods to improve the assessment and management of these rare but debilitating conditions. In particular, this work focuses on the detailed study of rehabilitation outcomes in a series of patients with a form of Frontotemporal Dementia known as Semantic Dementia.

To begin, Section 1.1 of this chapter introduces the clinical characteristics of each of the associated dementia syndromes, with particular reference to language processing deficits observed and the assessment of these symptoms. This is followed by a review of the neuropsychological profile and brain-related changes which occur in Semantic Dementia.

Next, in Section 1.2, the possibility of functional change in patients with neurodegenerative conditions is discussed in relation to current models of neuroplasticity and recent studies supporting improvements in patients who engage in cognitive interventions. In Section 1.3, studies of language interventions specific to Semantic Dementia are reviewed. Finally, an overview of the thesis is presented.

1.1. BACKGROUND

Introduction to Frontotemporal Dementia

Frontotemporal dementia (FTD) is the second most common form of early onset dementia (Ratnavalli, Brayne, Dawson, & Hodges, 2002), typically presenting in individuals aged in their 50s or 60s. Three distinct subforms have been identified (Neary et al., 1998), each differing from the clinical profile seen in patients with Alzheimer's Disease (Hodges et al., 1999). The most common form of FTD is the behavioural variant, where striking changes in behaviour and personality are prominent. Cognitive deficits may be relatively minor at presentation, but with disease progression typically involve executive dysfunction - particularly with respect to inhibitory control - attention and some forms of memory (Diehl-Schmid et al., 2011; Hornberger et al., 2010; Hornberger, Piguet, Kipps, & Hodges, 2009; Piguet, Hornberger, Mioshi, & Hodges, 2011). Patients often show limited or no insight into their changes, and may fail to acknowledge their medical condition (Hornberger et al., 2014). In this subtype, primarily the frontal lobes of the brain are affected (see Figure 1.1 A) below).

Figure 1.1: Magnetic resonance imaging (MRI) of typical brain atrophy patterns in FTD

Figure A) shows bilateral frontal lobe atrophy in behavioural variant Frontotemporal dementia, B) atrophy primarily within the temporal lobes (left > right) in Semantic Dementia, and C) left insular cortex atrophy in Progressive Nonfluent Aphasia. Note: left hemisphere is shown on the right.

The other two forms of FTD relate to language variants and are divided into those which affect speech fluency and grammar (nonfluent variant or Progressive Non-fluent Aphasia, PNFA) and those which affect word comprehension and conceptual knowledge (semantic variant or Semantic Dementia, SD), each accounting for approximately 12% of patients with FTD (Ratnavalli et al., 2002). These conditions are also referred to as forms of Primary Progressive Aphasia, given that the cognitive difficulties experienced are confined to the language domain at least in the first 2 years of presentation (Gorno-Tempini et al., 2004; Mesulam, 2001), and remain the dominant feature throughout the disease course. Unlike the behavioural variant of FTD, patients with Primary Progressive Aphasia are reportedly aware of their cognitive difficulties and diagnosis (Banks & Weintraub, 2009; Eslinger et al., 2005; Hornberger et al., 2014). Brain imaging studies identify damage principally in the temporal lobes (Figure 1.1 B & C), with an asymmetric pattern of atrophy of left greater than right most commonly reported in SD, and left insula atrophy in PNFA (Nestor et al., 2003; Rohrer et al., 2009; Rosen et al., 2002; Seeley et al., 2008).

While the three syndromes described above are all forms of FTD, an additional subtype of Primary Progressive Aphasia has also recently been identified – Logopenic Progressive Aphasia, LPA (Gorno-Tempini et al., 2008; Gorno-Tempini et al., 2004) (see Figure 1.2). This subtype shares some features of both SD and PNFA and is characterised by significant word retrieval problems and word finding pauses in association with reduced verbal attentional capacity (or verbal working memory), but relative sparing of comprehension and semantics. Unlike PNFA and SD, studies suggest that LPA is pathologically related to Alzheimer's Disease and involves more posterior temporal and parietal lobe changes (Leyton, Piguet, Savage, Burrell, & Hodges, 2012; Rohrer et al., 2010, 2013).

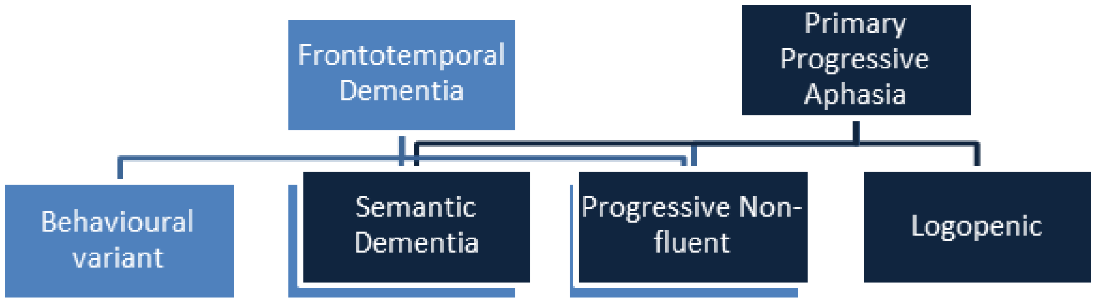

Figure 1.2: Subtypes of Frontotemporal Dementia and Primary Progressive Aphasia

Assessment and differentiation of Primary Progressive Aphasia subtypes

Despite the identification of these distinct subtypes of Primary Progressive Aphasia (PPA), it may be difficult in clinical practice to distinguish among them, particularly at first presentation. Brain imaging data may not be available or may not have been conducted using a protocol capable of detecting certain characteristic changes (e.g., slice thickness may be too large, images may be of poor resolution, changes may be too subtle to detect reliably using visual inspection methods). As a result, diagnosis may be based solely on information afforded through clinical assessment, with accuracy affected by both the presence of overlapping symptoms among the subtypes, as well as insensitivity of available measures to identify and differentiate subtle levels of impairment. For example, a word finding deficit known as anomia is common to all three subtypes of PPA (Mesulam, 2003). In addition, impairments in other aspects, such as repetition and comprehension, can arise in various ways across each of the three subtypes (see Table 1.1). While this may occur for differing underlying reasons, and at different points in the disease course, the need for careful testing is highlighted.

Table 1.1: Summary of linguistic features differentiating PPA subtypes

	PNFA	LPA	SD
Anomia	➢ Variable	➢ Moderate to severe	➢ Severe
Fluency of speech	➢ Non-fluent, agrammatic or laboured	➢ Slowed with word finding pauses	➢ Fluent, grammatical but may show word finding difficulty and substitutions
Repetition	➢ Problems with multisyllabic words (phoneme distortions, syllable segmentation) ➢ Some difficulties with sentences (if single word repetition is impaired)	➢ Problems with word strings (phonological errors) ➢ Some difficulties repeating sentences	➢ Preserved for single words and sentences (but errors with disease progression as words become less familiar)
Comprehension	➢ Preserved at single word level ➢ Impaired for complex syntactic structures	➢ Preserved at single word level ➢ Impaired syntactic comprehension, especially with increasing sentence length	➢ Impaired at single word level ➢ Preserved syntactic comprehension (if single word comprehension deficits do not intrude)
Semantic knowledge	➢ Preserved	➢ Some impairments	➢ Clear impairments

Although revisions have been made to criteria to improve the diagnosis of PPA, a recent study utilising the newest criteria reported that 19 patients (41%) in their study either did not meet criteria or fulfilled criteria for more than one variant (Sajjadi, Patterson, Arnold, Watson, & Nestor, 2012). In particular, misdiagnosis may occur between early SD and LPA if measures do not capture the differences in impairments across tasks of naming, semantic association, single-word comprehension and syntactic comprehension (Gorno-Tempini et al., 2004). Similarly, problems in differentiating between LPA and PNFA may arise, given that both can present with variable levels of anomia and relatively preserved word comprehension. Assessment of articulation difficulties assists the diagnosis in some cases, although this remains problematic as motor speech errors can be subtle in early stages of PNFA (Gorno-Tempini et al., 2011). In addition, some forms of PNFA present with agrammatism in the absence of apraxia of speech, and repetition deficits also occur in LPA. While these repetition deficits occur for different reasons, the causes may be misjudged; initiation problems (e.g., false starts, hesitancy) arising from word retrieval difficulties may sound similar to the groping speech identified in apraxia of speech (Croot, 2002; Ziegler, 2008). Likewise, phoneme and phonetic processing errors may be difficult to distinguish, leading to reports of phonological errors in both LPA and PNFA patients (Croot, Ballard, Leyton, & Hodges, 2012; Wilson et al., 2010). As a result, PNFA and LPA patients may produce equivalently reduced scores on simple measures of word repetition (e.g., Rohrer et al., 2010), although difficulty articulating multisyllabic words is typically considered diagnostic of apraxia of speech, which is characteristic of PNFA only (Gorno-Tempini et al., 2004). Likewise, assessment of sentence comprehension may be misleading if sentence complexity is confounded by working memory demands, thus lowering the performance of both PNFA and LPA patients (Leyton et al., 2011).

The easiest distinctions among PPA subtypes is between PNFA and SD, where the strongest dissociations between word repetition and comprehension can be demonstrated (Hodges, Martinos, Woollams, Patterson, & Adlam, 2008; Leyton et al., 2011). To exclude the possibility of LPA, however, it is important to test a range of cognitive and linguistic skills, with careful interpretation of both the level of deficit and relationship among measures required for accurate diagnosis.

Given these complexities in language deficits, reliable differentiation of PPA currently requires detailed speech and neuropsychological assessment, which may not always be available given practical constraints of time and resources. Thus, a need exists for the development of simple, yet effective tools to assist in this process - forming the first aim of this thesis (explored in detail in Chapter 3). Clarity in diagnosis may then lead to improvements in the management of these diseases.

Differential rates of decline in PPA

As noted earlier, PPA subtypes are associated with different underlying pathologies. In addition, it appears that the progression of symptoms may vary. Longitudinal studies indicate that the rate of change in SD is reportedly slower than in LPA (Leyton, Hsieh, Mioshi, & Hodges, 2013) and PNFA, where significantly greater declines occur over a 12-month period (Mioshi & Hodges, 2009). In addition, preservation of other cognitive domains may extend for a longer period of time in SD. As seen in Figure 1.3, over a 3-year period, despite having shown symptoms for 4.5 years on average, the rate of decline on a measure of overall cognitive ability was significantly slower for SD than matched LPA patients across each of the cognitive domains. Compared with controls, visuospatial skills in SD remained within normal limits and single-word repetition remained at ceiling (Leyton et al., 2013).

Over time, LPA patients may develop additional verbal memory and single word processing deficits (Rohrer et al., 2013), together with significant declines in episodic memory, which have not been observed in SD (Harciarek & Kertesz, 2011). Thus, despite such significant impairments in language, declines in SD may be gradual, evolving over 10 or more years (Hodges et al., 2010; Mioshi, Hsieh, Savage, Hornberger, & Hodges, 2010) and allow for a greater ongoing level of independence in everyday living (O’Connor, Ahmed, & Mioshi, 2014).

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Figure 1.3: Comparison of cognitive performance in Semantic Dementia (sv-PPA) and Logopenic Progressive Aphasia (lv-PPA) patients over time

Figure from Leyton et al., (2013). Graphs depict scores from the Addenbrooke's Cognitive Examination – Revised. The horizontal red lines represent a threshold of 3 standard deviations below healthy control performance.

No treatments are currently available either to reverse or halt the course of any of these dementias and the impact on the lives of the patients and caregivers is significant (Hsieh, Irish, Daveson, Hodges, & Piguet, 2013; Merrilees et al., 2013; Mioshi et al., 2007; Mioshi, Bristow, Cook, & Hodges, 2009). Given both the slow evolution of changes in SD and the residual cognitive strengths beyond the language domain, this subtype of PPA in particular may benefit from cognitive interventions. Chapters 4-7 of this thesis therefore focus specifically on the potential for remediation in this subtype. A more detailed description of Semantic Dementia follows.

Language and neuropsychological profile of Semantic Dementia

As noted above, Semantic Dementia (SD) is the form of FTD characterised by marked anomia and word comprehension difficulties (Hodges, Patterson, Oxbury, & Funnell, 1992). These difficulties are most prominent at a single word level, with other aspects of language, such as phonology, grammar and sentence-level processing, relatively well preserved (Garrard, Carroll, Vinson, & Vigliocco, 2004; Gorno-Tempini et al., 2004; Hodges & Patterson, 1996; Hodges et al., 1992; Rochon, Kavé, Cupit, Jokel, & Winocur, 2004). As such, speech may appear normal with respect to fluency and prosody, but may become increasingly vague or “empty” as key words are left out (Kavé, Leonard, Cupit, & Rochon, 2007; Kindell, Sage, Keady, & Wilkinson, 2013). Few problems may exist repeating words, although the meaning of the words is lost (Hodges et al., 2008). A classic diagnostic sign therefore relates to the need to clarify word meaning in order to complete requests – for example if asked to draw a clock, a patient may ask “what’s a clock?” (Harciarek & Kertesz, 2011). When the sentence structure provides sufficient context to follow the meaning, however, patients may be able to correctly identify items (Breedin & Saffran, 1999). By contrast, when faced with single word processing tasks, striking impairments are evident across multiple tasks, including picture naming, word generativity tasks - where words beginning with a specific letter or belonging to a particularly category must be provided under time pressure (Laisney et al., 2009) - and tests of word recognition, such as word-picture-matching tasks or semantic association tasks (Adlam, Patterson, Bozeat, & Hodges, 2010; Jefferies & Lambon Ralph, 2006). Spelling and reading are also affected, with the ability to read accurately or spell irregular words, which do not conform to spelling-to-sound rules, becoming increasingly impaired (Graham, Patterson, & Hodges, 2000; Noble, Glosser, & Grossman, 2000; Woollams, Lambon Ralph, Plaut, & Patterson, 2007).

As the disease progresses, the degradation of vocabulary appears strongly graded by word familiarity and word frequency, affecting both word retrieval and comprehension (Bird, Lambon Ralph, Patterson, & Hodges, 2000; Lambon Ralph, Graham, Ellis, & Hodges, 1998).

Related to this, higher order, superordinate terms become more heavily relied upon, as vocabulary becomes more general – for example "peanut" becomes "nut", then becomes "food" (Hodges, Graham, & Patterson, 1995). Speech may be reduced to stereotypical expressions, and patients may suffer a type of 'word deafness' (Hodges & Patterson, 2007).

While the impacts on language functioning are significant, importantly, the deficits found in SD are not purely linguistic in nature, but arise in the context of a progressive decay of underlying knowledge regarding words and concepts. As a result, difficulties are not solely the product of problems accessing and retrieving words from the store of known words (the lexicon), but relate to the integrity of the broader store of knowledge itself - semantic memory. Evidence of this can be found when testing patients using non-verbal measures, such as matching pictures of objects to their characteristic sounds (Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000; Garrard & Carroll, 2006; Hsieh, Hornberger, Piguet, & Hodges, 2011), recognising characteristic colours of objects (Rogers, Patterson, & Graham, 2007), or identifying correct versions of pictured objects or animals that have been altered in some way (Rogers, Lambon Ralph, Hodges, & Patterson, 2004).

In contrast to these difficulties with semantic memory, patients with SD demonstrate preservation in other key memory skills. Performance on non-verbal memory tasks typically fall within the normal range when asked to reproduce visual figures (Hodges et al., 1999), recognise photographs seen before (Graham, Simons, Pratt, Patterson, & Hodges, 2000), or complete topographical memory tasks (Pengas et al., 2010). The presence of good phonological short-term memory has recently been shown to aid the acquisition of new phoneme sequences, with positive implications for verbal learning (Jefferies, Bott, Ehsan, & Lambon Ralph, 2011). Studies have also demonstrated well preserved everyday, autobiographical memory (Adlam, Patterson, & Hodges, 2009; Graham & Hodges, 1997; Irish, Addis, Hodges, & Piguet, 2012; Mion et al., 2010), and the ability of these patients to learn new facts (Funnell, 1995) or retain unusual or low frequency words if they are part of everyday life, such as 'ibuprofen' (Snowden

& Neary, 2002). Episodic memory deficits may emerge with advanced disease, but are not typically reported early on (Tan et al., 2014).

In addition to these relative cognitive strengths in other forms of memory, patients with SD also perform well in core neuropsychological domains relating to visuoperceptual or visuoconstructional skills, basic attention and mental tracking (Hodges et al., 1999, 1992; Libon et al., 2007; Perry & Hodges, 2000). As a result, SD patients may excel at activities such as jigsaw puzzles (Green & Patterson, 2009) and show good problem solving skills on non-linguistic tasks, such as Sudoku (Papagno, Semenza, & Girelli, 2013). Some changes in executive function may occur over time, but are usually described with respect to behavioural changes in rigidity, apathy and disinhibition (Bozeat, Gregory, Ralph, & Hodges, 2000; Kashibayashi et al., 2010). Overall, this suggests that despite significant impairments to the semantic system, the neuropsychological profile of SD patients provides a good cognitive foundation on which to base remediation.

Brain-related changes in Semantic Dementia

The most prominent neuroanatomical feature of SD is the marked atrophy of the temporal lobes, which typically begins focally and asymmetrically (left more than right-sided), in the anterior and ventral portions (see Figure 1.4). Brain volume loss here is severe, with studies suggesting as much as 50% loss of the left temporal lobe compared to healthy age-matched controls within the first four years (Rohrer et al., 2008). While volume loss in the right temporal lobe is usually less pronounced over this period (with average estimates of a 25% reduction in volume compared with controls), a “catch up” process appears to occur within the next 1-2 years, to produce somewhat symmetrical involvement of the temporal lobes (Rohrer et al., 2008). In keeping with this, an autopsy of seven SD patients revealed no significant hemispheric differences (Davies, Halliday, Xuereb, Kril, & Hodges, 2009), with the most severe atrophy resulting in volume reductions of 59-66%, compared with healthy controls.

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Figure 1.4: Longitudinal structural MRI brain scans of a SD patient

Figure from Maguire et al. (2010). Coloured sections indicate areas of significant atrophy compared with healthy age-matched controls, using voxel-based morphometry.

Within the temporal lobes, imaging studies examining either atrophy or metabolic change have consistently indicated areas of abnormality in anterior, inferior aspects of the temporal lobes, with significant loss of grey matter in the polar and perirhinal cortices and the anterior fusiform gyri (Davies, Graham, Xuereb, Williams, & Hodges, 2004; Nestor, Fryer, & Hodges, 2006; Visser, Embleton, Jefferies, Parker, & Lambon Ralph, 2010). This has been confirmed by post-mortem analyses revealing the most severe atrophy in the temporal pole and perirhinal cortex (Davies et al., 2009; Tan et al., 2014). The pivotal role of these areas in the disease presentation has been highlighted by studies demonstrating that the degree of semantic impairments observed correlate with changes in these anterior temporal regions (Acosta-Cabronero et al., 2011; Davies et al., 2004; Mion et al., 2010; Rosen et al., 2002; Williams, Nestor, & Hodges, 2005).

Significant atrophy, however, has also been reported post-mortem in the entorhinal cortex, inferior and middle temporal cortices, amygdala and, notably, within the hippocampus (Davies et al., 2009). Changes in the hippocampus are present even early in the disease, typically beginning in the left and progressing to the right hemisphere (Maguire, Kumaran, Hassabis, & Kopelman, 2010; Rohrer et al., 2008), with autopsy studies measuring mean hippocampal atrophy around 35% loss of volume compared to healthy controls (Davies et al., 2009; Tan et al., 2014).

The involvement of the hippocampus has significant implications for memory processing. A number of explanations, however, have been put forth to account for the relative preservation of episodic memory observed in SD. Firstly, in comparison with Alzheimer's Disease patients, atrophy in SD patients appears more asymmetrical, with respect to laterality and rostral-caudal distribution (Chan et al., 2001). While the head of the hippocampus is significantly reduced by the end stage of the disease (43% of control volume), relative preservation is reported in the body and tail (85% preserved) (Tan et al., 2014). In addition, this recent post-mortem study demonstrated neural preservation in crucial memory relays involving the hippocampus, mammillary bodies and posterior cingulate throughout the course of the disease. Lastly, it has been argued that reductions in volume do not necessarily imply lack of function within a brain region, although few functional MRI studies in SD have been conducted. Importantly, however, one study by Maguire and colleagues (2010) looking at autobiographical memory has shown that despite significant atrophy in left temporal neocortical areas, residual tissue was still active. This was seen in the left hippocampus in the first year, as well as in the right hippocampus the following year, highlighting that hippocampal volume alone is insufficient for predicting functioning.

Beyond the temporal lobes, brain imaging studies suggest that other regions appear relatively spared. As seen in Figure 1.5 below, areas of significant abnormality, with respect to hypometabolism (pink), white matter changes (yellow), and grey matter atrophy (purple), concentrate heavily around the temporal lobes but do not appear to extend beyond this (Acosta-Cabronero et al., 2011).

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Figure 1.5: Representation of brain regions significantly affected in SD patients compared with age-matched controls

Figure from Acosta-Cabronero et al (2011). Coloured regions show brain regions of significant grey matter change, white matter change or hypometabolism.

In the final disease stage, post-mortem studies indicate additional frontal atrophy, particularly for the frontal pole (21% loss compared with control group) and the anterior cingulate gyrus (43% atrophy). Additional language processing areas found to be atrophic include the supramarginal and angular gyri (where 21-51% losses in volume are observed) (Davies et al., 2009). Encouragingly, however, results overall suggest that many different regions of the brain are relatively preserved and continue to support function throughout the disease course. The extent to which compensatory activity of the initially less affected hemisphere together with other extra-temporal brain regions could be utilised to reduce the impact of emerging cognitive deficits remains to be demonstrated, and is discussed further below.

1.2. NEUROPLASTICITY: THE POTENTIAL FOR POSITIVE BRAIN-RELATED CHANGE

The ability of the brain to reorganise its structure, function or connections in response to some form of stimuli is known as “neuroplasticity” (Cramer et al., 2011). Although initially thought to be hard-wired, increasing evidence over the last few decades has demonstrated the plastic nature of the adult brain in both healthy adults and those recovering from some form of neurological insult. Such reorganisation occurs in a variety of ways, including changes within the same hemisphere, altering the representational maps, as well as shifts in the balance of functions between hemispheres. Changes may also occur within the connections existing between network nodes. The discovery that cell genesis occurs in human brains also hints at the potential for self-renewal, although the function of the newly generated cells has not yet been clarified (Eriksson et al., 1998).

Within the context of rehabilitation, the potential for neuroplasticity provides hope that behavioural impairments resulting from pathological changes in brain structure and function may be lessened or ameliorated by adaptive changes in the brain. This may involve recruiting either nearby or contralateral areas of the brain within the functional network to support the behaviour. Evidence of such brain-related changes have come from stroke studies, with the robust finding of a “laterality shift”, wherein increases in activity are observed in the non-dominant hemisphere, together with increases in undamaged cortex within the dominant hemisphere (Vandenbulcke, Peeters, Van Hecke, & Vandenberghe, 2005). This has been demonstrated specifically within the context of the language network, where activation of both right and perilesional left regions have been shown to support language functions under specific circumstances (Crosson et al., 2007).

The stroke literature, however, has also highlighted that not all neuroplasticity may be viewed as adaptive, and increases in activation in some regions may be disruptive to language function. This appears to be moderated by the size of the lesion as well as the specific area activated. Specifically, for larger left hemisphere lesions, the lack of remaining adjacent cortex may result in increased activation within the right hemisphere, which can have differential effects to functioning. In certain areas of the right hemisphere, such as the pars triangularis, increased activation has been shown to impede word finding performance, while activity in the right pars opercularis is assistive (Crosson et al., 2007). Other positive outcomes associated with increased right hemisphere activation have included improved comprehension in a patient with Wernicke's aphasia when greater activity in the right superior temporal gyrus was observed (Musso et al., 1999), and increased word retrieval accuracy in association with greater activity in the right inferior frontal gyrus (Meinzer et al., 2006). Although increased activity in left hemisphere is typically associated with positive outcomes, in some instances, greater activation within the left frontal cortex, may be unhelpful (Crosson et al., 2007).

Remediation and neuroplasticity in ageing and dementia

The extent to which adaptive plasticity may be harnessed in the brains of older adults or those with neurodegenerative pathology is less clear. Although studies have suggested that engaging in cognitive activities, such as memory training, may support cognitive and psychosocial functioning (Doody et al., 2001) and potentially slow disease progression (Jean, Bergeron, Thivierge, & Simard, 2010; Mowszowski, Batchelor, & Naismith, 2010; Sitzer, Twamley, & Jeste, 2006), further high quality studies are needed (Bahar-Fuchs, Clare, & Woods, 2013).

In a study of 10 healthy adults (with a mean age of 70 years) who undertook a 5-week focused memory training, biochemical changes in the hippocampus were found using repeat magnetic resonance spectroscopy, compared with no changes observed in 10 healthy adults who did not complete the training (Valenzuela et al., 2003). Similarly, increases in brain activity post memory training have been observed using functional imaging, although older adults may not experience as great a potential for change (Nyberg et al., 2003).

A systematic review of cognitive interventions for mild cognitive impairment identified 3 studies using pre and post functional MRI scanning to examine patterns of brain activation (Simon, Yokomizo, & Bottino, 2012). In each case, significant changes in brain activity were associated with training, either with increases in activation levels within areas already active prior to intervention or in the recruitment of new brain regions post-intervention (Belleville et al., 2011; Clare et al., 2009; Hampstead et al., 2011). Two additional studies have reported similar findings for early dementia patients. In a functional MRI study of a LPA patient, concomitant increases in brain activity with improvements to word retrieval were found following a two-week intervention (Beeson et al., 2011) - in this case involving increased activation of the left dorsolateral prefrontal cortex. Intervention-related activation changes were also reported in a study of early Alzheimer's Disease patients completing an 8-week cognitive rehabilitation program (Clare et al., 2010). This suggests that a number of plasticity mechanisms are still present in older and mildly impaired populations.

Despite this positive evidence, not all studies have shown clear benefits of cognitive interventions in dementia populations. The limits of plasticity - the point at which the brain can no longer demonstrate such ability to adapt - is not yet known. While a review of cognitive training (without imaging) in Alzheimer's Disease, based mainly on mild cases of the disease, suggests an overall medium effect size on cognitive measures (Sitzer et al., 2006), little benefit was shown in two studies which included moderate to severe cases. Similarly, a recent meta-analysis focused exclusively on randomised controlled trials in Alzheimer's Disease and Vascular dementia reported "promising" results for a cognitive rehabilitation study involving patients in the early stages of dementia, but did not detect any significant differences in performance between cognitive training and control conditions when combining the results of eleven randomised control trials (Bahar-Fuchs et al., 2013). These trials included not only patients with mild, but also moderate (and in some cases a proportion of those with severe) disease stage. Thus more high quality studies at each disease stage are needed to clarify if and when such approaches are beneficial,

The failure to benefit from interventions in the later stages may reflect the loss of plasticity, as increasing pathological burden of disease may heavily compromise the brain's ability to adapt. As atrophy becomes more widespread, the existence of sufficient neural resources to take on functions previously supported elsewhere may be drastically reduced. Although the necessary studies which link brain imaging with behavioural abilities are limited at this stage, studies comparing task performance of Alzheimer's Disease patients in comparison to healthy controls suggest that plasticity continues at least in the early stages of the disease, with additional brain regions recruited to support function (Becker et al., 1996; Woodard et al., 1998).

The potential for remediation in Frontotemporal dementia

As FTD patients typically show less general cognitive impairment than other dementia types, such as Alzheimer's sufferers, an opportunity exists to capitalise on their cognitive strengths, at least in the early to mid-stages of the disease. While it is not yet known which mechanisms of neuroplasticity may be possible within the context of SD, results of two studies suggest that cognitive performance may be supported by a combination of up-regulation of brain networks, with residual tissue around atrophied areas activating as well as recruitment of additional brain areas into the network. In the SD case study by Maguire and colleagues (2010), completion of an autobiographical memory task activated both left and right hippocampi at the first assessment. The following year, both hemispheres were again involved but the right activation was now larger than the left and additional brain regions were recruited from prefrontal cortices, right temporal neocortex and left and right precuneus, suggesting compensatory mechanisms in an effort to maintain performance (Maguire et al., 2010) – at a point in time approximately 5 years post disease onset. This initial compensatory activity of the right hippocampus and other areas of the brain then appeared to reduce at a third annual follow up assessment, suggesting that plasticity effects, while present in the early to mid-stages of the disease course, begin to lessen with further disease progression.

In the only published study to date to investigate the neuro-functional correlates underlying cognitive training in SD using longitudinal functional MRI (Dressel et al., 2010), one mild SD patient who completed a 4-week training program showed improved picture naming associated with right-sided activation in superior, middle and inferior temporal gyrus and temporal pole at the immediate post-intervention assessment. Significant activations were also found in the right inferior, middle, superior and medial frontal gyrus, and right supramarginal gyrus, together with clusters of activation in left middle frontal gyrus, cingulate, putamen, and thalamus. The involvement of the right hemisphere is again suggestive of compensatory mechanisms, given the relative sparing of the right hemisphere earlier in the disease. This relationship between behavioural results and brain-related changes was also demonstrated at a 2-month follow up, when corresponding declines were observed in both naming performance and activation. Although this signals a need to investigate how to extend the benefits over time, as well as to determine the degree and nature of benefits later in the disease course, these initial findings are encouraging and support the value of further investigating cognitive remediation in SD.

1.3. WORD RETRAINING IN SD PATIENTS

A small, but growing literature of single case studies has now shown that patients with SD who engage in word retrieval interventions can improve their recall of object labels, at least in the short-term (Bier et al., 2009; Croot, Nickels, Laurence, & Manning, 2009; Dressel et al., 2010; Frattali, 2004; Funnell, 1995; Graham, Patterson, Pratt, & Hodges, 2001, 1999; Henry, Beeson, & Rapcsak, 2008b; Heredia, Sage, Lambon Ralph, & Berthier, 2009; Jokel & Anderson, 2012;

Jokel, Rochon, & Anderson, 2010; Jokel, Rochon, & Leonard, 2002, 2006; Jokel, Cupit, Rochon, & Graham, 2007; Newhart et al., 2009; Reilly, Martin, & Grossman, 2005; Robinson, Druks, Hodges, & Garrard, 2009; Senaha, Brucki, & Nitrini, 2010; Snowden & Neary, 2002). While group studies specific to SD are lacking, one non-randomised controlled trial involving a mixed progressive aphasic group has also provided support for such interventions (Farrajota et al., 2012). A detailed summary of each study's results is provided in Appendix 1.

While encouraging, this body of work raises many questions regarding the scope for rehabilitation (e.g., who can benefit, what items to select for training) and the methods to maximise outcomes (e.g., degree of initial training success, generalisation and maintenance). Studies have varied with respect to training technique, number of items trained, type of stimuli used (line pictures, photographs or objects), personal relevance of training items, and the number, frequency and length of treatment sessions. Some studies have conducted training within the clinic, while others are home-based, or include a mix of clinic and home practice. The majority of studies have focused on a single individual only, and have ranged from training as few as 6 and as many as 119 items under any one training approach (although most commonly, between 20-40 items are trained). As a result, comparison across studies is difficult. Nonetheless, recent reviews of this literature have been positive (Carthery-Goulart et al., 2013; Jokel, Graham, Rochon, & Leonard, 2014). Collectively, these single case studies provide insights regarding important aspects influencing treatment success, with key themes discussed below.

What factors affect treatment success?

Patient characteristics

To date, the training results for approximately 30 SD patients have been reported. Patients have ranged in age from 53 years to 87 years, encompassing those with basic schooling up to highly educated individuals, and with symptom durations from 1 to 7 years. Degree of anomia has varied from those patients unable to name any items on standardised tests, to those with some preservation. Similarly, some patients are reported to show severe semantic association losses (with scores close to chance on standardised tests), while others are only mildly affected. Three cases are reported as having asymmetrical temporal lobe atrophy on the right side, with 20 cases explicitly reported as having greater left-sided changes.

Surprisingly, despite this variability in patient profile, almost all reported cases have exhibited significant improvements following training, suggesting that word retraining can benefit a wide range of SD patients. To date, only three cases described in the literature appear not to have clearly benefited: patients AM (Graham, Patterson, et al., 1999), VH (Robinson et al., 2009), and Marian (Villanelli, Russo, Nemni, & Farina, 2011). In each case, aspects relating to the treatment method (AM: poor learning strategy, VH: insufficient sessions) or stimuli (VH and Marian: use of therapist versus patient derived materials) were identified as possible explanations.

Direct comparison across studies to determine patient characteristics which impact significantly on results is difficult, given the variability in clinical measures used to describe patients and the limited number of studies reporting effect sizes. The degree of underlying semantic impairment seems an obvious moderating factor, with reviews suggesting that cognitive retraining interventions may only be feasible in the early stages of the disease before pronounced comprehension deficits and declines in episodic memory occur (Henry et al., 2008b). This relationship, however, remains unclear given reports of "severe" cases demonstrating success (Heredia et al., 2009; Snowden & Neary, 2002). This is further complicated by the lack of clear guidelines for defining severity levels in this disease, with no universal measure(s) used to classify patients as mild, moderate or severe. It is also likely that patients at different stages of the disease may show differential responses to treatments – with some methods more effective when in the mild stages, and other methods better suited to those with severe deficits. This is yet to be investigated as it is rare for the same approach to be used in patients with different impairment levels.

In the small number of studies that have involved more than one case using the same clinical measures and method of training, the relative success of some individuals over others remains elusive. For example, Senaha and colleagues (2010) reported considerable treatment response for Case 3 in contrast to Cases 1 and 2, yet "it was not possible to associate the intensity of the therapeutic benefit to factors such as age, gender, rehabilitation time and severity of disturbance" (p 311). In the largest series reported prior to the current thesis, comprising 7 SD patients in the "mild to moderate" stage of the disease, individual differences were not commented upon (Jokel & Anderson, 2012). From inspection, however, the two lowest performers shared little in common demographically and were not the most semantically impaired in the series.

Variables such as education and age are likely to contribute to the degree of treatment success, given they are both commonly associated with performance on cognitive measures. The ability to investigate such relationships has been limited, however, given the small sample sizes of treatment studies to date. Another potential mediating variable is the relative preservation of executive function. As discussed by Visser and colleagues (2010), an important distinction in word retrieval processes may exist between the areas of the brain required to carry out the cognitive operations of controlling access and regulation of semantic knowledge (termed "semantic control"), from the regions which house this information ("semantic memory"). In this model, prefrontal and temporoparietal regions are important in performing tasks which require judgements of semantic material or where competing, alternative meanings need to be considered. In accordance, models of semantic cognition suggest that the presence of additional executive impairments may further impede performance on semantic tasks (Jefferies & Lambon Ralph, 2006). This has been demonstrated in stroke-aphasic patients, where executive skills predicted therapy success over and above the patients' language skills

(Fillingham, Sage, & Lambon Ralph, 2006). Although executive function is relatively preserved in SD patients, at least initially, the emergence of behavioural features and frontal atrophy over time suggests this could impact and limit treatment effects with disease progression. While this relationship has not been explored in SD, in at least one case reported (patient PA2), executive impairments appeared to have impeded the ability to engage in a semantic therapy, which involved switching between tasks, as well as reduced ability to perform the strategic retrieval required to demonstrate treatment effect (Henry, Beeson, & Rapcsak, 2008a).

Thus, important individual variables remain to be clarified, including the impact of demographic variables and the importance of preservation of other cognitive abilities such as executive function. By studying a large series of SD patients undertaking word retraining, this thesis begins to explore such issues (discussed further in Chapter 6). Encouragingly, however, current evidence suggests that cognitive interventions may be widely applied in this population.

Selection of therapy items

While studies have used different sets of training items (to focus on vocabulary which is specifically challenging for each individual patient), comparisons of sets of words within studies has provided clear evidence that the effectiveness of the intervention can be impacted by the choice of target words. Specifically, studies have demonstrated that words which are no longer comprehended are harder to relearn and maintain (Jokel et al., 2010, 2006; Snowden & Neary, 2002). This was observed in patient CR who at 6 months post-treatment could only name those items she was able to define (Snowden & Neary, 2002). Similarly, using a simple word-picture matching task to determine verbal comprehension (i.e., correct recognition in response to a spoken word), patients AK (Jokel et al., 2002) and CS (Jokel et al., 2010) correctly recalled and maintained a greater proportion of words that were recognised at baseline versus those words where verbal comprehension was poor. This suggests that improvements are more likely for words where some knowledge still exists by which to 'tag' the verbal labels (Snowden & Neary, 2002). Although it is still possible to show improvements, at least initially, for words that are no longer recognised, these gains may be more vulnerable to forgetting given the reduced ability to integrate this learning with existing knowledge.

Although one might expect that this ability to recognise a word form would be largely mediated by word frequency effects, given the relationship between semantic deficits and word frequency discussed earlier (Bird et al., 2000; Lambon Ralph et al., 1998), the effect of exposure to the item in day to day life also plays an important role (Snowden, Griffiths, & Neary, 1994). In support of this, when comparing named items versus non-named items patient KB showed no differences with respect to standardised measures of familiarity, visual complexity, word frequency, or age of acquisition, but was better at naming those items for which at least partial semantic knowledge remained (Snowden & Neary, 2002). Linked to this, anecdotally, Snowden and Neary (2002) observed that SD patients can learn the names of new, personally relevant, low frequency words, such as medication names (e.g., ibuprofen), despite no longer understanding high frequency objects (e.g., pen). Thus personal familiarity and relevance of items to daily living appears to play an important role. This may be due to repeated, frequent exposure to the concept or object resulting in a stronger and richer semantic representation (Lambon Ralph et al., 1998).

In addition, while not tested systematically, personal relevance of certain categories of words has been suggested as a contributing factor to performance, presumably linked with patient motivation. With patient PA2, for example, a very small overall treatment effect size was observed when results were combined across all categories trained. Examining within categories, however, revealed better performance when he was tested on a particular category of interest (dogs), where a medium effect size was reported (Henry et al., 2008a).

Aside from relevance and meaningfulness of the items, the number of items selected for practice may also contribute to the success reported. When paired with an intense practice (e.g., 5 days/week), training which focused on a smaller number of items (fewer than 30) often produced strong treatment outcomes. This was demonstrated by patients CR (Snowden & Neary, 2002), CUB (Heredia et al., 2009), Mrs P (Funnell, 1995), Case 3 (Senaha et al., 2010), NH and GE (Mayberry, Sage, Ehsan, & Lambon Ralph, 2011) – who each achieved 95-100% accuracy at their immediate post-intervention naming assessments. By contrast, Senaha and colleagues' Cases 1 and 2, who practised between 87-119 words, achieved at best 53% accuracy. In support of this, a negative relationship between the number of items provided in therapy and the proportion correctly recalled at treatment end was found in a meta-analysis of treatment studies in stroke-aphasic patients (Snell, Sage, & Lambon Ralph, 2010). A further empirical study by the same authors, however, found a similar level of performance at immediate and follow up assessments when comparing the effects of small (n = 20) versus larger (n = 60) word lists. How this may translate in a dementia population requires investigation.

In summary, the greatest treatment effects may be expected when the verbal label trained is associated with an object for which some level of semantic knowledge remains, the object is encountered regularly, and has relevance or interest to the person. This effect may be further enhanced if the word is of high frequency and is verbally comprehended. Focused practice on a small number of words may also yield better results, although this has not been systematically tested in SD.

Phonological and semantic training methods

The methods used to retrain words in SD have originated from those used in stroke patients. Such approaches focus on semantic, phonological or a combination of both processing levels, to improve word retrieval. Although the volume of literature in SD retraining is still small, studies already suggest that not all approaches are equally helpful and that the response to treatment may differ in some instances from post-stroke aphasics. This perhaps would be expected, given the naming impairments from these two types of patients arise from differing underlying mechanisms (Jefferies & Lambon Ralph, 2006) and anatomical changes. While SD patients show a specific pattern of dysfunction of temporal lobe grey and white matter in the ventral semantic pathway relative to the sparing of the dorsal fronto-parietal sub-lexical, phonological pathway, this pattern is not found in stroke-induced aphasic patients (Agosta et al., 2010).

Specifically, approaches that concentrate on semantically based methods and involve little practice of saying or hearing the word have appeared less successful. This has been observed in studies of stroke aphasic patients (Le Dor Ze, Boulay, Gaudreau, & Brassard, 1994; Lorenz & Ziegler, 2009) as well as in SD. Within respect to SD patients, this was first examined in a study by Fratalli (2004), the patient was given a semantic therapy using a conversational paradigm designed to engage higher order and associative skills through analysis of semantic features. No direct exposure of the word itself was provided, with word retrieval of targets seen as a by-product only. Although significant improvements were initially found for some of the trained lists, this effect was variable and was not maintained over time. In the formal-semantic therapy delivered to patient TBo by Bier and colleagues (2009), cues regarding category membership and specific attribute were often insufficient to assist with naming. As a result, TBo required additional phonemic cues and the full presentation of the word. Despite focusing on only 8 words throughout the training, mean accuracy during training was only 38%. Likewise, for patient PA2 (Henry et al., 2008a), the guided retrieval via identifying semantic attributes, comparing and contrasting exemplars and sorting pictures and words into categories did not prove an effective therapy. The reported effect size of $d = 2$ was substantially smaller than the effects seen in the two stroke-aphasic patients included in the study, who achieved medium to large effect sizes. In addition, observations were made regarding the difficulty experienced by this patient in engaging with the treatment tasks themselves. Thus, therapies which focus heavily on semantic tasks may be of limited value (Henry et al., 2008b). This is further supported by evidence to suggest that the facilitation effect of word-picture matching on picture naming ability does not occur at the level of semantic representations but by priming post-semantic processes in word retrieval (that is, by strengthening the links between the conceptual representation of the object and the word form)(Howard, Hickin, Redmond, Clark, & Best, 2006).

An argument may therefore be made for interventions which capitalise on the relative sparing of phonology in SD patients (Reilly, Cross, Troiani, & Grossman, 2007). Indeed, phonological approaches to naming therapy are well established within stroke aphasia (Nickels, 2002b), where the importance of exposure to the word form in improving naming performance has been demonstrated, with the number of production attempts made during therapy identified as an important factor to naming success (Fillingham, Sage, & Lambon Ralph, 2005). Phonology alone, however, also appears insufficient to produce significant improvements in word retraining – with patient AM unsuccessful in learning lists of words grouped according to initial letter (Graham, Patterson, et al., 1999).

Only one study to date has attempted to compare directly phonologically and semantically based approaches in the same SD patient (Dressel et al., 2010). In this case, naming improvements were found using both methods, with no significant advantage for either of the two approaches. A likely explanation for this result is that each method involved the combined presentation of a picture of the item and the word form, but with differing additional cues which were either phonologically based (e.g., syllable clapping) or semantic in nature (e.g., superordinate labels). Indeed, the majority of published studies in SD patients to date have included at least some combination by asking the participant to look at the object (or picture of the object), stimulating semantic processing, and repeat or read aloud the word, thereby engaging phonology (Graham et al., 2001; Heredia et al., 2009; Jokel & Anderson, 2012; Jokel et al., 2010, 2002, 2006; Mayberry, Sage, Ehsan, & Lambon Ralph, 2011; Senaha et al., 2010; Snowden & Neary, 2002; Suárez-González et al., 2014). In some studies, additional semantic processing has also been encouraged by providing item descriptions (e.g., as in Figure 1.6 below) or by grouping items of the same semantic category together. For these combined approaches to intervention, highly significant improvements have been reported, with naming accuracy at or above 80% (e.g., Heredia et al., 2009; Jokel et al., 2010; Mayberry et al., 2011; Suárez-González et al., 2014), and moderate effect sizes reported (Henry et al., 2013).

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Figure 1.6: Example of training stimuli combining semantic and phonological information

Figure from Jokel et al., (2010). In this program, the patient views the picture, accompanied by a written and software-generated spoken description, followed by the written target word.

Thus the best methods for retraining in SD appear to rely upon a combination of cues to phonological and semantic representations, thereby capitalising on unimpaired phonological processing and boosting a weakened semantic system.

Effortful and Errorless learning techniques

Many of the studies conducted have advocated for an errorless learning approach (Frattali, 2004; Jokel & Anderson, 2012; Jokel et al., 2010; Robinson et al., 2009; Senaha et al., 2010) or one in which errors are minimised during learning, for example by instructing the patient not to guess (Snowden & Neary, 2002). The rationale for this is based on the benefits observed in amnestic patient groups, such as Alzheimer's Disease (Clare, Wilson, Carter, Roth, & Hodges, 2002; Metzler-Baddeley & Snowden, 2005; Wilson, Baddeley, Evans, & Shiel, 1994), where the high frequency of errors made during the learning process may reinforce memory for erroneous rather than correct responses. When specifically studied, however, this proposed advantage of errorless learning over errorful methods may be limited to specific memory impaired groups only. A recent review reported benefits for patients with traumatic brain injury, but not in early Alzheimer's Disease, where patient performance was equivalent across the two methods (Clare & Jones, 2008).

The advantages of errorless learning are less clear in populations without memory problems (Fillingham, Hodgson, Sage, & Ralph, 2003; Fillingham et al., 2005, 2006), where again essentially equivalent performance has been observed under both errorless and error permitting methods. In keeping with this, one study in an LPA patient reported that error production was not detrimental to learning (Beeson et al., 2011). Importantly, the use of errorless learning when it is not necessary may introduce a significant drawback, given this style of learning is typically implemented using passive versus active approaches to avoid errors (Middleton & Schwartz, 2012). Numerous studies have demonstrated in the general population how effort or active engagement with materials during learning promotes better memory – arising from the generation effect, where self-generated information is better retained than information passively received (Bertsch, Pesta, Wiscott, & McDaniel, 2007; Jacoby, 1978; Slamecka & Graf, 1978) as well as the testing effect, where retrieval practice benefits both learning and long-term recall (Roediger & Butler, 2011). Studies in clinical populations such as early Alzheimer's Disease also indicate that active learning may be superior to passive, and that this effortful engagement may be more important than error elimination (Dunn & Clare, 2007). Further, by simply repeating spoken words and not engaging in effortful retrieval, it has been argued that brain plasticity effects may be lowered (Beeson et al., 2011). Errorless learning used in combination with active learning methods, however, may be assistive (Laffan, Metzler-Baddeley, Walker, & Jones, 2010).

Very little research has been conducted in SD to disentangle these aspects of effort and the potential impact of errors. Fratalli (2004) trialled an effortful, but errorless approach using a discourse therapy, where effort was required to inspect and analyse features, thereby engaging higher-order associative and analytical cognitive skills, but errors were avoided by explicitly telling the person "don't tell me the name of this". As this study did not compare the approach to any other method and the overall learning achieved by the patient was not superior to reports from other studies, no conclusions could be drawn regarding the relative benefits or otherwise of active and errorless methods.

Only one study to date has directly addressed this issue by comparing errorless and error-inducing methods, as well as methods which are passive versus those requiring active retrieval of information (Jokel & Anderson, 2012). In this study, errorless learning produced superior results to errorful learning at the immediate post- and 1 month post-intervention assessments (both at a group level, and at an individual level for 6 out of the 7 participants). At three months post-intervention, however, the benefits of errorless learning did not remain. Surprisingly, no main effect for active learning or interaction between errorless and active learning was present. In this study, however, errorless-active learning involved only answering “yes” to numerous questions which provided semantic and phonological information. Arguably this may not have been very ‘active’ as it did not require generation or retrieval of information. In the errorful-active condition, where effort was required in self-generating responses, patients may not have benefited due to the severity of their semantic impairments preventing them from meaningfully engaging in the task. Particularly in the case of items no longer verbally comprehended, patients would not have been able to generate appropriate responses to cues such as “where does it live?”. In such cases, the errorless-passive condition would appear more effective as it offered a method that all patients could at least comprehend and complete.

Thus, insufficient evidence exists to evaluate the relative benefits of errorless and effortful practices in SD patients. While minimising errors may be assistive, this approach does not appear necessary for successful outcomes. Overall, further investigation is needed to identify methods which are simple to complete but encourage patients to apply some effort in the learning process, and is focused upon in Chapter 4 of this thesis.

Generalisation: Can improvements in naming be applied to other contexts?

An important aspect to evaluate in any rehabilitation program is the degree to which improvements extend from the intervention to assist the person more generally. A consistent finding across the SD treatment studies is that words that are not explicitly trained do not improve (Croot et al., 2009; Jokel et al., 2014). This ability to generalise naming improvements to untrained words can occur in some aphasic populations, but only in the absence of significant semantic deficits (Best et al., 2013). Given the progressive deterioration of the semantic system in SD, the failure to find generalisation of this kind is not unexpected, as untrained words may no longer remain in memory to be retrieved. Instead, generalisation must be evaluated by measuring the extent to which trained words can be used in contexts which differ from the training format. Broadly, this may be divided into "near transfer" – wherein the demonstration of knowledge is highly similar to the original training context (e.g., asking the patient to produce the word in response to a different version of the stimuli – see Figure 1.7), or "far transfer" – where knowledge must be applied more flexibly (e.g., by completing a different kind of language task – such as verbal comprehension) (Subedi, 2004).

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Figure 1.7: Example of "near transfer" in testing the target word "banana" using different depictions of the item

Figure from Heredia et al., (2009).

Despite observations made during retraining that SD patients are rigid and stereotyped in their learning, little formal investigation has been conducted on the transfer of naming improvements following word retraining. Several studies have commented on the tendency for patients to rely upon rote learning methods to memorise lists of items rather than engaging semantic strategies to assist retrieval (Funnell, 1995; Graham et al., 2001; Henry et al., 2008a). As a result, the association between the object and the verbal label may not be learned, preventing transfer of knowledge to other contexts. In this way, list learning in patient DM was not meaningful, as he did not know that a Dalmatian was a dog or that a barge was a type of boat (Graham et al., 2001; Graham, Patterson, et al., 1999). In other cases, this may not be as extreme. For patient CR, improvements in naming were lessened (down to 75% accuracy) when testing occurred using a different order to training and when the colour of the paper of the training booklet was modified (Snowden & Neary, 2002). This appeared to relate, at least in part, to her focus on the temporal order of items in the training booklet when encoding the information – " it's the one after the duck, it's the bell" – rather than associating more salient, item-specific features with the label. While this can be avoided by randomising the presentation of items during training, (e.g., to avoid rote learning a word list order), it highlights that evaluations of generalisation are required both to demonstrate benefit of training and to improve training methods.

Aside from these observations, there are also theoretical reasons why generalisation in SD is likely to be reduced. One prominent theory of semantic memory suggests that the anterior temporal lobes act as a 'hub' for synthesising disparate knowledge or features of an object and evaluating commonality in order to build concepts (Patterson, Nestor, & Rogers, 2007; see Figure 1.8). With the erosion of this pivotal brain area, the ability to integrate what is learnt in one context to relevant information about the same object stored elsewhere may be lessened, impeding the flexible use of information. In support of this model, SD patients may recognise their own version of objects, but fail at times to realize that another visually dissimilar version is the same class of object (Bozeat, Lambon Ralph, Patterson, & Hodges, 2002; Snowden et al., 1994). Thus the degree or level of generalisation that can be achieved should be carefully investigated, as there are likely to be important limits.

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Figure 1.8: Illustration of the "distributed-plus-hub" model of semantic memory

Figure from Patterson et al., (2007). The anterior temporal lobe is represented in red as the semantic hub, linking each of the modality specific regions (coloured in blue, orange, yellow, green, purple etc.) centrally.

Of the small number of studies that have evaluated generalisation, preliminary evidence of some near and far transfers exists. Firstly, improvements in naming have been observed when patients are tested on alternative, line-drawing versions of trained items (Jokel & Anderson, 2012; Jokel et al., 2010), or are asked to name pictures of target items taken from different views (Heredia et al., 2009; Suárez-González et al., 2014). When visually dissimilar versions are tested, however, this ability to generalise may be markedly reduced (Mayberry et al., 2011). While in some cases (e.g., patient GE, Figure 1.9 b) this may result in significant, but smaller, improvements, for others (e.g., patient NH, Figure 1.9 a) there may be little or no evidence of transfer.

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Figure 1.9: Differences in picture naming accuracy when tested on trained stimuli versus an untrained visually dissimilar exemplar

Figure from Mayberry et al., (2011). Black bars represent pre-intervention accuracy; grey bars are for performance post-intervention. Figure a) shows no significant improvement from pre- to post-intervention for untrained versions for patient NH; Figure b) shows a significant, but smaller, improvement for untrained versions for patient GE.

The assessment of generalisation beyond picture naming tasks is rarer, but has been reported in some cases. A small improvement (from 0 up to 4 words) on a category fluency task (animals) was observed after word training in one patient (Jokel et al., 2010). Improvements in verbal comprehension may also occur. Patient CR was able to provide defining information for 60% of items trained at the end of treatment when queried using the spoken name alone (Snowden & Neary, 2002). On a standard word picture matching task – the Peabody Picture Vocabulary Test (Dunn & Dunn, 1997) - three of the seven SD participants significantly increased their score post-intervention (Jokel & Anderson, 2012). Lastly, a recent study of one patient undergoing both a standard word retrieval therapy and a conceptually enriched therapy showed improvements in both naming in response to a description and in providing a description in response to a name (Suárez-González et al., 2014).

Thus, while the existing evidence suggests some generalisation is possible, it is clear that not all improvements in naming will be transferred, and that this varies among individuals, although variables underlying these differences in generalisation are not currently known. Further exploration of both near and far forms of transfer is therefore warranted, and should ideally use ecologically valid tasks, enabling the participant to demonstrate transfer from a laboratory style learning environment to a functional use or understanding of trained words. Here, functional language refers to "communication skills necessary for communicating adequately and appropriately within an individual's own environment" (Worrall & Frattali, 2000, p. 5). This would involve participants using trained words in an everyday context, or recognising the verbal labels used by others. Assessment tools of this kind, unfortunately, are currently lacking. The problems of trying to capture generalisation through conversational speech samples has been documented in other populations (Mason et al., 2011), and structured interviews designed to elicit certain words may still provide too little output for a meaningful assessment. The best evidence of functional use of retrained words for SD patients currently rests upon anecdotal reports that patients incorporated some of the relearned words into their daily activities (Henry et al., 2013; Heredia et al., 2009; Jokel & Anderson, 2012). Thus, alternative measures of expressive and receptive language skills need to be developed to provide clearer evidence of real benefit to SD patients following word retraining. Chapter 5 addresses this important issue by evaluating generalisation of word retraining through the use of novel, ecologically valid tasks.

Maintenance: How long do treatment effects last and can this be extended?

The majority of studies have clearly demonstrated that significant improvements in naming can be achieved within a matter of weeks. Initially, these improvements appear well maintained post-intervention (Bier et al., 2009; Jokel & Anderson, 2012; Jokel et al., 2010; Mayberry et al., 2011). Beyond the first month, however, varying levels of performance have been reported if practice does not continue. Some participants experience non-significant reductions in naming accuracy, with 73-82% of the words named at the end of treatment still maintained 3 to 6 months later (Heredia et al., 2009; Jokel et al., 2010). In others, larger drops in naming proficiency are observed (e.g., with retention around 65%), although ongoing benefits of training are clear when comparing performance with baseline scores or against a control set of words (Dressel et al., 2010; Jokel et al., 2006). Finally, a last group of patients show substantial declines over this period (e.g., where only 10-40% of words are still maintained) (Frattali, 2004; Graham et al., 2001; Snowden & Neary, 2002).

The reason for this variability across patients is currently unclear. As discussed earlier with respect to initial improvements, meaningfulness of items appears to impact retention over time. For example, at her 6-month post-intervention assessment, the only pictures that patient CR could name when tested in randomised order were those items where meaning remained (Snowden & Neary, 2002). While disease severity is a logical mediating variable, the reported case with the best retention, patient CUB (Heredia et al., 2009), had severe semantic impairments. This suggests that aspects of the training method also play an important role.

One such variable could relate to the intensity of practice, with respect to the frequency and length of time spent during the intervention phase. While patient CUB completed a daily practice of one word list for 4 weeks, in previous studies intervention periods have been restricted to 2 or 3 weeks per word list (Dressel et al., 2010; Graham et al., 2001; Henry et al., 2008a; Jokel et al., 2006; Snowden & Neary, 2002), and/or required only a few sessions per week (Bier et al., 2009; Jokel et al., 2007). While improvements in naming often occur rapidly regardless of the intensity of practice, patient CUB's continued rehearsal of items over a longer period of time may have been a significant factor in extending the maintenance of her improvements. Certainly, principles relating to repetition and intensity of practice have been highlighted in animal models of successful learning and may be important for inducing experience-dependent plasticity in the brain (as outlined by Kleim and Jones, 2008). Despite this, no published studies have attempted to explore the effect of an intense practice over varying lengths of time in SD word retraining.

Another important factor for maintenance of words relates to their ongoing use. As stated by Cramer and colleagues: “skills training can improve behavioural outcomes on the backbone of neuroplasticity; in many cases, maintenance of behavioural gains depends on continued therapeutic exposure” (Cramer et al., 2011, p. 1603). Given the continuing degeneration of the temporal lobes associated with the disease, some decline in performance in the absence of practice would be expected. Indeed, this pattern of fast improvements in performance followed by declines over the medium term may be predicted, according to the Complementary Learning Systems Theory (McClelland, McNaughton, & O’Reilly, 1995). Under this theory, learning occurs as a result of the relatively intact hippocampal system, which is involved in the rapid acquisition of novel information. As a result of degradation to the temporal neocortex, however, the slower process of consolidation of learning into long-term semantic storage is impeded. As a result, once training ceases, if insufficient consolidation has occurred, this rapid, hippocampal learning may be over-written unless the material is rehearsed (Graham, Patterson, et al., 1999). This suggests an important role for ongoing training in this disease group, yet no studies to date have specifically focused on practices which may enable improvements to be sustained over time.

Ideally, continued practice and exposure would be achieved through generalisation of trained words into everyday speech, as this mechanism allows for incidental practice after formal training ends. This is also consistent with the observations that autobiographical experience and subsequent conversations regarding such experiences may enhance semantic knowledge and preserve these words over time (Snowden et al., 1994). However, household words that are practically helpful for patients to recall (e.g., stove, plate) may not naturally form part of everyday conversation. As recent experience with the object alone, without direct use of the word, may prove insufficient for maintenance (Graham, Lambon Ralph, & Hodges, 1999), some form of ongoing practice may be necessary to continually refresh memory of the words to aid retrieval. Studies describing methods to bridge the gap between formal practice and a sustaining, everyday use of words are currently lacking. Some attempt in stroke patients with aphasia has been described (Hickin, Herbert, Best, Howard, & Osborne, 2007), with exercises such as making shopping inventories, reminiscing or telling anecdotes about a chosen item, or engaging in conversation with the therapist regarding specific items. Similarly, in a recent study of an SD patient, the generative naming approach included recounting personal experiences with items as part of the therapy (Henry et al., 2013). Such approaches involve significant therapist input over multiple sessions and again may not lend themselves to all types of everyday words (e.g., patients are unlikely to have conversations or reminisce about kitchen utensils, bathroom items, etc.). Development of alternative methods which promote day to day use but are less resource intensive are therefore needed.

One obvious solution may be to recommence some schedule of home practice to prolong the benefits. When patient DM began training again, his improvements in performance returned. (Graham et al., 2001). Although he continued his daily practice for a further 2 years, reinstating full practice over such a long interval may be impractical, burdensome and potentially unnecessary. Whether reduced levels of training, or revision at certain intervals, may assist in sustaining performance over time is yet to be investigated. Determining how best to provide ongoing exposure at the level required to maintain training benefits is therefore an important area to explore, and is addressed in Chapter 6 of this thesis.

How aware are SD patients about their language deficits?

Although generally not discussed within the SD training literature, level of awareness into deficits is a variable known to affect rehabilitation outcomes in other patient groups (Leung & Liu, 2011; Ownsworth & Clare, 2006), including those with Alzheimer's Disease (Clare, Wilson, Carter, Roth, & Hodges, 2004). Awareness of deficits can affect motivation to engage in therapy, as patients who lack awareness of their cognitive changes may be less willing to engage in programs (if perceived as unnecessary). An additional consideration in the context of

SD relates to the development of tailored programs and the degree to which patients can contribute to decisions regarding the selection of words to retrain.

Reduced self-awareness can arise in many neurological conditions, including dementia syndromes (Rosen, 2011), and can cause variable impairments that result in a person being aware of declines in one area of functioning (e.g., memory), but not in another (e.g., personality change) (Aalten, van Valen, Clare, Kenny, & Verhey, 2005; Hannesdottir & Morris, 2007). In recent years, comprehensive models, such as the Cognitive Awareness System model (see Figure 1.10), have been developed to account for cognitive mechanisms– involving a complex interplay among perceptual, memory, and executive processes.

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Figure 1.10: Cognitive Awareness System model

Figure from Agnew & Morris (1998).

Of particular note, such models include a role for semantic memory, as a storage of self-knowledge which is drawn upon when making comparisons between past and current skills, and when updating knowledge of one's abilities (Agnew & Morris, 1998; Hannesdottir & Morris, 2007). Evidence for a relationship between semantic memory and self-awareness has also been provided in a study of Primary Progressive Aphasia (primarily LPA) patients, where scores on a semantic association task and reduced information content in speech were predictive of larger discrepancies between patients and carers when rating the patients' current behaviour (Banks & Weintraub, 2008).

While impairments to semantic memory may suggest an increased risk of reduced self-awareness, little investigation has specifically focused on this in patients with SD. Anecdotally, SD patients are described as "very aware" of their deficits (for example, patient EC in Bier et al., 2011). Accordingly, results from two questionnaire-based evaluations have suggested that awareness of diagnosis, language problems (Hornberger et al., 2014) and functioning in other broad cognitive domains (Eslinger et al., 2005) appears preserved.

However, incidental observations noted in some studies provide indications that awareness of cognitive changes may be impacted. Patient CR, for example, when shown her own rolling pin "expressed a lack of familiarity and denial that she had seen it before" (Snowden & Neary, 2002, p. 1723). Impairments regarding awareness of changes in apathy, empathy (Eslinger et al., 2005) or social interaction (Hornberger et al., 2014) have also been noted.

As a result, SD patients may not always be able to reliably recognise and identify areas of semantic loss. This has not been specifically explored in SD patients and forms the final component of investigation in the current thesis.

1.4. SUMMARY AND OVERVIEW

In summary, Frontotemporal Dementia is a form of younger onset dementia for which no treatments currently exist. Patients with the language variant of Semantic Dementia display difficulties in naming and comprehension of words, in the context of good attention, non-verbal memory and visuospatial abilities. This preservation in other cognitive skills equips SD patients with a strong foundation to support cognitive intervention. Furthermore, compared with other PPA patients, the evolution of the disease appears slower. Patients are often willing to engage in treatments to address their language disorder, and early evidence suggests that this might be useful. Recent studies of cognitive training in older adults, those with mild cognitive impairments, and case studies of SD patients completing word retraining have all yielded positive results, although the extent to which SD patients of differing severities can benefit from this is an area which is under-explored.

The results of previous single subject studies into word retraining in SD have provided guidance regarding approaches to improve naming, with the best outcomes arising when practice involves both semantic and phonological processing of items and selected words are meaningful for the participant. Methods which incorporate both error minimisation and effortful retrieval practice may further enhance results. The extent to which improvements in picture naming generalise beyond the training context and provide real-world improvements, however, is unclear. Maintenance of benefits is likely to depend upon some form of continued engagement with the items, although schedules of practice designed to promote maintenance have not yet been investigated. Many questions remain unanswered regarding the patient characteristics or minimum requirements to maximise treatment success, with few studies using the same training method in more than one person, or reporting standard metrics such as an effect size, to allow comparison across individuals or studies. Thus, the key variables for success, and the intervention strategies most effective, are yet to be identified. Finally, awareness of deficits can affect both motivation and ability to participate in intervention planning. While patients are generally considered insightful about their language difficulties, this has yet to be explored in detail.

Aims

In light of these issues, this thesis had five aims, which are addressed in the following experimental chapters:

1. To develop a simple assessment tool which firstly distinguishes the language processing deficits in the three main subtypes of Primary Progressive Aphasia, and then

characterises each language profile with respect to single-word processing skills (Chapter 3).

2. To refine current methods used in word retraining to identify simple but effective methods which can be applied across a range of Semantic Dementia patients (Chapter 4).

3. To examine generalisation of word retraining using novel and ecologically valid methods to assess improvements in the use and understanding of words in a variety of contexts beyond the therapy practice itself (Chapter 5).

4. To investigate maintenance of word retraining gains and explore methods which may assist in preserving these gains over a longer time period (Chapter 6).

5. To investigate levels of awareness regarding language deficits in patients with Semantic Dementia (Chapter 7).

The methods used to investigate these aims are described in Chapter 2.

CHAPTER 2. Experimental Methods

This chapter details methodological aspects in common across the experimental chapters regarding procedures for participant entry to the study (eligibility, including diagnostic criteria), ethics, and cognitive assessment. In addition, an overview of the single case experimental design methodology used in Chapters 4, 5 and 6 is provided.

2.1. PARTICIPANT RECRUITMENT AND ELIGIBILITY

All participants were recruited through FRONTIER, the Frontotemporal Dementia Research Group clinic at Neuroscience Research Australia, Sydney. Patient referrals to the clinic were obtained via their treating clinician (e.g., a neurologist or neuropsychologist), with healthy control participants sourced through local community clubs, or in some cases via association with the patients. All patients were assessed and provided with a diagnosis by an experienced behavioural neurologist, based upon detailed clinical assessment, neuropsychological assessment and, where possible, structural brain magnetic resonance (MR) imaging. Healthy controls also completed detailed neuropsychological assessment and were invited to undergo brain MR imaging.

To be considered for inclusion in the current studies, all participants were required to show adequate English proficiency to complete the tasks and have attained a basic level of education (a minimum of 6 years of primary school). Additional criteria for healthy control participants included adequate performance on cognitive screening, requiring a score of 88/100 or above on the Addenbrooke's Cognitive Examination – Revised (ACE-R) (Mioshi et al. 2006), and the absence of structural abnormalities on brain imaging, when conducted. For participants who were referred as patients, it was necessary to meet international consensus criteria for Primary Progressive Aphasia (PPA). This involves satisfying the following inclusion and exclusion criteria, as outlined by Gorno-Tempini and colleagues (2011):

Inclusion criteria for a diagnosis of PPA

- Language difficulty is the most prominent clinical feature;
- Deficits in language are the principal cause of impaired daily living activities;
- These deficits remain the most prominent form of deficit during at least the initial phases of the disease.

Exclusion criteria for a diagnosis of PPA

- The pattern of deficits is not better accounted for by a non-degenerative medical disorder;
- The cognitive disturbance is not better accounted for by a psychiatric diagnosis;
- Initial disturbances do not include prominent episodic memory, visual memory or visual perceptual impairments;
- There is no prominent behavioural disturbance in the initial phases of the disease.

Patients satisfying the overall criteria for PPA were then classified further into one of the three subtypes (Gorno-Tempini et al., 2011; Neary et al., 1998). The specific criteria for each of these are provided below (see Table 2.1, Table 2.2 and Table 2.3).

Table 2.1: International consensus criteria for diagnosis of Semantic Dementia (referred to as semantic variant primary progressive aphasia)

I. Clinical diagnosis of semantic variant primary progressive aphasia Both of the following core features must be present: ▪ Impaired confrontation naming ▪ Impaired single-word comprehension At least 3 of the following other diagnostic features must be present: ▪ Impaired object knowledge, particularly for low-frequency or low-familiarity items ▪ Surface dyslexia or dysgraphia ▪ Spared repetition ▪ Spared speech production (grammar and motor speech)
II. Imaging-supported semantic variant primary progressive aphasia diagnosis Both of the following criteria must be present: ▪ Clinical diagnosis of semantic variant primary progressive aphasia ▪ Imaging results must show one or more of the following: - Predominant anterior temporal lobe atrophy - Predominant anterior temporal hypoperfusion or hypometabolism of SPECT or PET
III. Semantic variant primary progressive aphasia with definite pathology Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present: ▪ Clinical diagnosis of semantic variant primary progressive aphasia ▪ Histopathologic evidence of a specific neurodegenerative pathology (e.g., FTLD-tau, FTLD-TDP, AD, other) ▪ Presence of known pathogenic mutation

Note: Taken from Gorno-Tempini et al., (2011)

Table 2.2: International consensus criteria for diagnosis of Progressive Non-fluent Aphasia (referred to as nonfluent/agrammatic variant primary progressive aphasia)

I. Clinical diagnosis of nonfluent/agrammatic variant primary progressive aphasia At least one of the following core features must be present: ▪ Agrammatism in language production ▪ Effortful, halting speech with inconsistent speech sound errors (apraxia of speech) At least 2 of 3 of the following other features must be present: ▪ Impaired comprehension of syntactically complex sentences ▪ Spared single-word comprehension ▪ Spared object knowledge
II. Imaging-supported nonfluent/agrammatic variant diagnosis Both of the following criteria must be present: ▪ Clinical diagnosis of nonfluent/agrammatic variant primary progressive aphasia ▪ Imaging must show one or more of the following results: - Predominant left posterior fronto-insular atrophy on MRI or - Predominant left posterior fronto-insular hypoperfusion or hypometabolism on SPECT or PET
III. Nonfluent/agrammatic variant primary progressive aphasia with definite pathology Clinical diagnosis (criterion 1) below and either criterion 2 or 3 must be present: ▪ Clinical diagnosis of nonfluent/agrammatic variant primary progressive aphasia ▪ Histopathologic evidence of a specific neurodegenerative pathology (e.g., FTLD-tau, FTLD-TDP, AD, other) ▪ Presence of a known pathogenic mutation

Note: Taken from Gorno-Tempini et al., (2011)

Table 2.3: International consensus criteria for diagnosis of Logopenic Progressive Aphasia (referred to as logopenic variant primary progressive aphasia)

I. Clinical diagnosis of logopenic variant primary progressive aphasia Both of the following core features must be present: ▪ Impaired single-word retrieval in spontaneous speech and naming ▪ Impaired repetition of sentences and phrases At least 3 of the following other diagnostic features must be present: ▪ Speech (phonologic) errors in spontaneous speech and naming ▪ Spared single-word comprehension and object knowledge ▪ Spared motor speech ▪ Absence of frank agrammaticism
II. Imaging-supported logopenic variant primary progressive aphasia Both criteria must be present: ▪ Clinical diagnosis of logopenic variant primary progressive aphasia ▪ Imaging must show one or more of the following results: – Predominant left posterior perisylvian or parietal atrophy on MRI – Predominant left posterior perisylvian or parietal hypoperfusion or hypometabolism on SPECT or PET
III. Logopenic variant primary progressive aphasia with definite pathology Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present: ▪ Clinical diagnosis of logopenic variant primary progressive aphasia ▪ Histopathologic evidence of a specific neurodegenerative pathology (e.g., AD, FTLD-tau, FTLD-TDP, other) ▪ Presence of a known pathogenic mutation

Note: Taken from Gorno-Tempini et al., (2011)

Exclusion criteria for all participants related to presence of any of the following: significant psychiatric conditions such as bipolar disorder, schizophrenia, or severe depression; a history of substance abuse; dementia or neurological disease (excluding a diagnosis of Primary Progressive Aphasia in the patient group).

2.2. ETHICS

The studies were approved by the Human Research Ethics Committees of South Eastern Sydney Illawarra Area Health Service and the University of New South Wales. All participants gave written informed consent themselves and/or through their Person Responsible (usually the next of kin).

2.3. COGNITIVE ASSESSMENT

A standardised battery of validated cognitive tests was administered to all participants. This battery was designed to cover a range of neuropsychological domains, suitable for participants of varying cognitive ability, and for which the majority of participants could complete within a 2-3 hour period. For patients, this was usually conducted over a series of short 1-hour sessions, interspersed with breaks across the day, to minimise fatigue.

General cognitive ability

To begin, all participants were administered the Addenbrooke's Cognitive Examination – Revised (ACE-R; Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006) as a screening and general measure of cognitive functioning. This test incorporates and expands upon the Mini Mental State Examination, to provide subscales regarding attention and orientation, verbal memory, verbal fluency, language and visuospatial abilities. The maximum overall score is 100, with higher scores reflecting better cognitive ability. Scores of 88 or above have been shown to discriminate between healthy control participants and dementia patients with high sensitivity and specificity (Mioshi, et al. 2006).

Attention and working memory

To assess verbal attention span and working memory, the Digit Span subtest from the Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler, 1997) was administered. In the first part (Digit Span Forwards), participants repeat aloud a string of numbers of increasing length, read by the examiner. For a correct response, the numbers must be recalled in the exact order presented. Attention span is then measured as the longest string of numbers (between two and nine) that was repeated without error. In Digit Span Backwards, working memory is evaluated. Participants repeat strings of numbers of increasing length, but do so in the reverse order of presentation (e.g., if the examiner read 3-4-1 the participant must respond 1-4-3 to score the item correctly). A maximum span score of 8 can be achieved. In addition, an overall age scaled score for the Digit Span subtest can be derived, based upon comparing overall item scores with a standardised normative group provided with the test (Wechsler, 1997). Scores of 8 to 12 indicate average or expected performance within a given age bracket; scores of 4 or below signal significant impairment.

Psychomotor or processing speed

To measure mental speed, Part A of the Trail Making Test (TMT A; Tombaugh, 2004) was administered. This is a paper and pencil task requiring participants to draw a line to connect circles containing the numbers 1 to 24, in order, as quickly as possible. Numbers are spread out of order across the page (Figure 2.1). Performance is measured in seconds.

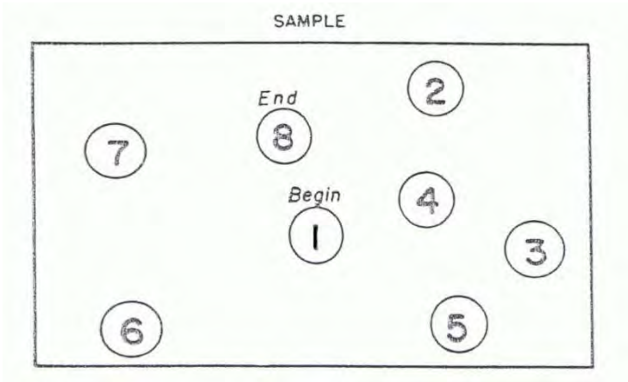

Figure 2.1: Sample of Trail Making Test – Part A

Visuospatial skills

The copy task of the Rey Complex Figure (Meyers & Meyers, 1995) was used to assess visuoconstructional skills. Participants are instructed to copy carefully a complex geometric figure (Figure 2.2). The figure remains in view for the duration of the task. Completion time is recorded. Scoring of the design is based on the correct positioning and rendering of 18 discrete units, producing a maximum score of 36.

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Figure 2.2: The Rey-Osterrieth Complex Figure

Figure from Meyers & Meyers (1995) The Meyers scoring system for the Rey Complex Figure and the recognition trial: Professional manual.

Memory

Memory was assessed using a combination of visual and verbal tasks, where appropriate, to measure free recall (unprompted retrieval of information) and recognition memory (where cues may be provided to assist in memory retrieval). Free recall of visual information was measured via the 3 minute delay condition of the Rey Complex Figure (Meyers & Meyers, 1995). Having completed the copy of the figure (as described above), participants are asked to reproduce the drawing again from memory 3 minutes later. A score is given for the inclusion and correct placement of each element. To assess visual recognition memory, the Doors subtest of the Doors and People test was administered (Baddeley, Emslie, & Nimmo-Smith, 1994). In this task, photographs of different doors are shown for 3 seconds each. Immediately after viewing a set of 12 doors, participants are asked to identify those doors, one at a time, by selecting each from an array of 4 pictures (one target and 3 distractors per page). The test includes a basic set of doors (Part A) and a challenging set (Part B). Each set is scored out of 12 and can be converted to a standard score.

For healthy control participants, an assessment of verbal memory was also conducted, using the Rey Auditory Verbal Learning Test (RAVLT; Schmidt, 1996). In this test, participants attempt to learn a list of 15 words (List A) read aloud by the examiner over 5 trials. After the fifth learning trial of List A, free recall of a second list of 15 words (List B) is examined. Free recall of List A is then immediately tested again, with a final free recall test of List A conducted 20-30-minutes later, as a measure of delayed recall. Finally, recognition of List A is also assessed after this delay by reading a list of words (including List A, List B and distractor items), and asking the participant to respond "yes" or "no" to indicate if the word had been part of the original list. Verbal memory in PPA patients was not assessed given performance would have been confounded by their significant language deficits.

Language

Language was primarily assessed using the Sydney Language Battery (SYDBAT) – described in detail in the following chapter. This battery involves four subtests of single-word processing: picture naming, word repetition, word-picture-matching, and associative picture-picture matching. Each of the subtests comprises 30 items, creating a maximum score of 30 per subtest. Items are graded into 3 blocks of 10 words, ranging from higher frequency nouns (e.g., potato, bicycle) to those of lower frequency (e.g., orangutan, pagoda). The Naming subtest provides a measure of expressive ability and requires participants to view pictures one at a time and correctly retrieve the name of each item. Ability to correctly articulate each of the target words is then assessed in the Repetition subtest. Here, the examiner asks the participant to repeat each of the 30 multi-syllabic words to detect any difficulties in pronunciation or motor control in speech. The final two subtests provide measures of semantic knowledge which do not rely upon spoken ability or retrieval of words. Firstly, the word comprehension subtest requires participants to match the word spoken by the examiner to one of seven pictures. Lastly, conceptual knowledge is assessed by asking participants to form associations in meaning by matching each target picture with one of four other pictures. Pictures may be associated with respect to how they are used (e.g., Radio-Ear), location (e.g., Kangaroo-Opera House) or common properties (e.g., Escalator-Ferris Wheel both involving moving up).

As another measure of semantic memory, category fluency scores were extracted from the ACE-R. In this task, participants must name as many different types of animals as possible within a one minute timeframe. The total score generated reflects the number of correct responses provided (i.e., total words excluding errors such as repetitions of the same word, or words outside the category).

To further assess language skills in the PPA patients, grammatical comprehension was also examined using the Test for Receptive Grammar (Bishop, 1983, 2003). Here, the examiner reads aloud a statement (e.g., "The boy chasing the horse is fat" – see Figure 2.3 below) and the participant must select which of four colour drawings best matches the statement. Each drawing combines different elements of the statement, to provide challenging distractors (e.g., varying whether it is the boy or the horse that is fat, or varying who is being chased, etc.). The test is divided into twenty blocks comprising 4 items each, producing a total score of 80.

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Figure 2.3: Example item from the Test of Receptive Grammar

Figure from Bishop (1983) Test for Receptive Grammar, for the item: "The boy chasing the horse is fat".

Lastly, during the development of the SYDBAT, some additional language tests were administered to a subset of healthy control and PPA participants. These included an alternative picture naming task, the 15-item Boston Naming Test (Mack, Freed, Williams, & Henderson, 1992), wherein participants are asked to name items in response to 15 black and white line drawings within a 20-second time limit. The 10-item Repeat and Point test (Hodges et al., 2008) was also administered to assess performance on single-word repetition and comprehension abilities. Participants must firstly repeat a word spoken by the examiner and then point to the matching picture from an array of 7 colour photographs. Finally, the Pyramids and Palm Trees (Howard & Patterson, 1992) was used as an alternative measure of associative knowledge, wherein the participant must select which of two black and white drawings is related in meaning to each of the 52 target drawings.

Executive functions / mental flexibility

Higher order cognitive abilities, or "executive functions", were assessed firstly using Part B of the Trail Making Test (TMT B; Tombaugh, 2004). Here, participants are required to find and connect circles to form ascending sequences as quickly as possible. However, unlike in Part A (as described above under Psychomotor and Processing Speed), the circles contain either a number or a letter (see Figure 2.4) and the participant must alternate between these sequences to complete the task correctly (i.e., 1-A-2-B-3-C...). Time to complete is measured in seconds and a tally is kept of any errors made.

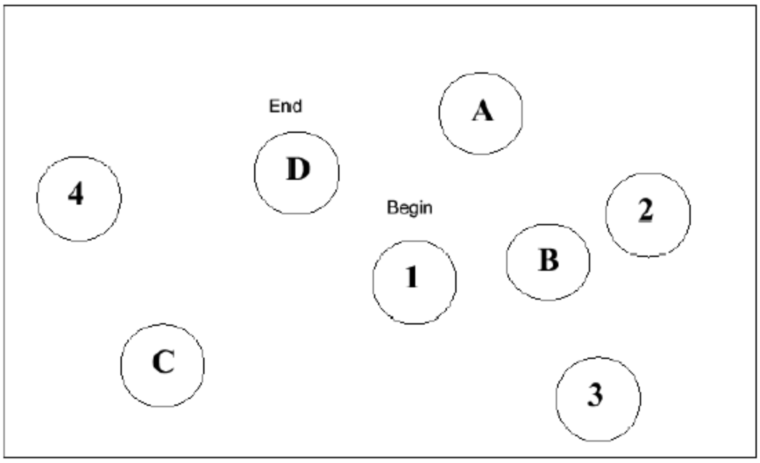


Figure 2.4: Sample item from the Trail Making Test - Part B

A second measure of executive functioning administered was letter fluency, or the Controlled Oral Word Association Test (COWAT; Strauss, Sherman, & Spreen, 2006). In this task, participants are given 1 minute per trial to generate as many words as possible that start with a specified letter (firstly 'F' then 'A', then 'S'). Words must not include proper nouns or numbers, or extensions upon previous words (e.g., if "speak" is said, then "speaks" or "speaking" would be counted as repetition errors). The final score is the total number of words correctly generated across all three letters.

2.4. FUNCTIONAL & BEHAVIOURAL ASSESSMENT

To provide additional indicators of disease severity in the patient groups, a number of carer based assessments were also conducted. These were based on questionnaires and interviews completed with family members or a close informant using measures known to be sensitive to the behavioural and functional disturbances which arise in Frontotemporal dementia.

Firstly, the Clinical Dementia Rating scale (CDR; Morris, 1997; or the modified FTLD-CDR; Knopman et al., 2008) was completed. This quantifies the severity of symptoms of dementia across a range of cognitive and functional performance domains including: memory, orientation, judgement and problem solving, community affairs, home and hobbies, personal care, language, and behaviour comportment and personality. Each domain is given a score ranging from '0' (normal function) to '3' (severe disturbances). An example of this scoring system is provided in Figure 2.5 below, for the additional FTD specific domains:

SCORE	Healthy CDR 0	Questionable Dementia CDR 0.5	Mild Dementia CDR 1	Moderate Dementia CDR 2	Severe Dementia CDR 3
BEHAVIOR, COMPORTMENT AND PERSONALITY	Socially appropriate behavior	Questionable changes in comportment, empathy, appropriateness of actions	Mild but definite changes in behavior, comportment, empathy, appropriateness of actions	Moderate behavioral changes, affecting interpersonal relationships and interactions in a significant manner	Severe behavioral changes, making interpersonal interactions all unidirectional
LANGUAGE	Normal speech, normal comprehension	Minimal but noticeable word finding, minimal non-fluency. Comprehension normal in ordinary conversation	Mild word finding problems event frequently, but does not significantly degrade spoken speech. Or mild comprehension difficulties	Moderate word-finding problems, interferes significantly with communication or moderate nonfluency or moderate comprehension difficulty in ordinary conversation.	Severe deficits in word finding, expressive speech, comprehension making communication virtually nil

Figure 2.5: FTD specific domains of the FTLD-CDR

From: Knopman et al., (2008). Ratings range from '0' for normal function, '0.5' for questionable or very mild abnormalities, to '3' indicating severe disturbances.

In both versions of the scale, an overall composite score can be derived, based on the original six domains, where '0' reflects no evidence of dementia and '3' is indicative of severe dementia (Morris, 1997). However, as disturbances in language and/or behaviour are important when considering disease severity in FTD, the FTLD-CDR "sum of boxes" score was also calculated, where possible, to increase the sensitivity of this measure and incorporate changes across all 8 domains.

In addition, the Frontotemporal dementia Rating Scale (FRS; Mioshi, Hsieh, Savage, Hornberger, & Hodges, 2010) was used as a further measure of disease severity. This 30-item scale comprises a specific subset of questions from the Disability Assessment for Dementia (Gélinas, Gauthier, McIntyre, & Gauthier, 1999) and the Cambridge Behavioural Inventory (Wedderburn et al., 2008) to provide a reliable and valid measure of ability in FTD. High scores reflect greater functioning, with lower scores indicative of declines in everyday skills and marked behavioural change. The resulting logit scores are divided into 6 severity categories for clinical interpretation: very mild ($\geq$ 4.12), mild (4.11 to 1.92), moderate (1.91 to -0.40), severe (-0.39 to -2.58), very severe (-2.57 to -4.99), and profound (below -4.99).

Finally, severity was also considered with respect to disease duration. This was estimated by reports provided from the patient and their informant as part of the clinical assessment conducted with the neurologist. Here, disease duration was calculated in years based on the interval of time between the clinical assessment and when the first symptoms of the disease were observed. Time since diagnosis was also recorded.

2.5. SINGLE CASE EXPERIMENTAL DESIGN

The word retraining studies presented in Chapters 4, 5 and 6 were all conducted using a single-case experimental design methodology, providing a detailed investigation of each individual's response to intervention over time, as it was systematically applied and withdrawn.

Rationale for using single case experimental designs

While large group-level, randomised controlled trials (RCTs) are generally considered a gold standard in rehabilitation studies, these designs are not always feasible in rare conditions, and may mask or distort individual responses in some instances (e.g., if variability in patient characteristics produces a group average that does not accurately reflect the treatment response observed for any individual participant in practice, or if changes in response to an intervention occur initially but then subside and are not captured within the small number of measurements collected in group studies versus single subject designs)(Wilson, 1987). By contrast, single case experimental designs provide a detailed examination of the extent and timing of changes in performance for each individual, which can readily be applied into clinical practice (Tate et al., 2008).

As Semantic Dementia is a rare condition, wherein the impact of individual characteristics (such as disease duration, level of semantic impairment, or left versus right predominant anterior temporal lobe atrophy) is largely unknown, a single case experimental approach is an appropriate methodology to study responses to intervention in this population. In addition, such a design provides the ability to tailor measures to the needs of each person, allowing for each individual's intervention to focus on the specific vocabulary that requires remediation, and to create measures sensitive to capture changes specific to these items. While the ability to generalise findings to a whole population is limited by the focus on the individual, replication across multiple individuals provides evidence of the applicability of results. This may be particularly informative in conditions such as SD, where the general profile has been noted as fairly homogenous (Woollams et al., 2007). Finally, single subject designs are valuable in the early stages of exploring potential interventions, by identifying those approaches which warrant further confirmation in larger samples, and have a well-established tradition in the literature for language and communication disorders (Beeson & Robey, 2006).

Multiple baseline across behaviours design

It is important to distinguish among different forms of single participant designs, as these vary in the methodological rigour afforded. While a broad range of designs has been described (Barlow, Hersen, Barlow, Andrasik, & Nock, 2008), the main forms include (Perdices & Tate, 2009):

1. *Pre-post designs*: performance of an individual is measured prior to intervention and then following treatment end. Treatment is not systematically manipulated and there is no attempt to demonstrate stability of responses, or control for extraneous events over time.
2. *Bi-phase or AB designs*: multiple measurements are taken during a baseline (‘A’ phase) and during treatment (‘B’ phase). This allows for an examination of baseline stability and observations of change within the treatment phase. However, there is no control for extraneous, confounding events over time.
3. *Multi-phase ABA designs*: multiple measurements are taken during an initial baseline (A1), during treatment (B), and during a withdrawal or ‘return to baseline’ phase (A2). Some demonstration of cause and effect may be demonstrated by the replication of the baseline phase to show a relationship between the behaviour measured and the presence of the intervention, manipulated by the systematic application and withdrawal of the treatment.
4. *Multiple baseline designs* (using either AB or ABA style designs): performance is systematically measured over A and B phases as an intervention is introduced

sequentially across a series of behaviours, settings or individuals (see Figure 2.6 below). This builds a further level of control, as the observed effects of the intervention are replicated multiple times within the same design. The possible bias of extraneous variables is additionally controlled by measuring the effect of the intervention on the specific behaviour/setting/individual while simultaneously observing the other behaviours/settings/individuals at that same point in time.

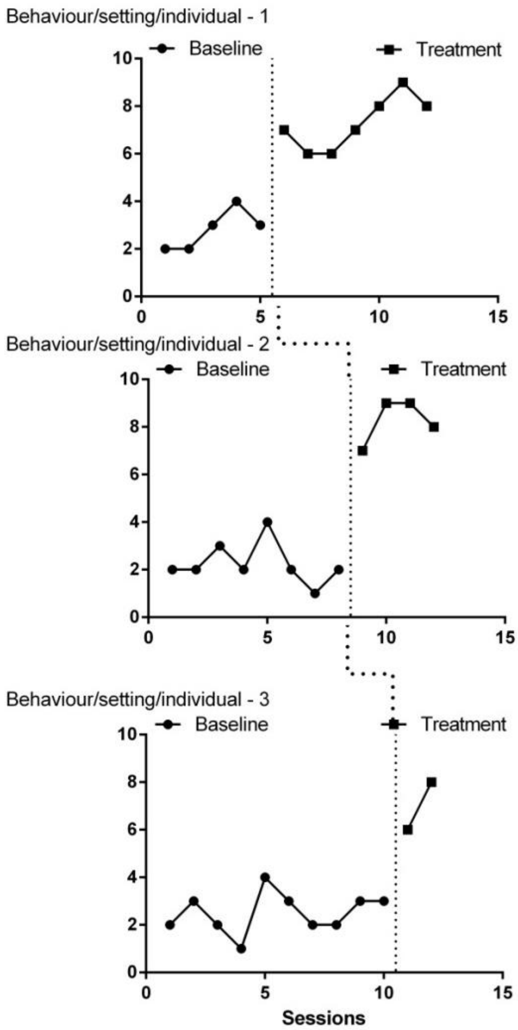


Figure 2.6: Example of a multiple baseline design

Dotted lines indicate the time points in which the treatment is introduced to each behavioural set, location or individual. Treatment effect is demonstrated when change repeatedly occurs only following the introduction of the B (treatment) phase.

Design overview for the current studies

Within the current set of studies (Chapters 4, 5, 6), a series of multiple-baseline-across-behaviours designs were implemented to provide the clearest evidence by which to evaluate the impact of word retraining on an individual's naming ability. In each participant, the replication of behaviour involved measuring the effect of retraining on different sets of word lists. Word lists were constructed to be matched on key variables found to affect word retrieval in Semantic Dementia, such as semantic category, word frequency, and familiarity (Capitani, Laiacona, Mahon, & Caramazza, 2003; Hirsh & Funnell, 1995; Lambon Ralph et al., 1998; Robinson et al., 2009). Word frequency measures were obtained from the SUBTLEX database (Brysbaert & New, 2009) and familiarity was operationalised by measuring the personal frequency of use on a 6-point scale (1 = daily, 2 = several times per week, 3 = once a week, 4 = once a fortnight, 5 = monthly, 6 = seasonally or less frequently) Variables regarding imageability, phoneme length, and visual complexity were not matched upon, given these do not appear to significantly impact naming performance in this population (Lambon Ralph et al., 1998; Snowden & Neary, 2002).

Multiple baseline assessments of naming each of the items were completed for all lists, followed by the sequential implementation of training to List 1 and List 2. List 3, however, remained untreated as a control list throughout to provide a measure of general naming performance over the same time period. Due to the progressive nature of the disease, this was an important consideration given the potential for treatment effects to be measured not only by improvement in performance over time from baseline, but also in relative preservation of performance versus possible declines in untreated items (as raised in the review by Croot and colleagues, 2009).

The target behaviour measured throughout the study of each participant was naming accuracy, where each item tested was scored either '1' for correct performance, or a '0' if incorrect. Responses were strictly scored such that approximations were considered incorrect (e.g., if shown a picture of an iron, the response "ironing" would get a score of 0).

Consistent with the methodological rating and guidelines set out in Tate and colleagues (2008), additional design considerations included:

- Baseline phase comprised at least 3 data points, where possible, to allow for an adequate assessment of stability. Baseline stability was assessed using non-parametric statistics (Cochrane's Q), applied to each list.
- Intervention phases comprised at least 3 data points to allow a visual assessment of variability of performance.
- Assessments of the target behaviour (naming accuracy) were conducted either by an independent assessor or were collected via computer recordings of responses, thereby limiting the possible biases introduced by assessment directly with the treating clinician.
- Reporting of results involved not only description of changes over time, but also statistical confirmation using non-parametric statistical methods.

This basic design was then repeated across multiple participants, providing evidence of treatment effects both within and between individuals.

CHAPTER 3. Language assessment in Primary Progressive Aphasia

The aim of this study was to develop a simple assessment tool for evaluating language skills at a single word level, to be assistive in the diagnosis and planning of interventions for patients with Primary Progressive Aphasia. As discussed in Chapter 1, Semantic Dementia patients show striking deficits in these skills, with a distinct pattern of performance expected when comparing speech fluency with word comprehension and knowledge. An effective assessment tool to distinguish this profile among other types of PPA and characterise the severity of impairments across patients is important for rehabilitation planning. This study describes the development and validation of this test, including an evaluation of its ability to distinguish different profiles within PPA, as well as basic psychometric properties of test validity and reliability.

3.1. INTRODUCTION

Despite apparent differences in the clinical features of each PPA subtype (PNFA, LPA and SD - as defined by the clinical criteria in Chapter 2), diagnosis remains difficult, given overlapping symptoms. Patients with SD and LPA both show marked anomia, with the distinction resting upon semantic impairment in the former versus impaired auditory verbal span in the latter syndrome. Distinguishing between PNFA and LPA may rest upon detecting differences between coordination of speech movement, known as apraxia of speech (in the former), and the finding of phonological errors (in the latter) – a subtle distinction which is not free from controversy (Gorno-Tempini et al., 2011). Differentiation of the subtypes, however, is of considerable clinical importance given differences in pathology, which can affect the time course and the effectiveness of different treatments.

Current neuropsychological tests (as described in Chapter 2) may be helpful in ruling out a diagnosis of PPA by identifying the presence of significant deficits in other cognitive domains, but are less efficient in distinguishing among the subtypes of PPA. Performance on one of the most common language tests used – the Boston Naming Test (Kaplan, Goodglass, Weintraub, & Goodglass, 1983) – is likely to be reduced in the majority of PPA patients, given anomia presents as the single most common sign (Mesulam, 2003). More extensive language batteries, such as the Western Aphasia Battery (Kertesz, 1980) or the Psycholinguistic Assessments of Language Processing in Aphasia (PALPA; Kay, Coltheart, & Lesser, 1992), are usually outside the scope of most neuropsychological assessments.

The combination of various tests from different sources to compare the integrity of various linguistic processes (e.g., Boston Naming Test in combination with the Pyramid and Palm Trees Test; Howard & Patterson, 1992, or Repeat and Point Test; Hodges et al., 2008), which may be relevant both to diagnosis and in identifying different strengths and weaknesses to guide the most appropriate forms of rehabilitation, is also problematic. Interpretation of results is complicated by the use of different norms across tasks and the potential for each item set to introduce confounding variables, due to differing levels of word frequency, familiarity and syllable length. The Cambridge Semantic Memory Battery (Adlam et al., 2010) was introduced to address these issues, and while effective in evaluating semantic processing, remains lengthy to administer and cannot distinguish well among all PPA subtypes.

Study design and hypotheses

The current study introduces a new language battery of single-word processing that is simple and quick to administer as part of a standard cognitive battery, which targets key features of confrontational naming, single-word comprehension and word repetition skills. These features not only assist in distinguishing subtypes of PPA, but provide information regarding the severity of semantic impairment and the integrity of speech fluency, which is important when considering word retraining programs that rely upon repeating words aloud.

The battery was applied to a consecutive series of patients meeting core criteria for PPA. It was hypothesised that each PPA subtype would demonstrate a distinct profile across these tasks, with the most striking impairments in naming and comprehension expected in SD. Conversely PNFA patients were expected to perform well on comprehension tasks, but perform poorly on speech related tasks. Lastly, LPA patients were expected to perform at an intermediate level on all tasks, but with deficits most evident on naming.

3.2. METHOD

Participants

Fifty-seven patients meeting clinical diagnostic criteria for Primary Progressive Aphasia (Gorno-Tempini et al., 2011), were included from the FRONTIER Research Clinic (PNFA = 22; SD = 20; LPA = 15). As outlined in Chapter 2, the clinical diagnoses were established following a comprehensive multi-disciplinary assessment including neurological, neuropsychological, and language testing in conjunction with MR imaging. Specifically, detailed examination of each participant's language was conducted or reviewed by an experienced clinician, using both qualitative assessment methods to judge speech quality, as well as tests of syntax and sentence repetition. Diagnosis was reached at a consensus meeting.

Exclusion criteria for this study were: (a) extremely limited speech or mutism; (b) significant overall cognitive impairment, defined as scores below 45 on the Addenbrooke's Cognitive Examination-Revised (Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006); (c) limited or no formal education in English; and (d) a dual diagnosis of Frontotemporal dementia and motor neuron disease.

Fifty-four healthy individuals, matched on age, years of education, and sex, were also recruited.

Neuropsychological assessment

A standard battery of cognitive tests was administered to capture general cognition, together with specific measures of memory, attention, visuospatial skills and executive function. The tests included the ACE-R (Mioshi et al., 2006), Rey Complex Figure Test (RCFT; Meyers & Meyers, 1995), Trail Making Test (TMT A and B; Tombaugh, 2004), letter fluency (Controlled Oral Word Association Test; Strauss, Sherman, & Spreen, 2006) and the Digit Span subtest of the Wechsler Adult Intelligence Scale (Wechsler, 1997). Full descriptions of these tests can be found in Chapter 2.

Approximately half of the participants also completed additional language assessment, including a short form of the Boston Naming Test (BNT-15; Mack, Freed, White Williams, & Henderson, 1992), the Pyramids and Palm Trees test (PPT; Howard & Patterson, 1992), and the Repeat and Point test (Hodges et al., 2008) for reliability and validity analyses.

Experimental study: Stimuli and design

The Sydney Language Battery (SYDBAT) was designed to test expressive and receptive single-word processing skills. Words were sourced by consulting previous language assessment tools, and conducting searches on the MRC Psycholinguistic Database (http://websites.psychology.uwa.edu.au/school/MRCDatabase/uwa_mrc.htm). Target words were required to be imageable nouns of three or more syllables, and included a mix of both living and non-living items. It was also necessary for each item to be represented in four different subtests (which incorporated visually and semantically related distractors). Only words where sufficient distractor items could be generated were selected. Coloured pictures were obtained from the Shutterstock image database (http://www.shutterstock.com). The resulting words were graded into three blocks of difficulty, based on decreasing word frequency (using the Sydney Morning Herald word database http://www2.psy.uq.edu.au/CogPsych/Noetica/OpenForumIssue4/SMH.html, where frequency is estimated upon occurrences per million).

Based on these criteria, test items for forty-two nouns were piloted in a separate sample of PPA patients (n = 6), other non-aphasic FTD patients (n = 4), as well as in five healthy controls. Items where pictures were unclear or responses were highly variable were removed. A final subset of 30 items which appeared to discriminate well between patients and controls and showed the expected overall pattern of increasing difficulty across blocks was selected for the test. A full list of items, together with mean word frequency per block, is presented in Appendix 2.

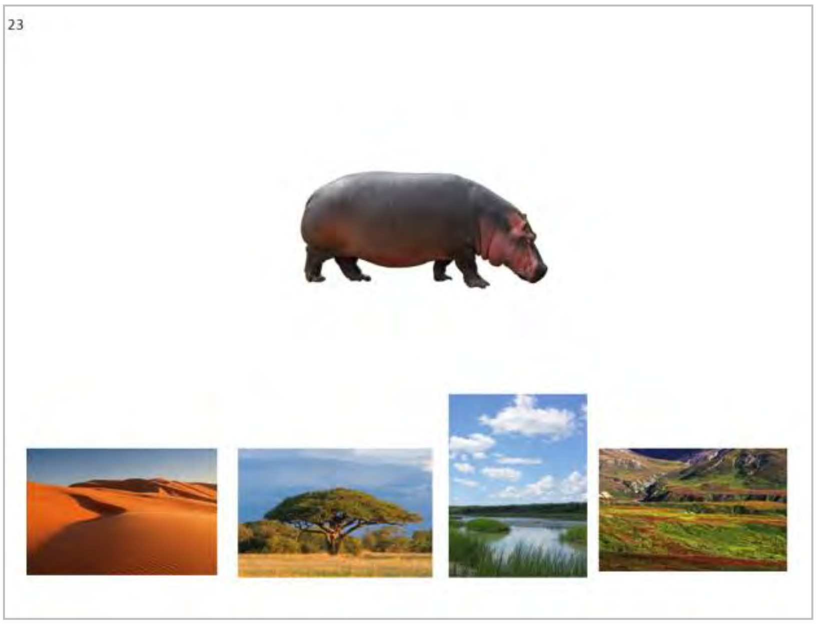
Four subtests were created: naming, word comprehension, semantic association and repetition. Each subtest yielded a total score of 30. An example of the stimuli used for the item "Hippopotamus" is provided below.

1. **Naming task** - Participants provide the name of the item shown in a colour photograph, one at a time. This subtest is always administered first. For example, for the following picture, participants are asked: "What is this called?".

Responses are untimed and can be self-corrected, with no penalty for minor distortions in sound (e.g., slurring of words).

2. **Word Comprehension task** (Word-Picture Matching) – Participants select the picture which best matches the word spoken by the examiner when presented with arrays of photographs containing the target item and six foils. Targets are presented in a random location. Foils are either semantically close to the target (e.g., for the target item *hippopotamus* foils included other large African animals) or visually similar. This subtest is always administered before the Semantic Association task. For example, for the picture below, participants are asked to: "Point to the hippopotamus".

3. **Semantic Association task** (Picture-Picture Matching) – participants select the picture which is most closely associated with the target picture from a set of four options. The four options are semantically related to each other, but only one option relates closely to the target. For example, for the picture below, participants are asked. "Which picture below best goes with the hippopotamus?" (where the correct response is the third picture, depicting an environment in which this animal would be found).



4. **Repetition task** – participants listen and repeat each word, one at a time, after the examiner (e.g., "Say the word *hippopotamus*"). Words must be repeated correctly and fluently, without pausing or re-starts. Full scoring criteria are provided in Appendix 3.

The same images were used for each target in the Naming and Semantic Association subtests. The Word Comprehension task, however, used alternative images of the same items so that participants could not identify the item based on visual memory.

The administration of all four subtests took approximately 20 minutes, and a short break was given between administering the Naming and Word Comprehension subtests. Given the graded nature of the test, subtest administration was discontinued in cases where the participant made 6 consecutive failures and showed signs of possible distress.

Data analysis

IBM SPSS Statistics 20.0 was used for data analysis. Between-group comparisons for neuropsychological tests and total scores on the SYDBAT tasks were performed using univariate analysis of variance (ANOVA), followed by Tukey *post hoc* tests. Comparisons on sociodemographic variables were conducted using either parametric or non-parametric tests, as appropriate. Impairment profiles for each patient group were examined firstly by classifying SYDBAT scores as either impaired or unimpaired, based on a threshold of two standard deviations below the control mean, and then calculating the proportion of impaired cases within each diagnostic group. A discriminant function analysis was also conducted to investigate how well the test distinguished among the three patient groups.

Basic psychometric properties of the SYDBAT were also evaluated. Convergent validity was established through correlations between Naming and BNT-15, Repetition and the Repeat Score from Repeat and Point Test, Word Comprehension and the Point score from Repeat and Point Test, and Semantic Association and PPT. Given the potentially subjective nature of the Repetition scoring, scores for 29 PPA cases were obtained from two independent raters (1 neurologist and 1 neuropsychologist) who were blind to the clinical diagnosis. Inter-rater reliability was assessed using a two-way random effects model intra-class correlation coefficient based on absolute agreement. With regard to test-retest reliability, a small number of participants in the current sample were available within a short time for a re-assessment. Additional patients attending the FRONTIER clinic who also could be tested twice over a short time period (2-4 weeks) were included in this analysis. These patients included other diagnoses within the spectrum of Frontotemporal dementia and Alzheimer's Disease. Test-retest reliability was assessed by correlating test performance on the first administration with scores obtained at a second administration.

3.3. RESULTS

Participants

No significant group differences were present for age, years of education, or distribution of sex (all p values > .05; Table 3.1). The PPA subgroups did not differ with regard to time since diagnosis (p = .375) or severity of dementia symptoms as measured by the Clinical Dementia Rating scale (p = .053), although there was a significant difference in disease duration (H (2) = 12.8, p = .002), with SD patients reporting a longer history of language difficulties.

Table 3.1: Demographic details by group

	PNFA	SD	LPA	Controls
Males / Females (n)	11 / 9	16 / 6	5 / 10	28 / 26
Age	67.7 ± 10.1	63.9 ± 7.2	65.7 ± 7.8	67.8 ± 6.0
Education (years)	13.5 ± 3.0	12.7 ± 2.8	14.5 ± 3.2	13.6 ± 3.0
Time since diagnosis (years)	0.3 ± 0.4	1.0 ± 1.3	0.8 ± 1.0	N/A
Disease duration (years)	2.7 ± 1.4	4.9 ± 2.0	3.8 ± 2.7	N/A
CDR[a]	0.3 ± 0.3	0.6 ± 0.2	0.5 ± 0.4	N/A

Values are Mean ± Standard Deviation. [a] CDR = Clinical Dementia Rating scale, 0 indicates no impairment, where 0.5, 1, 2, and 3 indicate Very Mild, Mild, Moderate and Severe Dementia

Neuropsychological test results

As expected, all PPA groups were significantly impaired on the cognitive screening measure (ACE-R) compared to controls (Table 3.2). Among the patient groups, PNFA patients performed significantly better than both LPA and SD patients (p < .001), with no other significant differences found. On neuropsychological assessment, PNFA and LPA patients displayed similar impairments relative to controls on forward and backward Digit Span, Trail Making Test A and B, and letter fluency.

Table 3.2: Neuropsychological test results by group

	PNFA		SD		LPA		Controls		F	Post hoc tests	
	M	StD	M	StD	M	StD	M	StD		below controls	other differences
ACE-R (100)	**81.4**	2.8	**64.3**	13.4	**62.7**	8.0	**95.1**	3.3	114.6	All groups [b]	PNFA > SD = LPA [b]
Category fluency	**11.0**	4.1	**7.5**	4.4	**6.9**	3.3	**21.0**	4.7	78.9	All groups [b]	PNFA > LPA = SD[a]
Letter fluency (FAS)	**19.9**	13.6	**25.7**	12.0	**22.6**	9.7	**46.5**	11.5	36.5	All groups [b]	
Digits (max forwards)	**5.3**	1.4	**7.0**	1.5	**4.4**	1.4	**7.2**	1.3	21.9	PNFA, LPA [b]	SD > PNFA = LPA [b]
Digits (max backwards)	**3.6**	1.0	**5.1**	1.1	**3.2**	1.1	**5.5**	1.3	22.4	PNFA, LPA [b]	SD > PNFA = LPA [b]
RCFT – copy (36)	**30.0**	5.4	**32.4**	2.6	**28.0**	5.7	**32.5**	3.0	6.5	LPA [b]	SD > LPA [b]
RCFT – recall (36)	**15.1**	8.4	**13.1**	6.9	**8.0**	6.1	**17.4**	6.3	8.1	LPA [b]	PNFA > LPA[a]
TMT A (seconds taken)	**65.7**	28.5	**40.1**	17.3	**60.1**	36.7	**33.8**	12.1	13.7	PNFA, LPA [b]	SD < PNFA [b]; SD < LPA[a]
TMT B (seconds taken)	**164.3**	97.7	**94.5**	45.4	**202.3**	105.4	**79.3**	30.3	18.5	PNFA, LPA [b]	SD < LPA [b]; SD < PNFA[a]

Note: maximum scores in brackets where relevant; M refers to Mean, StD refers to Standard Deviation; ACE-R = Addenbrooke's Cognitive Examination-Revised; RCFT = Rey Complex Figure Test; TMT = Trail Making Test; [a]$p < .05$ [b] $p \le .005$ [c] *excludes patients with significant apraxia reported in the dominant hand*

Differences in profile, however, were seen on tasks of visual memory, where only LPA patients were significantly below the controls (*p* <.001), and on category fluency, where PNFA were least impaired of the patient groups, followed by equivalent performances by SD and LPA patients. Patients with SD, by contrast, performed normally on tasks of attention, visual memory, and executive function (with the exception of fluency tasks).

SYDBAT results

As expected, significant group differences were found on all four subtests of the SYDBAT. All PPA groups were significantly impaired on the Naming subtest compared with healthy controls (F (3,107) = 178.5, p <.001), with pair-wise comparisons showing differences among each of the patient groups (SD < LPA < PNFA, p <.001). While all SD patients (100%) and virtually all LPA patients (14 out of 15, 93%) showed impairment on this subtest (scoring below two standard deviations of the control mean), only 40% of the PNFA patients performed below this range, with only 2 patients scoring below 20 (Figure 3.1).

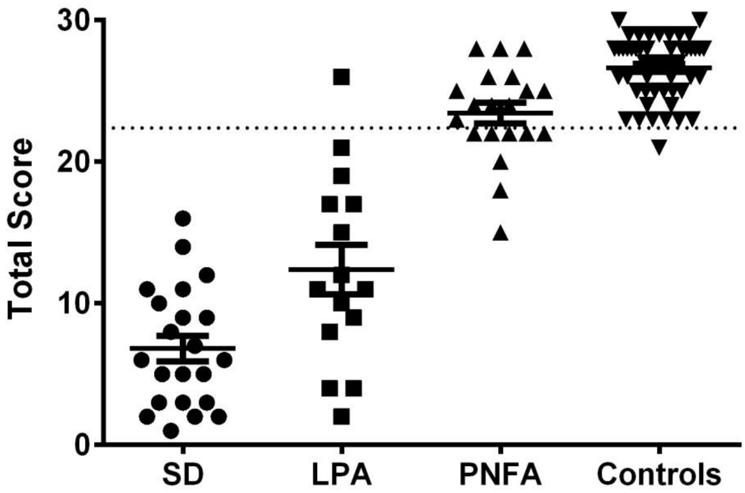


Figure 3.1: Naming performance by group

The dotted line indicates scores 2 standard deviations below the mean of healthy controls. Error bars represent the Standard Error of Measurement.

Overall group differences were found for Repetition (F (3,106) = 16.9, p <.001), but contrary to expectation, both PNFA and LPA patients were impaired relative to controls (both $p \leq .001$) and relative to SD patients (p < .001; p = .042 respectively), with no other significant differences between groups. The majority of PNFA and LPA patients made at least one error on this subtest (65% and 60% of cases respectively). Although one third (36%) of SD patients also made some repetition errors, these were infrequent with no patient scoring below 25 out of 30 (Figure 3.2).

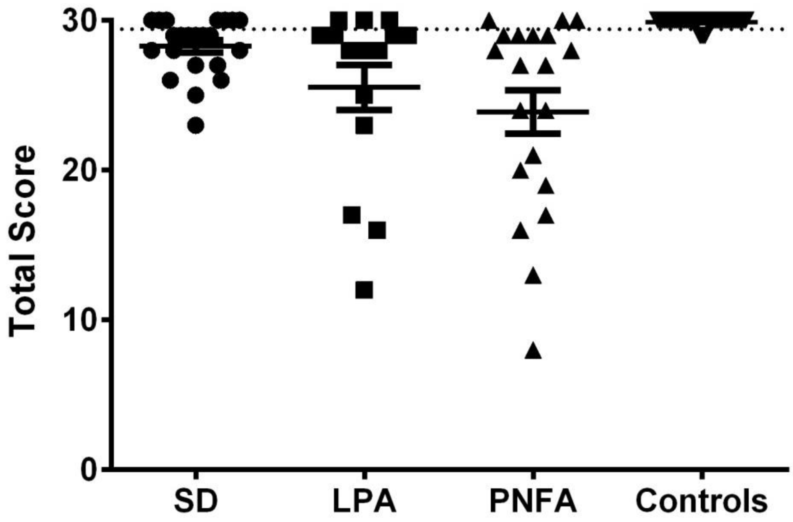


Figure 3.2: Word repetition performance by group

The dotted line indicates scores 2 standard deviations below the mean of healthy controls. Error bars represent the Standard Error of Measurement.

Group differences were also observed for the Word Comprehension and Semantic Association subtests (F (3,107) = 58.1, p < .001; F (3,105) = 60.5, p < .001). SD patients were significantly impaired on both tasks compared with all other groups (all p values < .001), with a majority scoring below the normal range (82% and 90% of cases respectively). The reverse pattern was observed in PNFA patients, where only a small proportion of patients fell within the impaired range (15% and 10% respectively). For the LPA patients, performance on the Word

Comprehension task was significantly lower than controls (p = .001) and PNFA patients (p = .049), with half of the patients (53%) classified as impaired (including some well below the normal range). By contrast, only 4 LPA patients (27%) fell within the impaired range on the Semantic Association task (Figure 3.3).

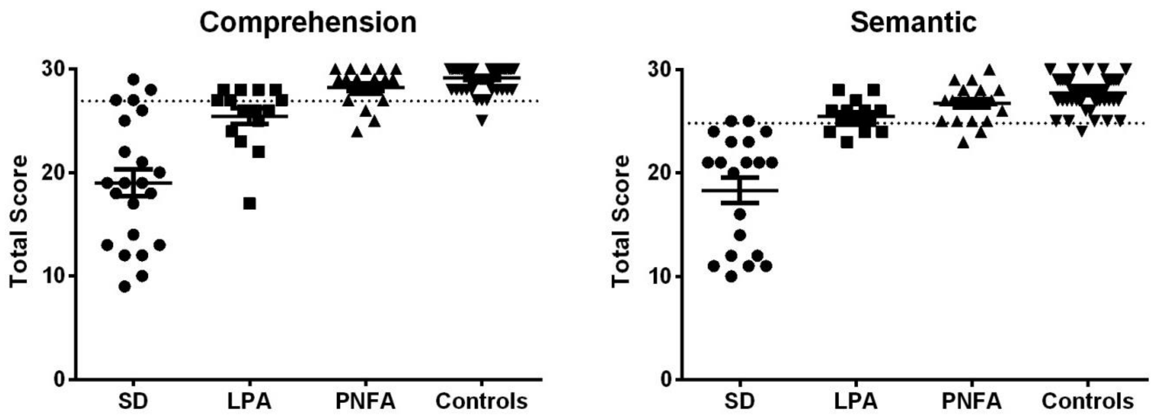


Figure 3.3: Word comprehension and Semantic Association performance by group.

The dotted line indicates scores 2 standard deviations below the mean of healthy controls. Error bars represent the Standard Error of Measurement.

In order to explore whether patients could be classified into diagnostic groups using a combination of SYDBAT scores, a discriminant function analysis was conducted based upon Naming, Repetition and Semantic Association tasks. The Word Comprehension subtest was not included given the greater overlap in scores across the patient groups, compared with the other semantic task. The predictive capacity of this function was significant (X^2 = 86.3, p < .001), with the cross-validated classification resulting in 80% of cases (44 out of 55) correctly classified. The majority of classification errors related to the diagnosis of LPA, where only two-thirds (10 out of 15) were correctly classified from SYDBAT scores alone. Of the 6 diagnostic errors made across the two other groups, all errors involved an incorrect classification of LPA. If LPA patients were removed from the sample, 100% of the PNFA and SD cases were classified correctly in the cross-validated analysis.

While discriminant analysis provides a robust statistical method to demonstrate classification accuracy, it does not provide easily applicable diagnostic rules. To aid clinically, some simple decision rules were created from these findings (Figure 3.4):

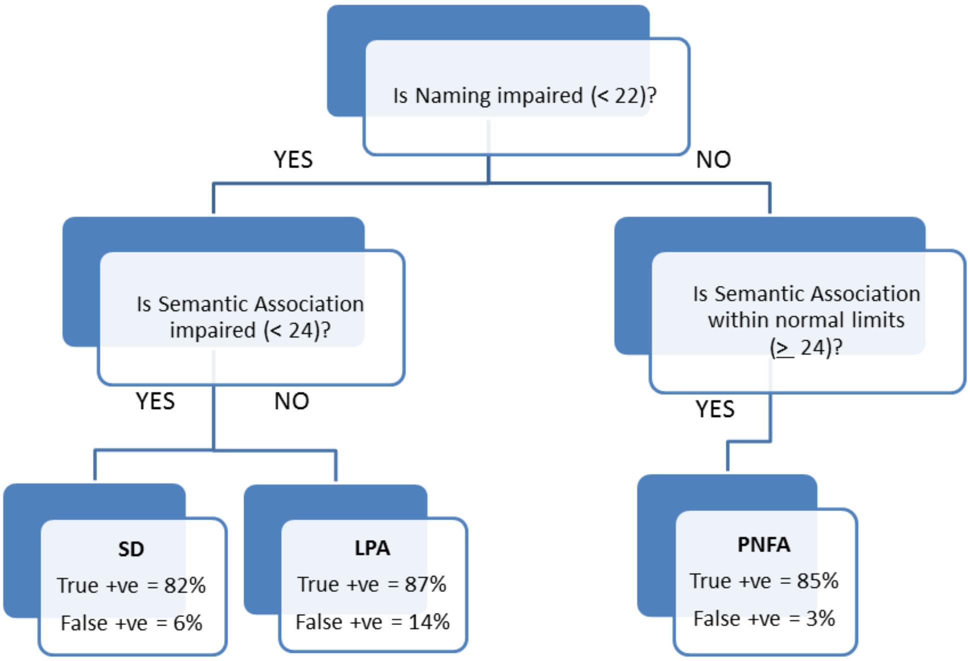


Figure 3.4: Decision tree for diagnosing PPA subtypes.

Note: +ve = Positive

1. If scores on the Naming and Semantic Association subtests are 2 standard deviations or more below the control mean (below 22 and 24 respectively), the most likely diagnosis is SD. Application of this rule correctly classified 18 out of 22 (82%), while including 2 (6%) LPA cases (i.e., false positives). A diagnosis of SD is further supported by good Repetition and normal performance on other neuropsychological tests such as RFCT and Digit Span.

2. If Naming is below 22 but Semantic Association is within 2 standard deviations of the control mean (i.e., ≥ 24), the diagnosis is most likely LPA. This simple rule correctly identified 13 out of the 15 (87%) LPA cases, but also produced the highest false

positive rate (6 cases – 4 PNFA and 2 SD patients, 14%). Reductions on other neuropsychological tests such as RCFT and Digit Span further support the diagnosis of LPA.

3. If Naming and Semantic Association are both within 2 standard deviations, the diagnosis is most likely PNFA. This rule produced an 85% true positive rate and misdiagnosed only 1 LPA case (3%). This diagnosis is then supported by errors in Repetition, particularly with laboured, segmented delivery.

SYDBAT means and standard deviations for all four groups are provided in Table 3.3 below.

Table 3.3: SYDBAT means (M) and standard deviations (StD) by diagnostic group

	PNFA (n =20)		**SD** (n = 22)		**LPA** (n =15)		**Controls** (n = 54)	
	M	StD	M	StD	M	StD	M	StD
Naming	**23.5**	3.3	**6.8**	4.2	**12.4**	6.8	**26.6**	2.1
Word Comprehension	**28.3**	1.7	**19.0**	6.1	**25.4**	3.0	**29.1**	1.1
Semantic Association	**26.7**	1.8	**18.3**	5.5	**25.5**	1.5	**27.7**	1.4
Repetition	**23.9**	6.5	**28.6**	1.5	**25.4**	5.9	**29.9**	0.3

SYDBAT psychometric properties

Investigation of the psychometric properties revealed good convergent validity when comparing SYDBAT subtest scores with other established language measures, with all Pearson correlation coefficients ranging from $r = .67$ for Repetition to $r = .95$ for Naming (all p values $< .01$, Table 3.4). High test-retest reliability was also demonstrated over a mean interval of 27 days across each of the subtests yielding .89 and above. Inter-rater reliability for repetition scoring also showed excellent results with an intra-class correlation coefficient of .96.

Table 3.4: SYDBAT convergent validity and test-retest reliability results

SYDBAT	BNT-15	Repeat & Point - Repeat	Repeat & Point - Point	Pyramids & Palm Trees	Test-Retest (n = 23)
Naming (n = 82)	.95**				.94**
Repetition (n = 72)		.67**			.94**
Word Comprehension (n = 73)			.74**		.90**
Semantic Association (n = 31)				.89**	.92**

*All values are Pearson's r; ** correlation is significant at .01 level (2-tailed); BNT-15 = Boston Naming Test – 15 item version*

3.4. DISCUSSION

As predicted, the application of the SYDBAT revealed different patterns of performance across groups of PPA patients, with significant group differences found for each subtest. A discriminant function analysis revealed that 80% of PPA participants were correctly classified based on scores on three SYDBAT subtests alone. Based upon these results, a simple rule based algorithm capable of diagnosing the vast majority of cases was devised. While the true positive rate was equivalent across the three syndromes (82-87%), the highest false positive rate was for LPA (14%).

Discussion of PPA profiles

As found in previous studies (Hodges et al., 2008), SD was characterised by a clear discrepancy between word repetition and tasks which require semantic knowledge. This pattern was most evident in the comparison of the Naming and Repetition subtests scores, although accurate diagnosis of this group required consideration of the Semantic Association score as significant discrepancies between naming and repetition can also be observed in some LPA cases. The majority of SD patients performed well below the normal range on semantic tasks, providing a clear diagnosis. When this result was combined with naming performance, 82% of SD cases were classified correctly using the simple algorithm. It should be noted however that a small but distinct subgroup (4 of 22) were classified as LPA as their semantic deficits were very mild. To correctly classify these cases it may have been necessary to test naming and comprehension of very low frequency nouns (e.g., proper names) not included here. Such cases were however distinguished from those with LPA on the basis of their preserved auditory verbal short-term memory, as evident from cognitive measures such as superior backward digit span and sentence repetition (Gorno-Tempini et al., 2004; Leyton et al., 2011; Wilson et al., 2010).

As expected, the profile of PNFA reflected a reverse pattern to SD. Overall, these patients performed well on tasks requiring word comprehension and associative knowledge in the context of several speech abnormalities. It should be noted that overall almost two thirds of the PNFA patients were within normal limits on the Naming test, providing a clear distinction from the two other PPA variants. While patients with PNFA typically manifest severe disruption of conversational speech, they frequently perform well on naming tasks requiring the production of a single word in response to a specific target (Croot, Patterson, & Hodges, 1998; Graham, Patterson, & Hodges, 2004). The lack of a clear differentiation between PNFA and LPA groups on the Repetition task was somewhat surprising. This failure may in part reflect the two forms of PNFA which have been defined within the diagnostic criteria - agrammatism and apraxia of speech – which may co-occur, but of which only one needs to be present for diagnosis (Gorno-

Tempini et al., 2011). As a result, not all PNFA patients demonstrated the striking difficulties in articulating multi-syllabic words which have often been described. While the SYDBAT cannot replace a full assessment of speech quality to determine the presence or absence of a motor speech disorder (speech apraxia), as well as elements of agrammatism, as needed to meet recent consensus criteria for a diagnosis of PNFA, the SYDBAT was successful in identifying 85% of the non-fluent cases within the PPA sample.

The most difficult group to classify on the basis of the SYDBAT was LPA. The profile of these patients was somewhat intermediate, showing moderate to severe impairments on naming, reductions in word repetition, and mild deficits on word comprehension. Although repetition problems have previously been reported in this group with respect to word strings or sentence level tasks (Gorno-Tempini et al., 2008), significant difficulties with multi-syllabic words were not expected. Close examination revealed that these errors were phonological in nature or included the need to re-start words. While not distinguished in the scoring of this subtest, LPA patients typically did not produce segmented or aprosodic errors, providing a qualitative distinction which may further assist in differentiating between PNFA and LPA. A similar pattern of performance has been observed when analysing speech samples in PPA (Wilson et al., 2010), where approximately half of the PNFA and LPA patients were found to make phonological paraphasias. False starts were common in LPA, but distorted speech was rarely found outside of the PNFA group.

In considering the distinction between SD and LPA patients, it was interesting to note the mild impairment in word picture matching observed in half of the LPA sample. While LPA patients are generally reported to show preserved word comprehension, some reductions on tasks of word-picture matching have been reported previously, which although not as severe as SD patients, are greater than what is observed for PNFA (Rohrer et al., 2010), and progress over time (Rohrer et al., 2013). Only SD patients show severe impairments (scoring at or below 50% correct on this subtest); however, a large proportion of LPA and SD patients showed a similar level of impairment on this test. Given the relatively preserved performance on Semantic Association, this reduction in performance in LPA could reflect a mild impairment in lexical semantics, relative to intact conceptual semantics (that is, intact understanding of the underlying concepts but a breakdown in the relationships between meaning and word form). Alternatively, this difference could suggest subtle attentional problems, or working memory issues, associated with the difficulty in maintaining in memory the spoken word (target word) while scanning the 7 response options presented. Other tasks used to assess single-word comprehension (e.g., Peabody Picture Vocabulary Test) are easier to complete as they present only 4 response options (Mesulam et al., 2009). To distinguish these LPA cases clearly from mild SD patients, results on SYDBAT should be coupled with other neuropsychological tests, where additional reductions in visuospatial tasks and verbal working memory and span may be detected. In particular, administration of tests of auditory short-term memory such as sentence repetition and digit or word span may improve sensitivity (Leyton et al., 2014). Despite LPA being a challenging group to identify, the SYDBAT was still able to identify correctly a majority of these cases in the sample.

Conclusions

In summary, the results of the current study indicate that the SYDBAT provides a fast and simple tool for assessing single-word language processing, which can be easily incorporated within the time constraints of a cognitive assessment. Used in conjunction with broad neuropsychological results, this battery can assist in differentiating PPA subtypes, and increase diagnostic certainty.

A clear profile for Semantic Dementia was found, illustrating the relative strengths of word repetition in contrast to word retrieval (naming). While this pattern was found in all participants, the Word Comprehension and Semantic Association subtests showed a broad range of performance, with some SD patients displaying relatively mild deficits, while others were very severe. This highlights the importance of measuring not only naming performance but other indicators of semantic impairment to capture disease severity within this group. As discussed in Chapter 1, word comprehension and degree of remaining semantic network have been posited as factors affecting the success of word retraining interventions. The SYDBAT therefore also provides a simple tool for considering the relationship between training outcomes and broader measures of semantic memory.

CHAPTER 4. Word Retraining Methods – *simple effective practices to restore words*

The aim of this study was to investigate how length of practice, as well as different components of practice, may affect word retraining outcomes in SD. As part of this investigation, the study also aimed to identify the simplest forms of practice to achieve effective results, while reducing burden for clinicians involved in the therapy and maximising inclusiveness for patients.

4.1. INTRODUCTION

As discussed in Chapter 1, case studies to date have demonstrated the potential for patients with Semantic Dementia to improve their naming skills while engaging in a word retrieval therapy. The specific key variables for success, however, remain largely unidentified. This is due to the difficulty in comparing across individuals or studies published to date. Few studies have applied the same training method to more than one person, or reported a standard metric, such as an effect size, to allow comparison across individuals or studies.

Review of the literature has, however, provided some guidance regarding effective training methods. It appears important to incorporate both phonological and semantic aspects of the target word, and focus on vocabulary that is of relevance to the individual, thereby providing the opportunity for the relearnt information (word label) to be integrated with existing semantic knowledge. Methods which minimise intrusive errors during the intervention may also be beneficial for some patients (Jokel & Anderson, 2012), although this does not seem vital to the treatment success.

Other aspects of retraining, such as the intensity of practice, have not been specifically studied, despite the suggestion from animal models of learning that repetition may be an important factor in promoting brain plasticity (Kleim & Jones, 2008). One of the most successful reported cases to date, patient CUB (Heredia et al., 2009), utilised one of the most intense practice regimes (as discussed in Chapter 1). As yet, however, no published studies have directly compared the effectiveness of intense practice over different lengths of time in SD retraining.

One reason for the lack of studies in this area may relate to practical constraints of therapist availability and expense. With recent advances in technology, however, a growing trend exists towards interventions which can be run on home computers (Cherney et al., 2007; Jokel et al., 2010, 2006; Katz, 2010; Mason et al., 2011). This approach appears to have a number of important advantages. Firstly, the combination of phonologic and semantic inputs assistive in word retrieval interventions is readily adaptable to computer programs, allowing the patient to see, hear and practice the word ("*Look, Listen and Repeat*" method) all independent of a therapist's presence. Thus a person could engage in daily, multi-modal practice over an extended period of time without significant expense or therapist's time. Secondly, training at home in a naturalistic setting may enhance the success of the intervention, given learning in this patient group can be context dependent (Graham, Lambon Ralph, et al., 1999; Snowden & Neary, 2002).

Another under-explored variable likely to impact on the success of word retraining relates to identifying methods of practice that encourage generalisation into everyday speech. This integration of learning into a broader context of daily life may assist in the maintenance of treatment effects by providing a mechanism for ongoing rehearsal. Intervention studies in SD have not yet investigated methods to bridge the gap between formal practice and naturalistic use of words. As sentence processing is often spared in this patient group, and related to the functional goal of carrying trained words into speech, one approach could be to include sentence generation into the word retraining. By modelling target words into sentences, this form of practice could provide a stepping stone to everyday use. This may have additional benefits to word recall by promoting an active form of learning (as discussed in Wilson et al., 1994), which could result in deeper memory processing (Craik & Lockhart, 1972; Craik & Rose, 2012). Thus, through the addition of a simple daily writing task, with the instruction to repeat the sentence aloud once complete, learning and maintenance of target words may be enhanced.

Study design and hypotheses

The current study therefore sought to investigate two therapy approaches:

1. Look, Listen, Repeat (LLR)
2. Look, Listen, Repeat + sentence generation exercise (LLR + SGE)

over two time lengths (3 weeks versus 6 weeks). It was hypothesised that:

- an intense daily practice would improve naming ability, with effect size related to severity of semantic impairment;
- while a 3-week period may improve naming of trained items, greater maintenance would be demonstrated for items which are trained over a longer interval of time;
- the combined practice of sentence generation and naming would result in stronger maintenance for these items at 4 weeks post-therapy.

To identify the simplest methods, the study was divided into two components – firstly utilising a rich semantic practice; then secondly exploring the impact of removing certain elements of the practice to identify the most basic yet effective method of training.

4.2. GENERAL METHOD

Participants

Four patients meeting diagnostic criteria for Semantic Dementia (Gorno-Tempini et al., 2011) were recruited from the FRONTIER Research Clinic. The age of participants ranged between 54 and 69 years. Participants were similar with respect to level of education, sex, and duration of symptoms (Table 4.1). While two participants had pacemakers and were therefore unable to have MRI scans, the other two participants (SD1 and SD4) showed the typical pattern of anterior temporal lobe atrophy, with left greater than right volume loss.

Table 4.1: Demographic characteristics of study participants

	SD1 (Study 1)	**SD2 (Study 1)**	**SD3 (Study 2)**	**SD4 (Study 2)**
Sex	M	M	M	M
Age	61	69	65	54
Education (years)	11	11	9	11
Disease duration (years)	4	5	5	4

All participants completed a standard neuropsychological and language assessment (as outlined in Chapter 2). On these assessments, participants showed the expected preservation of visuospatial skills, basic attention and executive function. Syntactic comprehension and word repetition remained generally intact, but each participant showed significant impairment on confrontation naming. Other measures of semantic impairment, as assessed using the SYDBAT, revealed a range of performances, from mild to severe (Table 4.2).

Table 4.2: Neuropsychological and language profile of study participants

	SD1 (Study 1)	SD2 (Study 1)	SD3 Study 2)	SD4 (Study 2)
Cognitive ability				
ACE–R (100)	65	46	68	56
RCFT - Copy (36)	35	34	34	34
RCFT - 3 minute recall (36)	12	16.5	2	30
Digit Span (WAIS-III) -				
Max. Fwds Span, Max. Bwds Span	6, 5	7, 5	7, 5	8, 6
Language assessment				
Category fluency - Animals	5	2	12	8
SYDBAT Naming (30)	4	3	6	5
SYDBAT Repetition (30)	29	26	30	29
SYDBAT Word Comprehension (30)	15	10	22	23
SYDBAT Semantic Association (30)	15	10	21	22
SYDBAT Total (120)	63	49	79	79
Test for Reception Grammar - 2 (80)	66	56	76	76

Note: maximum scores in brackets where relevant; Abbreviations: MMSE = Mini-mental State Examination; ACE-R = Addenbrooke's Cognitive Examination-Revised; RCFT = Rey Complex Figure Test; WAIS-III = Wechsler Adult Intelligence Scale, 3rd edition; SYDBAT = Sydney Language Battery (cut-offs for 2StDs below control mean: Naming = 22; Repetition = 29; Comprehension =26, Semantic = 24)

Experimental study: Stimuli and design

A single subject experimental design was conducted, using a 'multiple-baseline-across-behaviours' with 3 word lists (as described in Chapter 2). Naming was tested over a 3-4-week period to establish baseline performance. Following the baseline period, participants were trained on their first word list for three weeks. Training was then extended to include a second list for three weeks, with both lists withdrawn from treatment at week 6 (T6). During the same period of time the third list remained untreated as a control. During the training period, participants were re-assessed at the end of each therapy week. Follow-up assessments were undertaken 4 weeks later, with further follow up assessments 7-8 weeks post-intervention for participants SD1 and SD3 (participant SD2 was unavailable at this point in time).

4.3. STUDY 1 METHOD

SD1 and SD2 - Rich practice (orthographic, phonological, and semantic input)

A tailored program was developed for each participant, following an initial session with the researcher (SS) to select items and collect the materials.

Materials

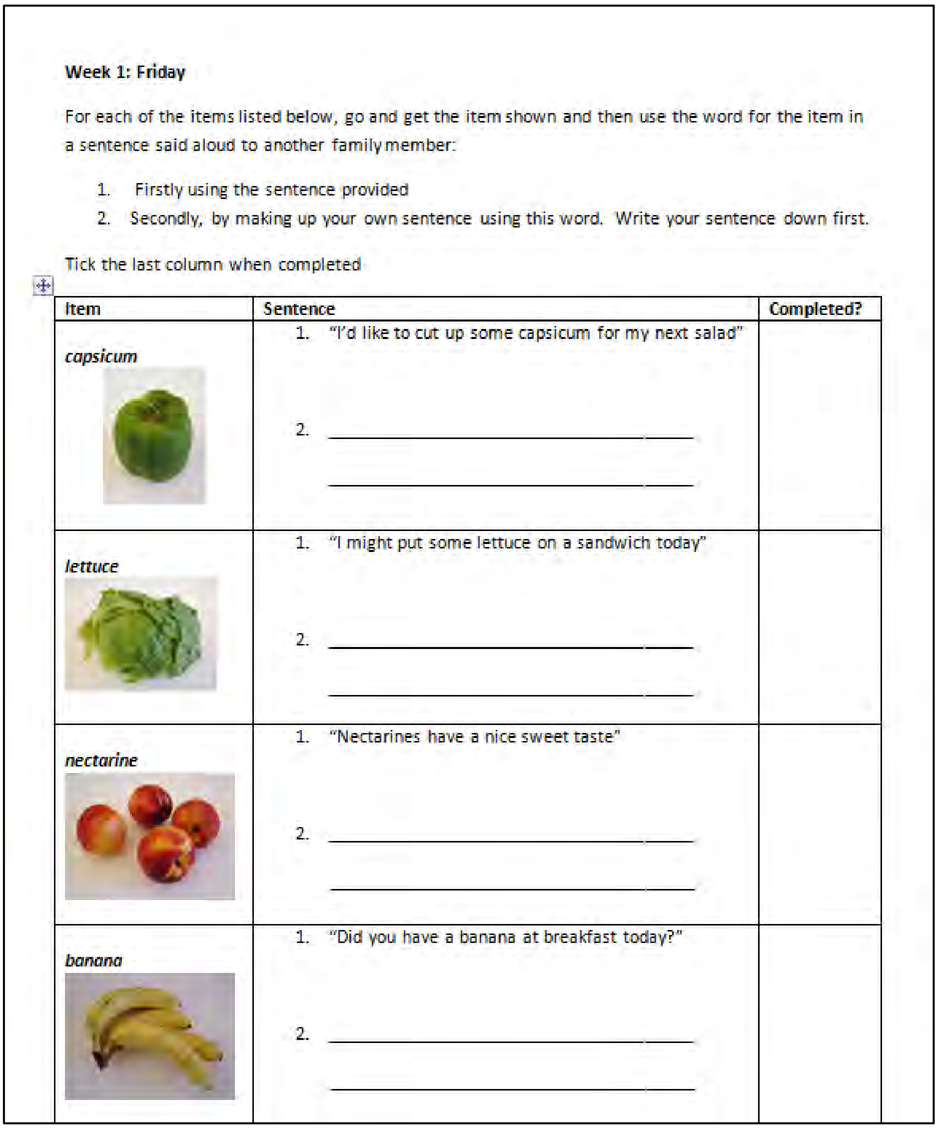
Digital photographs of household objects were taken at the participant's home and included: food, household appliances, kitchen utensils, outdoor tools and clothing. Items were included only if they were considered relevant by the family and participant, and if the participant could demonstrate semantic knowledge either by miming the use of the item or describing it. To measure item familiarity, the exposure or use of each item for each participant was rated by a family member on a frequency scale: daily, several times per week, once a week, once a fortnight, monthly, seasonally or less frequently.

Items were then ranked in relation to this scale and assigned to one of three lists, so that lists were matched for frequency of exposure/use. Each of the two training lists comprised approximately 15-20 words, with a minimum of 2 items named correctly during baseline testing, to provide the participant some sense of success when tested. The remaining items were assigned to the third list, as a control, such that all categories featured in the training lists also appeared within this list.

For each treated word, the participant provided a personally meaningful description, drawing on autobiographical memory, personal tastes or other associations. This was summarised into a short paragraph. An audio recording of the object name and this description was made by the researcher. Photographs and audio recordings were then incorporated into a computer program to produce a slideshow for use in therapy. An example slide is shown in Figure 4.1. To prevent participants from rote learning the lists, the order of item presentation was varied each time, but items from the same category were blocked together to help stimulate semantic processing during training.

Figure 4.1: Example training slide for the item "lemon"

Approximately half of the items from the two training lists were then selected for the additional sentence generation exercise. Photographs of these items were arranged on paper handouts, with 4 to 5 images per page. Beside each photograph was the name of the item, an example sentence using the word, and blank lines for the participant to write their own sentence, incorporating the target word (Figure 4.2).



Week 1: Friday

For each of the items listed below, go and get the item shown and then use the word for the item in a sentence said aloud to another family member:

1. Firstly using the sentence provided
2. Secondly, by making up your own sentence using this word. Write your sentence down first.

Tick the last column when completed

Item	Sentence	Completed?
capsicum	1. "I'd like to cut up some capsicum for my next salad" 2. ______________________ ______________________	
lettuce	1. "I might put some lettuce on a sandwich today" 2. ______________________ ______________________	
nectarine	1. "Nectarines have a nice sweet taste" 2. ______________________ ______________________	
banana	1. "Did you have a banana at breakfast today?" 2. ______________________ ______________________	

Figure 4.2: Example Sentence Generation Exercise sheet

Training procedures

Based on the two sets of training materials (computer slideshow and paper handouts), two training procedures were developed. The first relied solely upon the "look, listen, repeat" (LLR) approach using the computer slideshow, repeated 3 times per item. The second, more effortful, approach incorporated the LLR strategy for 2 repetitions of the item, but used the sentence generation exercise (SGE) for the third exposure. Both procedures aimed for errorless learning (Fillingham et al., 2003) that was self-paced.

During the LLR practice, target items were presented one at a time on the screen, in five steps as shown in Table 4.3. For the SGE items, participants were asked to generate a sentence using the word by completing a daily worksheet. Participants were then instructed to read the sentence aloud. The completed activity sheets were returned to the researcher at the end of each week.

Table 4.3: "Look, Listen, Repeat" (LLR) self-paced procedure

Step	Display	Response
1	A photograph of a training item appears.	The participant is asked to recall the name if possible, but not to guess. When ready, the participant clicks a button.
2	The word appears beside the photograph and a voice recording of the word plays.	The participant repeats the word out aloud then clicks a button to proceed.
3	The written form and audio recording of the item description provided by the participant is presented.	The participant listens and when ready clicks a button to continue.
4	The word beside the photograph disappears.	The participant is encouraged to concentrate on the word and when ready, click a button.
5	The word and voice recording of the word are re-presented.	The participant repeats the word out aloud. When ready, the participant clicks a button and the next item is shown.

Participants were encouraged to practise once a day throughout the training period, initially for 30 minutes and then up to an hour when both lists were introduced. During the first three weeks of training, participants were provided with the slideshow and sentence worksheets for List 1.

For weeks 4 to 6, the slideshow and worksheets were extended to include items from both List 1 and List 2. At the end of the six-week period, all training materials were collected by the researcher so that no further structured practice could be carried out.

Assessment measures

The primary outcome measure was naming accuracy. At each assessment, participants were asked to provide the name of each item (treated and untreated), presented in a randomised slideshow, in the absence of the verbal label or description. Assessments were conducted by an independent researcher (at least 2 hours after completing training for the day) or through a computer program (immediately following the last training session for the week) which recorded verbal responses for later scoring. Responses were given a score of 1 if the target word or a common synonym was provided, with all other responses, including minor phonemic errors (such as the addition, omission, or substitution of a sound), scored as incorrect (a score of 0). Examples of errors include saying "ironer" instead of "iron" or "trouser" instead of "trousers".

Data analysis

Baseline stability of naming scores was established using Cochran's Q Test. To examine the effectiveness of therapy length (List 1 for 6 weeks or List 2 for 3 weeks) and for each therapy approach (LLR only or LLR+SGE), the final pre-treatment results were compared to the post-treatment results using McNemar's Test for related samples. Similarly, to evaluate maintenance, follow-up results were compared with the immediate-post treatment results using McNemar's Test.

To compare treatment results between participants and provide a measure of the relative strength of the treatment, effect sizes were calculated following the approach advised by Beeson and Robey (2006) using Busk and Serlin's d:

$$d = \frac{\bar{x}_{A2} - \bar{x}_{A1}}{S_{A1}}$$

where $\bar{x}$A2 is the mean of the data collected post-treatment (here, immediate post-treatment and 1 month follow up), $\bar{x}$A1 is the mean of the data collected pre-treatment (here, the average of three baseline measurements) and *S*A1 is the standard deviation at pre-treatment (Busk & Serlin, 1992). Separate effect size calculations were made for each treatment list and then averaged to represent the overall treatment effect for each participant. The results were then compared with benchmarks provided by Beeson and Robey (2006), based on a meta-analysis of 12 studies in lexical retrieval studies (small d = 4.0; medium d = 7.0, large d = 10.1).

4.4. STUDY 1 RESULTS

Overall training effect

A clear improvement in naming performance was observed in the trained lists, with no change in performance on the untreated items over the same period (see Figure 4.3 and Figure 4.4). This was confirmed in both patients statistically, with significant increases after both 3 and 6 weeks of training for List 1 compared with baseline performance (all McNemar Tests $p \leq .004$), and at the end of the training period for List 2 (McNemar Tests - final baseline assessment vs T6: $p \leq .001$), as expected from the treatment schedule. No significant differences were found for the untreated list (all p values > .55), nor in the pre-treatment baseline period for any item lists (Cochran's Q, exact probability two-tailed, $p > .05$, for all comparisons). The magnitude of change in performance, as measured by the overall effect size, was large for both participants (SD1 = 10.9; SD2 = 11.6), regardless of their level of semantic impairment.

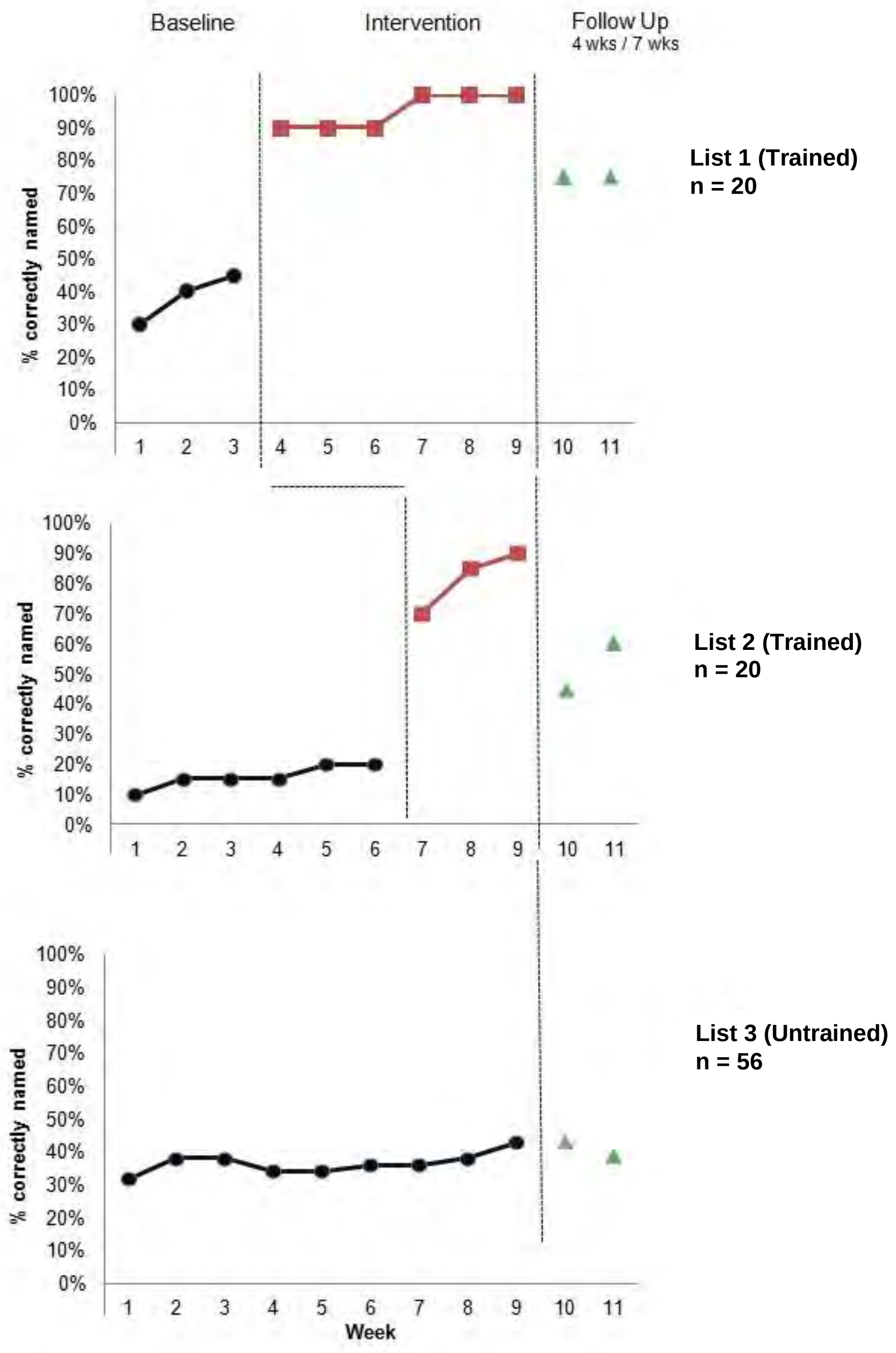


Figure 4.3: Word retraining results for Case SD1

Dotted lines mark the three phases of the study. Follow-up period is for 4 weeks and 7 weeks.

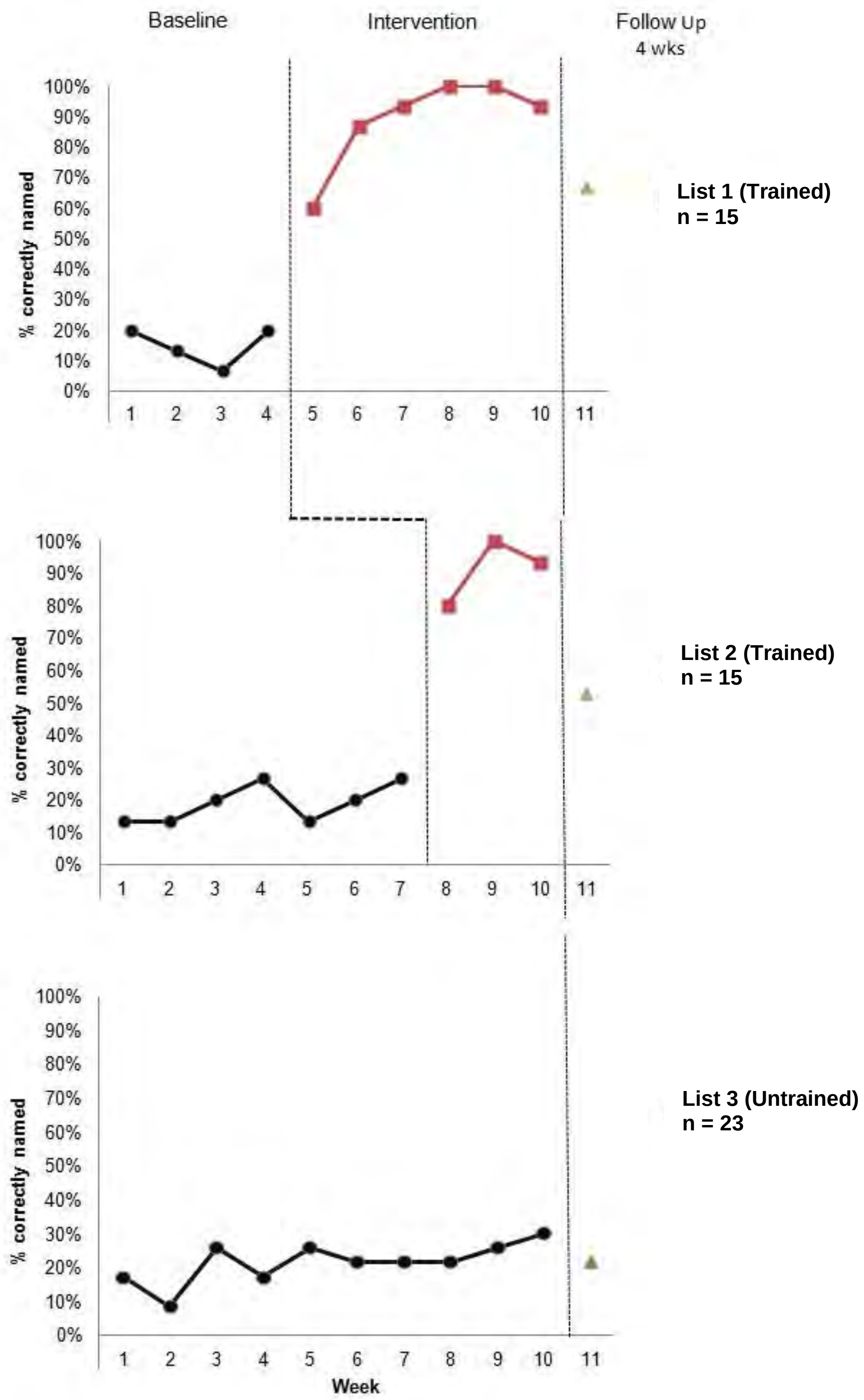


Figure 4.4: Word retraining results for Case SD2

Dotted lines mark the three phases of the study. Follow-up period is 4 weeks.

Length of training effect

The length of training (6 weeks versus 3 weeks) had equivalent benefit during the treatment phase, with equally high levels of attainment despite fewer sessions for List 2 (see Figure 4.3 and Figure 4.4). The maintenance of this improvement, however, appeared less robust for the shorter trained list. Comparisons of naming performance at treatment end (T6) with follow up showed a significant drop for the shorter-trained List 2 for SD1 at both 4 weeks (p = .022) and 7 weeks (p = .031) post-treatment, and at the follow up assessment for SD2 (p = .031). While some declines were also observed for the longer-trained List 1, these were not significant for either SD1 or SD2, supporting the hypothesis that better maintenance may be achieved with longer training.

Type of training effect

With regard to the two training procedures, both forms of practice delivered strongly significant increases from baseline to post-treatment (all McNemar's Tests: $p \leq .002$). While not yielding a statistically significant difference, a higher final level of attainment was consistently observed for items engaged in the combined LLR +SGE practice (up to 100% for both SD1 and SD2, compared to 90% and 88% respectively on the LLR only items, Table 4.4). This difference was also reflected in larger effect sizes for LLR+SGE items than LLR only items (SD1: d = 11.8 vs 7.5; SD2: d = 8.6 vs 8.1, respectively).

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Table 4.4 Naming performance by type of practice versus untrained words

	Naming performance over time (% correct)											
	BL1	**BL2**	**BL3**		**T1**	**T2**	**T3**	**T4**	**T5**	**T6**	**Follow up - 4wks**	**Follow up - 7wks**
SD1												
LLR (n = 20)	20%	25%	30%		55%	55%	60%	80%	90%	90%	60%	50%
LLR+SGE (n = 20)	20%	30%	30%		50%	55%	50%	90%	95%	100%	60%	85%
Untrained (n = 56)	32%	38%	38%		34%	34%	36%	36%	38%	43%	43%	39%[a]
SD2	**BL1**	**BL2**	**BL3**	**BL4**	**T1**	**T2**	**T3**	**T4**	**T5**	**T6**	**Follow up - 4wks**	
LLR (n = 17)	35%	12%	18%	24%	53%	53%	53%	88%	88%	88%	59%	
LLR+SGE (n = 13)	8%	8%	0%	15%	31%	46%	54%	85%	100%	100%	62%	
Untrained (n = 23)	17%	13%	26%	22%	26%	26%	26%	22%	22%	26%	22%	

BL1 to BL4: baseline assessments conducted prior to commencing treatment; T1 to T6: assessments conducted during at the end of each treatment week

[a] *The items within the control list reduced to 36 as a result of the introduction of practice on a third training list for SD1 between the two follow up periods*

Evaluating the longer term benefits, however, did not reveal a consistent pattern of advantage for words trained under the combined LLR+SGE approach. The expected result was found for SD2, with only the list of words in the combined approach successfully maintained at follow up 4 weeks later (McNemar's Tests - LLR only: p = .016; LLR+SGE: p = .375). For SD1, results were variable across the two follow up periods; while at 4 weeks post-intervention LLR only items appeared better maintained compared with results immediately following the end of intervention (LLR only: p = .11; LLR+SGE: p =.008), the reverse was observed at 7 weeks post (LLR only: p = .008; LLR+SGE: p = .25).

4.5. STUDY 2

SD3 and SD4 - Exploring key variables

To begin exploring the minimal requirements for effective practice, two further participants (SD3 and SD4) were recruited. In particular, this series examined: a) whether the inclusion of a semantic description of the item is a key component of retraining; and b) whether a simple LLR training approach, without semantic descriptors or the SGE, is sufficient (given results of Study 1 did not demonstrate as clear an effect of training type on maintenance as expected).

Case SD3 – LLR with picture and word only (no semantic description) + SGE

Materials and measures for case SD3 were assembled using the same approach as in Study 1, with the exception that no semantic descriptions were obtained for training. All other aspects of the design and intervention approach remained identical, with half of the trained words including the SGE, and the other half using LLR only. Follow up was conducted at 1 month and 2 months post-intervention. Naming assessments during the training phase were conducted following the final training session for the week.

Once again, clear improvements in naming scores were observed in the trained lists as compared to the untreated list (see Figure 4.5). For List 1, baseline stability was confirmed (Cochran's Q, p = .311), and a significant improvement in naming was found at the end of the third week of training (T3, McNemar's Test, p = .002) and at the immediate post treatment assessment (T6, McNemar's Test, p = .002), with 100% of the words correctly named throughout the training period. Improvements were well maintained at 1 and 2 months post-treatment. For List 2, SD3 was pre-exposed to some items prior to training commencement at week 4, as a result of receiving the SGE sheets for List 2 one week early. This affected baseline stability (Cochran's Q, p = .007 over the 6 week baseline period), such that while an improvement was found, it was not significant at the immediate post-treatment assessment (McNemar's Test, p = .125). Items in the Control list remained unchanged throughout the study period (McNemar's, p > .500). List 2 items were well maintained over the 1 and 2 month follow up periods (p = 1.00 for both follow up periods). The weighted effect size was small to medium (d = 4.9).

No additional benefits were found for items trained under the combined LLR+SGE training approach, with both procedures resulting in similar improvements in naming accuracy by the end of week 6 (Table 4.5), and maintenance at 1 and 2-month follow up assessments (all McNemar Tests $p \geq .500$).

Thus, the results of SD3 support the hypothesis that the semantic description is not a necessary component to the success of improved naming or maintenance.

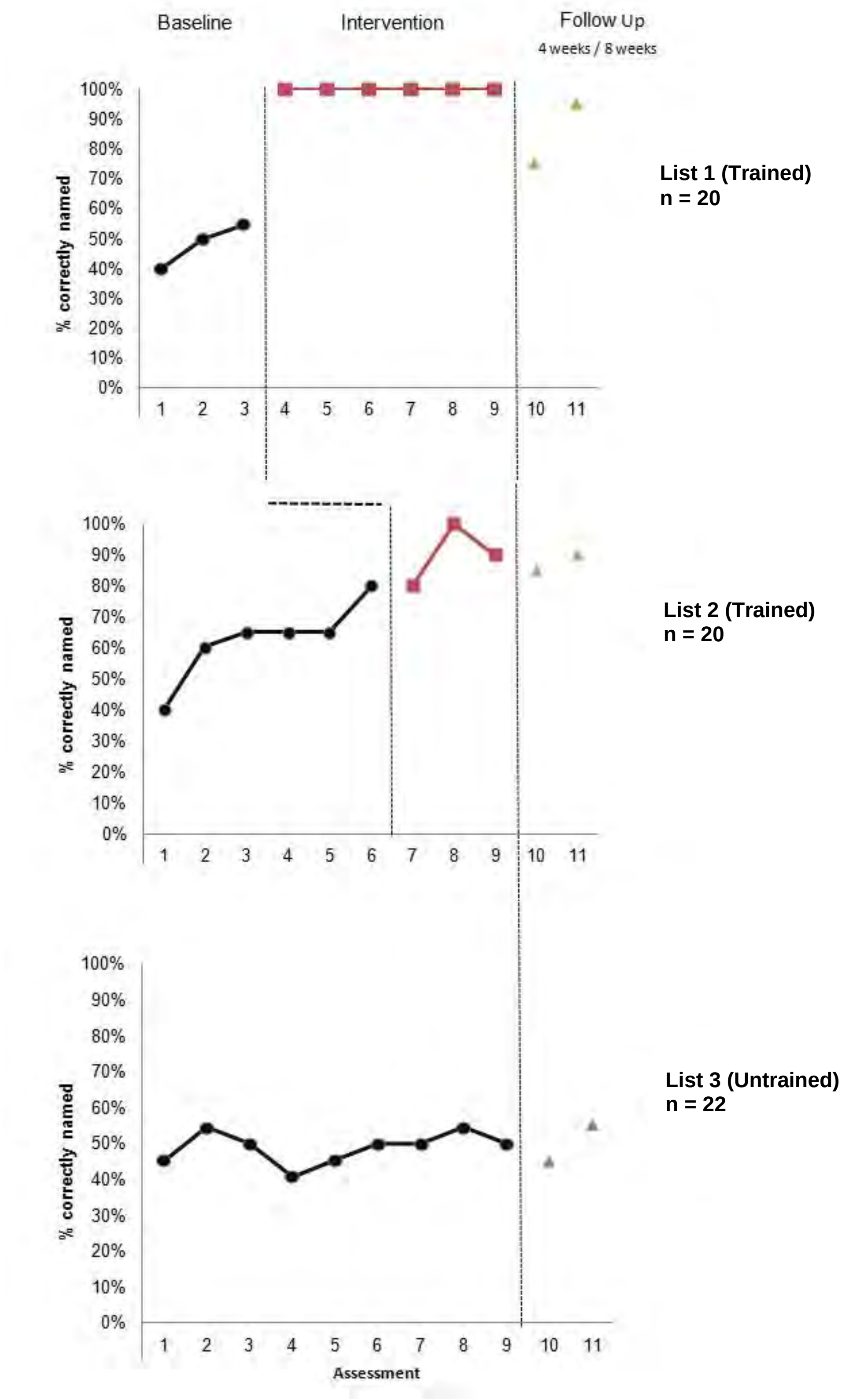

Figure 4.5: Word retraining results for Case SD3

Dotted lines mark the three phases of the study. Follow-up period is at 1 month and 2 months.

Table 4.5: SD3 – Naming performance by type of practice

	Naming performance over time (% correct)										
	BL1	BL2	BL3	T1	T2	T3	T4	T5	T6	Follow up 1 month	Follow up 2 months
LLR (n = 20)	35%	55%	50%	80%	80%	85%	85%	100%	90%	80%	95%
LLR+SGE (n = 20)	45%	60%	65%	85%	85%	95%	95%	100%	100%	80%	90%
Untrained (n = 56)	45%	55%	50%	41%	45%	50%	50%	55%	50%	45%	55%

BL1 to BL3: baseline assessments conducted at the end of each week prior to commencing treatment; T1 to T6: assessments conducted at the end of each treatment week ; Follow up: assessments after treatment withdrawn

Case SD4 – LLR with picture and word only (no semantic description), no SGE

Materials and measures for case SD4 were identical to those used for SD1 in Study 1, with the exception that no semantic descriptions were obtained for training and all items were practised using the Look, Listen, Repeat approach only. As SD4 was living interstate, the training procedure and schedule were modified slightly. Data were collected once at baseline, three times at the conclusion of the treatment, and finally at a 3-week follow up. Post-treatment assessments were conducted on 3 consecutive days, 2 weeks after the final training session was completed.

Once again, clear improvements in naming accuracy were observed for both trained lists (McNemar's Test, Baseline vs T6: $p \leq .002$), but not for the untreated items ($p = 1.00$, see Table 4.6). Only List 1, practised over the 6-week period, was maintained at follow up (no significant difference between T6 and Fl-U, $p = .375$), while performance on List 2, practised for only 3 weeks, fell back to baseline levels ($p = .004$).

Table 4.6: SD4 - Pre- versus post-treatment naming of trained and untrained lists

	Naming performance over time (% correct)					**McNemar's Test**	
	BL	T6-1st	T6-2nd	T6-3rd	Follow up – 3 weeks	Baseline vs T6	Fl-U vs T6
List 1 (n = 20)	**30%**	**85%**	**80%**	**80%**	**65%**	**p = .002**	p = .375
List 2 (n = 20)	**35%**	**60%**	**90%**	**80%**	**35%**	**p = .004**	**p = .004**
Untrained (n = 51)	**29%**	**24%**	**29%**	**29%**	**37%**	p = 1.00	p = .454

Note: Post-intervention assessments (T6-1st, T6-2nd and T6-3rd) were conducted over 3 consecutive days, 2 weeks after treatment end.

4.6. DISCUSSION

Overall summary

This study sought to identify simple but effective methods to retrain words in patients with Semantic Dementia. Using intense, daily practice conducted at home, improvements in word production were observed in a range of patients with SD, over a 3-6-week period. All participants improved significantly, regardless of level of semantic impairment, consistent with prior case reports where significant improvements have been demonstrated in patients even with severe semantic losses (Frattali, 2004; Jokel et al., 2010; Snowden & Neary, 2002). In these studies, however, the effectiveness of learning varied according to patients' comprehension for the items being trained. This study focused exclusively on items at least partially still meaningful to participants, thereby providing the greatest utility and maximising the likely effect. Significant improvements were observed under both 3- and 6-week therapy durations and when using the Look, Listen, Repeat approach with or without sentence generation. Implications of these findings are discussed below.

Discussion of findings

Contrary to expectation, disease severity did not have a negative impact on the effect size of treatment, with severely impaired participants showing the greatest level of change over time. While the only other studies to have quoted an effect size in SD patients found either a very small effect on the treated list (d = 2.00 for PA2, Henry et al., 2008) or small to medium effect sizes (d = 4.74 for NG, Macoir, Leroy, Routhier, Auclair-Ouellet, Houde, & Laforce, 2014; d = 7.22 for SV, Henry et al., 2013), the current study demonstrated large effect sizes for participants SD1 and SD2, and a small to medium effect for the milder participant, SD3. Although surprising at first glance, this difference in effectiveness can readily be explained by the differing levels of opportunity for improvement. While all participants in the current study demonstrated equally high levels of achievement - between 80 to 100% correct by the end of training - higher performance at baseline provided SD3 with fewer words from which to improve. That patients with differing levels of semantic impairments may benefit from word practice most likely reflects the similar level of preservation in other cognitive skills necessary to engage meaningfully in the program, such as everyday memory and attention. Importantly, this finding has implications for treatment planning, and suggests that patients with severe semantic impairments should not be overlooked when considering word retraining programs.

Rapid improvement was observed consistently across participants, with high levels of achievement produced within a three-week period. The majority of previous studies have likewise demonstrated significant improvements following a one to two-week practice period per list (Dressel et al., 2010; Graham et al., 2001; Henry et al., 2008a; Jokel et al., 2006; Snowden & Neary, 2002). While Heredia and colleagues' patient CUB was reported to improve quickly, practice continued for a further two-week period after having learned the full list. Whether this additional practice beyond simply attaining the words contributed to the successful maintenance over time has not previously been explored. In directly investigating the impact of length of practice (in this case either 3 or 6 weeks of training), the current study provides the first opportunity to consider this, with results suggesting this is the case: SD1, SD2 and SD4 all showed better maintenance for words practised over 6 weeks, with losses in learning experienced for words practised over a 3-week interval. While not significant for SD3, fewer words were retained from the list practised for 3 weeks only.

Improved results following a longer period of practice makes sense, as it allows for greater reinforcement of the material learned. It is also consistent with connectionist semantic memory models of SD wherein patients experience a weakened consolidation memory system, and longer term links within the neocortex may be difficult to form (Murre, Graham, & Hodges, 2001). While a longer period assisted in strengthening or establishing stronger links within the memory system, participants in the current study still experienced some losses over time. This finding suggests that simply increasing the length of consolidation is insufficient to maintain benefit and that without some ongoing practice, benefits will fade over time. The nature and level of ongoing practice required once words have been sufficiently re-attained, however, remains unclear, and will form the focus of investigation in Chapter 6.

The benefit of different components of practice was also explored by comparing results both within and between individuals, to identify the simplest methods to achieve significant improvements. The results illustrate that methods to improve naming can be simply constructed, by the pairing of a picture of an object with the word form, presented both visually and aurally. While more elaborate materials, including semantic descriptions may support learning, such additional elements do not appear necessary for words where some conceptual knowledge still remains. This result was demonstrated by the improvements shown by participants SD3 and SD4, whose practice did not involve this component at any stage. Evidence from related studies in aphasic stroke patients also supports the finding that pairing of the object and word form is perhaps the crucial element of training, with reduced learning demonstrated for interventions which focus on semantic associations without reference to the phonological presentation of the word (Crofts et al., 2004). Enriched practice, involving additional semantic information, may be more important where the training goal is to relearn concepts rather than the labels. Preliminary evidence of this has recently been demonstrated by Suárez-González and colleagues (2014), in a case study focused on retraining words which had become meaningless to the person. Here, conceptually enriched therapy provided greater improvements to word retrieval and comprehension than the “standard” word-picture approach. A corresponding drawback, however, relates to the time required by the clinician in creating and testing the training materials for each individual. Thus for the purposes of a simple, home-based program where the goal is to restore words associated with at least partially known concepts, the current study’s simple approach appears sufficient.

Maintenance of naming improvements was demonstrated using both the "Look, Listen, Repeat" method alone, as well as when practised in conjunction with the Sentence Generation Exercise. For SD1, SD2 and SD3, 100% of the words were learned using the LLR + SGE technique by week 6, but after one month the level of retention was not consistently above words practised on the computer alone. Further, patient SD4 was able to relearn words in the absence of this form of practice. While the results therefore do not support a clear benefit to maintenance, consideration of methods to promote transference of learning into everyday life remains important.

Conclusions

The results of this study provide evidence for the effectiveness of basic strategies to reinstate or refresh vocabulary in SD patients. Improvements may be achieved quickly and viably through home practice that involves simple, imitative naming of salient vocabulary, which can easily be set up on patients' home computers. At its most basic level, the pairing of the picture with the word was sufficient to promote significant improvements in naming, and allowed patients with severe semantic impairments to participate and benefit from this approach, with strong treatment effects observed. The translation of these naming improvements into everyday contexts, however, is an important consideration. The extent to which this simple word-picture practice may generalise to other uses of the word is thus explored within the next chapter. Finally, while the current study focused on immediate learning and a short-term follow up of 2 months, how benefits may be maintained into the longer term requires further investigation (and is discussed in Chapter 6).

CHAPTER 5. Generalisation of retrained words

Following on from the previous chapter, the aim of this study was to demonstrate whether words gained through a basic word training program could be applied in contexts other than picture naming. While this is an important issue within the word retraining field, little investigation into verifying the usefulness of these programs has been conducted to date.

5.1. INTRODUCTION

As demonstrated in Chapter 4 (and in previous studies discussed within Chapter 1), SD patients can improve their ability to name pictures following a simple, repetitive practice of associating the picture of the object with the word. In milder stages of the disease, the mechanism by which training assists naming may reflect an improved ability to access target words within the existing store of words (lexicon). In later stages, as this lexicon degrades, training may help by reinstating words that are no longer recognised. Although the loss of words from vocabulary signals a decline in memory functioning, the ability of SD patients to learn and remember new verbal information has been demonstrated more broadly in studies of episodic and autobiographical memory (Irish et al., 2011; Jefferies et al., 2011). Collectively, these studies demonstrate a clear capacity for learning in SD patients. This process of learning, however, appears rigid and context-dependent – only the trained words improve, and programs need to be carefully structured to ensure that the patient learns to associate the picture with the word rather merely learning a list order.

A crucial issue which remains unanswered is whether the improvements in word retrieval (whether achieved by enhancing access to existing words or by relearning words) are specific to the training environment or whether it can be applied to other contexts, given that generalisation depends upon the semantic system which is being increasingly compromised (Hodges & Patterson, 2007; Lambon Ralph, Cipolotti, Manes, & Patterson, 2010). As discussed in Chapter 1, some examples of “near transfer” – the ability to apply learning to contexts that are similar in nature to the training condition (Subedi, 2004) - such as other picture naming tests, have been reported. Little investigation, however, has been conducted into “far transfer”, where tasks differ in nature to the mode of training and thus require a demonstration of flexible learning. Where some attempt has been made to measure this, tasks bear little resemblance to everyday life, making it difficult to draw conclusions regarding the potential usefulness of training at a practical level. The ability to integrate training improvements into everyday use is also important, as it is likely to assist in maintaining the benefits of word retraining over time. The degree to which patients are able to use trained words in varied conditions which simulate everyday scenarios is therefore an area of interest that requires further investigation. To achieve this requires ecologically valid measurement tools to capture this functional language change, as standard neuropsychological test approaches may not accurately reflect everyday performance.

Study design and hypotheses

This study aimed to establish the degree to which improvements from word retraining can extend beyond the specific training stimuli in a series of SD patients, using both traditional and novel approaches to assess transfer of naming improvements to expressive and receptive language skills. A video description task was created to capture word retrieval in a naturalistic form. To assess single word comprehension, a word-to-picture matching task using alternative images was constructed. To maximise ecological validity, a verbal requests task was created wherein participants were asked by a family member to follow simple verbal instructions relating to objects around the house.

In line with theories of transfer, it was hypothesised that patients would show the greatest ability to apply their learning on the video description task, followed by the word picture matching task (where verbal labels are associated with picture cues thereby providing a closer correspondence between training and assessment tasks). The verbal instructions task was predicted to be the most difficult, given the greater requirements to adapt acquired knowledge (naming to picture) into a significantly different situation (verbal comprehension in the absence of a picture cue).

5.2. METHOD

Participants

Five patients meeting clinical criteria for a diagnosis of SD (Gorno-Tempini et al., 2011; Neary et al., 1998) were recruited to the study, including two patients who had been involved in the initial study described in Chapter 4 (but who had not been practising words for over 12 months). Participants ranged in age from 56 to 71 years, with disease duration from 6.5 to 9.5 years (Table 5.1).

Table 5.1: Demographic characteristics of study participants

Participant	SD-G1	SD-J2	SD-J3[a]	SD-T4[b]	SD-J5
Sex	M	F	M	M	M
Age	63	71	56	63	56
Education (years)	16	16	11	11.5	19
Disease duration (years)	6.5	9.5	7.5	6.5	9.0

[a] Participant SD4 from Chapter 4; [b] Participant SD1 from Chapter 4

All five showed the typical pattern of anterior temporal lobe atrophy, with left greater than right volume loss at presentation, but in two (SD-T4, SD-J5) the atrophy appeared to have progressed to affect both temporal lobes significantly (Figure 5.1).

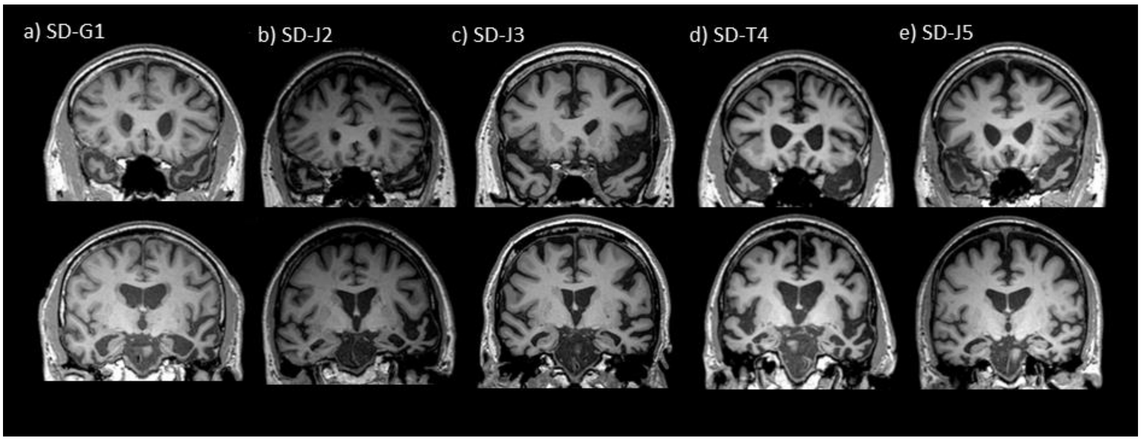

Figure 5.1: Coronal T1 weighted MRI of the anterior (top) and medial (bottom) temporal lobe for each participant.

Note the left hemisphere is shown on the right.

Participants completed the standard neuropsychological and language assessment, as described in Chapter 2. Cognitive testing revealed the expected pattern of preserved visuospatial skills, non-verbal memory and basic attention, but marked impairments on semantic processing tasks– namely, category fluency, picture naming, spoken word-picture matching, and a semantic association picture-picture matching task (subtests from the Sydney Language Battery), where performances consistently fell below the first percentile (with the exception of category fluency for SD-J2, who had completed pilot word training on the category of Animals). Executive function impairments were also evident for patient SD-J5 (Table 5.2). Based on performances across the language tasks and an overall dementia scale sensitive to changes in Frontotemporal dementia (Knopman et al., 2008), patients were ranked relative to each other and classified as having mild-moderate (SD-G1 and SD-J2) or severe (SD-J3, SD-T4, SD-J5) impairments.

Table 5.2: Neuropsychological and language profile of study participants

Participant	SD-G1	SD-J2	SD-J3	SD-T4	SD-J5
ACE-R (100)	68	56	45	49	32
Digit Span – WAIS-III (ASS)	10	8	13	7	7
RCFT - Copy (36)	33	35	36	34	32
RCFT - 3 minute recall (36)	22.5	25.5	27.5	12	18.5
TMT - A (seconds)	34	35	33	31	50
TMT - B (seconds)	80	111	113	88	225
Letter Fluency - F,A,S	13, 13, 13	11, 11, 11	6, 5, 9	5, 2, 5	7, 4, 8
Category fluency - Animals	7	13*	3	3	2
SYDBAT Naming (30)	8	8	1	2	2
SYDBAT Repetition (30)	29	29	25	25	24
SYDBAT Word Comprehension (30)	17	17	13	12	15
SYDBAT Semantic Association (30)	17	15	12	7	14
SYDBAT Total (120)	71	69	51	46	55
FTLD-CDR - Sum of boxes	2	6	12	15.5	11.5

*Note: maximum scores in brackets where relevant; Abbreviations: ACE-R = Addenbrooke's Cognitive Examination-Revised; WAIS-III = Wechsler Adult Intelligence Scale, 3rd edition; ASS = Age Scaled Score; RCF = Rey Complex Figure test; TMT = Trail Making Test; SYDBAT = Sydney Language Battery (cut-offs for 2StDs below control mean: Naming = 22; Repetition = 29; Comprehension =26, Semantic = 24);FTLD-CDR = modified Clinical Dementia Rating, * SD-J2 had participated in a pilot study where animal names had been trained*

Experimental study: Stimuli and design

As described in Chapter 4, word retraining was tailored for each individual and delivered using a single subject experimental design ('multiple-baseline-across-behaviours' - 3 word lists).

Training materials were based on digital photographs of everyday items (e.g., food, household appliances, clothing) that the participant still used or could correctly describe. This was assessed informally through discussions with the participant, family members, and through responses made during the initial baseline picture naming assessments (as participants tended to provide facts or describe how items were used when they were unable to recall the name). For each person, approximately 75-100 items were selected and divided into three words lists, matched for word frequency, personal familiarity (using the frequency of use rating scale described in Chapter 4, completed by family members), baseline naming performance, and categories (proportion of words in each list relating to food, kitchen items, etc.). See Appendix 4 for an example of the words used for participant SD-G1.

Although the primary objective was to retrain forgotten words, each list included approximately 10-15 objects that could be named correctly for the majority of baseline assessments. This served both to encourage participants (by providing a less daunting start point), and to potentially support the maintenance of these currently known words in the two training lists (discussed in more detail in Chapter 6). Baseline assessments were conducted two to three weeks prior to commencing training, with stability of performance confirmed using Cochran's Q Test (all p values > .05, see Appendix 5). Where possible, baseline assessments were conducted several times per week (with a minimum of 4 and maximum of 15 assessments in total conducted for each participant prior to training), using a custom-built computer program run via the internet (described further below). A final baseline test was also completed face-to-face with the researcher (SS).

Training procedures

As in the previous study, two of the lists received training (n = 50-65 words), with one list left untrained (n = 25-35 words). Following the success of the "Look, Listen, Repeat" approach in Chapter 4, each session involved this simple, repetitive practice of pairing the photograph of the target item with the item label, presented on the computer both in written format and via an audio recording of the spoken word. As before, items from the same category were blocked together to help stimulate semantic processing during training and rote learning list order was prevented by randomising both the order of categories and the within-category order each time. For this program, however, each item from the training list was presented only twice per session, with a short naming test immediately following. In this short test, each picture from the training list was presented in a random order one at a time and the participant was asked to say the name of each trained picture within a 10 second time limit (or say "Don't know" if they were uncertain) and then type their answer. This allowed for the training to incorporate two passive exposures of the training material, followed by an active retrieval of the word.

To allow as many participants as possible to take part in the program, given the geographical distance of participants from the FRONTIER clinic, new software was designed and developed to enable the training program to be run over the internet on the participants' home computer (with programming provided by Syntonic, www.syntonic.net.au). Specifically, this custom built software allowed the researcher control over the accessibility and content of each session, and produced detailed logging and audio recordings of participant responses (e.g., with date and time stamps to verify treatment compliance, as well as additional information about length of time spent per item). Participants logged in to each session via their web browser, with de-identified data automatically uploaded to a server as they progressed through each session.

Sessions were designed to be self-paced and typically took around 20-30 minutes to complete. Participants practised List 1 for 5 days/week for 4 weeks, followed then by List 2 for 4 weeks. This duration of practice was selected to balance between maximising retention of words (given the finding of the previous study that with longer training more words were maintained), and the need to maintain participant interest (given words are typically learnt within the first two weeks).

At the end of each week, participants logged onto the program to complete a full naming test (items from all 3 lists). As with the short tests at the end of training sessions, each picture was presented one at a time, in random order, with the participant given 10 seconds to say the name. Responses were audio recorded and later transcribed and scored. At the end of the 8-week training period, a face-to-face assessment was also conducted with the researcher. The final weekly pre-training baseline and the immediate post-training assessment scores were used to evaluate treatment success. Full data sets, however, are presented in Appendix 6.

Generalisation measures

Generalisation beyond the confines of picture naming was examined using both expressive and receptive language tasks. In each task, participants were assessed on approximately 20 trained and 10 untrained items from their respective lists.

1. **Word retrieval - Video description:** a series of 6 short videos (each 2 to 3 minutes in length) was created to depict different everyday household scenes involving food, appliances, kitchen and bathroom items (e.g., setting the dinner table, making a cup of tea – see Figure 5.2 for example screenshots). Scenes were created to capture as many different items as possible within each scenario and to include those items most likely to be in common across participants' programs. Between 3 and 5 of these videos were used to assess each participant's word retrieval (based upon the categories covered, and to ensure both trained and untrained items were included). Participants watched the videos and then described in detail what they saw, by naming objects and reporting what the person was doing with each object. Where necessary, general prompts were

given (e.g., "what did you see next?"), as well as more specific prompts (e.g., "what is this called?") if participants did not address all elements of the video (see example in Appendix 6 for a response given to one video). Every item correctly named received a score of 1 (see Appendix 7).


A)


B)


C)

Figure 5.2: Example scenes from the video description task

A) Making a hot drink; B) Cooking on the barbecue; C) Getting ready in the bathroom

2. Word comprehension tasks

a. **Household requests**: items were selected from each participant's program to form sentences, requesting the participant to carry out an action in the home. Each sentence was carefully worded to not include any additional clues regarding the nature of the item (e.g., "Could you please take out 2 *plates*?" or "Could you get me an *orange*?"). A family member was asked to administer the items over a few days, in as natural a way as possible. Participants were only scored as correct ('1' point) if they were able to complete the request correctly without any further information.

b. **Word Picture Matching** (WPM): participants were presented with a series of 3 x 3 arrays of photographs and asked to select the picture which best matched the word spoken by the examiner (e.g., "Which picture shows: ….[apple]?". If the participant says "Don't know", he/she is encouraged to guess). Arrays contained alternative versions of the target item and semantically or visually related foils – of which the majority consisted of different versions of items within the program (Figure 5.3). This design was used to minimise the possibility that participants could select the most visually familiar target, without recognising the word itself. One point was awarded for each correct response.

Participants were assessed on these measures prior to word training and then immediately following completion of the practice.

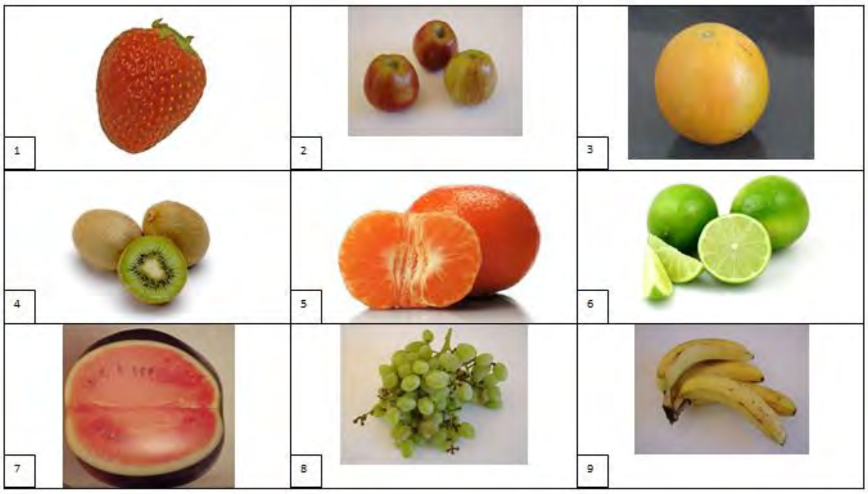

Figure 5.3: Word Picture Matching example

Data analysis

IBM SPSS Statistics 20.0 was used. Results were firstly analysed at an individual case level, using McNemar's Test for related samples to evaluate change from pre-treatment to post-treatment scores for both trained and untrained words (with $p < .05$ used to indicate statistical significance). Group results were then analysed using the paired sample Wilcoxon signed rank test, based on the percent accuracy scores at each time point.

To compare change over time across participants, the proportion of words gained out of those "available to be learned" was computed (Snell et al., 2010), to indicate each individual's therapy response or degree of success relative to their baseline performance:

$$\textit{Proportion Gained} = \frac{\text{(Total words correctly named post-therapy) - (Baseline score)}}{\text{(Total number of words provided) - (Baseline score)}}$$

This procedure took into account individual differences in baseline performance and the number of items assessed, given tailoring of each training program. "Baseline score" for picture naming was defined as performance on the final baseline completed prior to commencing intervention; "post-therapy score" related to the immediate post-assessment.

5.3. RESULTS

Word training effect

All participants showed significant improvements in naming trained pictures post-intervention. As expected, no significant improvements were seen on the control (untrained) list over the same period (Table 5.3). Patients with mild-moderate semantic impairments (SD-G1 and SD-J2) were able to correctly name most (90% or more) of the words they did not know initially. Level of achievement was variable in severely impaired patients, ranging between 48% and 84%.

Generalisation of word retrieval (Video description task)

On the video description task, significant increases in successful word retrieval for trained items were observed in all but one participant (Table 5.3). No significant improvements were seen in untrained items. These increases were comparable in magnitude to the proportion of words gained on the training program stimuli for two of the participants (SD-G1, SD-J3), indicating good transference of learning across tasks (Figure 5.4). Although the proportions gained for SD-J2 and SD-T4 appeared smaller than what was demonstrated on the word program stimuli (50% vs. 94% and 32% vs. 84%), a relative advantage of 83% and 57% was achieved respectively, after considering the declines seen on the untrained words for this task. Taken at a group level, the percentage change over time in trained items was significant, $z = 2.02$, $r = 0.64$, $p = .031$, one-tailed, whereas a non-significant result was found for untrained items, $z = 0.55$, $p = .375$, one-tailed.

***Table 5.3**: Baseline and immediate post-intervention scores – expressive language*

	Trained words (BL vs Post)				Untrained words (BL vs Post)			
	BL	Post	Gain (%)	p	BL	Post	Gain (%)	p
	Word retraining picture-naming scores (total correct / total items assessed)*							
SD-G1	34 / 64	61 / 64	**90**	<.001	15 / 32	19 / 32	24	.219
SD-J2	29 /63	61 / 63	**94**	<.001	19 / 36	25 / 36	35	.07
SD-J3	3 / 43	22 / 43	**48**	<.001	13 / 54	14 / 54	2	1.00
SD-T4	17 / 66	58 / 66	**84**	<.001	14 / 41	10 / 41	-10	.125
SD-J5	9 / 52	34 / 52	**58**	<.001	5 / 25	6 / 25	5	1.00
	Video description task (total correct / total items assessed)							
SD-G1	13 / 26	24 / 36	**85**	.001	7 /10	7 / 10	0	1.00
SD-J2	17 / 32	24 / 32	**50**	.039	10 / 16	8 / 16	-33	.625
SD-J3	2 / 22	13 / 22	**55**	.001	2 / 12	3 / 12	10	1.00
SD-T4	11 / 30	17 / 30	**32**	.03	2 / 10	0 / 10	-25	.5
SD-J5	2 / 13	6 / 13	**36**	.125	1 / 7	2 / 7	17	1.00

*Abbreviations: BL = Baseline score * For picture-naming, baseline is defined as the final baseline assessment prior to commencing training*

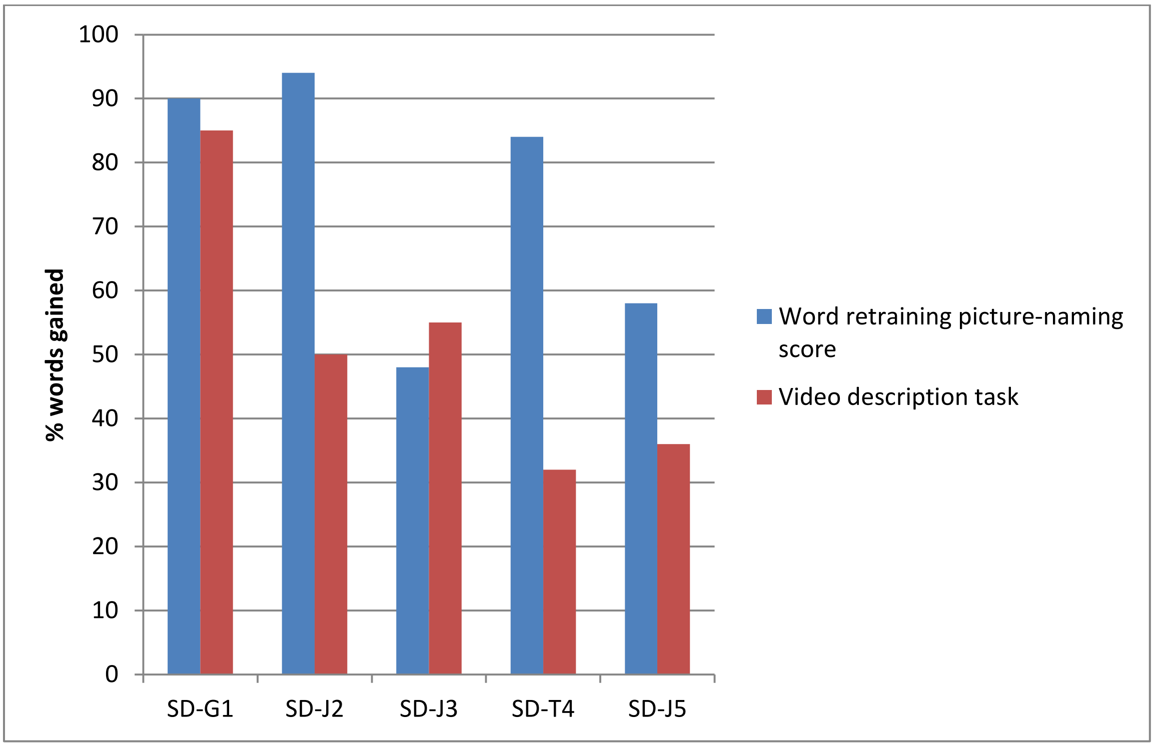

Figure 5.4: Comparison of gains made from pre- to post-intervention on the word retraining stimuli versus those made pre- to post-intervention on the video description task

Generalisation to word comprehension tasks

Improvements were also found for trained items on comprehension tasks (Table 5.4). When patients were required to comprehend words from speech alone (household requests task), patients with milder impairments (SD-G1 and SD-J2) showed significantly increased accuracy in their ability to follow instructions for trained words. The magnitude of the gain was similar to the overall gains seen in naming (Figure 5.5). While not reaching significance, SD-T4 also showed improvements on trained items and reductions on untrained items. For the other severely impaired SD patients, either mild improvements were seen across both trained and untrained items, or untrained items improved relative to trained items. Taken as a group, a significant improvement was observed for trained items over time, $z = 2.02$, $r = 0.64$, $p = .031$, but not for untrained items, $z = 1.40$, $p = .125$.

Table 5.4: Baseline and immediate post-intervention scores - comprehension

	Trained words (BL vs Post)				Untrained words (BL vs Post)			
	BL	Post	Gain (%)	p	BL	Post	Gain (%)	p
	Household requests task (total correct / total items assessed)							
SD-G1	11 / 19	17 / 19	75	.031	11 / 13	11 / 13	0	1.00
SD-J2	13 / 21	20 / 21	88	.016	6 / 10	8 / 10	50	.5
SD-J3	5 / 14	8 / 14	33	.25	2 / 16	6 / 16	29	.125
SD-T4	3 / 20	7 / 20	24	.219	1 / 10	0 / 10	-11	1.00
SD-J5	5 / 18	8 / 18	7	.219	1 / 7	4 / 7	57	.125
	Word-Picture Matching task (total correct / total items assessed)							
SD-G1	22 / 28	25 / 28	50	.375	10 / 12	10 / 12	0	1.00
SD-J2	19 / 25	23 / 25	67	.219	12 / 15	13 / 15	33	.5
SD-J3	4 / 22	13 / 22	50	.004	5 / 18	6 / 18	8	1.00
SD-T4	13 / 28	21 / 28	53	.039	7 / 12	5 / 12	-40	.687
SD-J5	9 / 17	13 / 17	50	.219	4 / 9	4 / 9	0	1.00

Abbreviations: BL = Baseline score

** For picture-naming, baseline is defined as the final baseline assessment prior to commencing training*

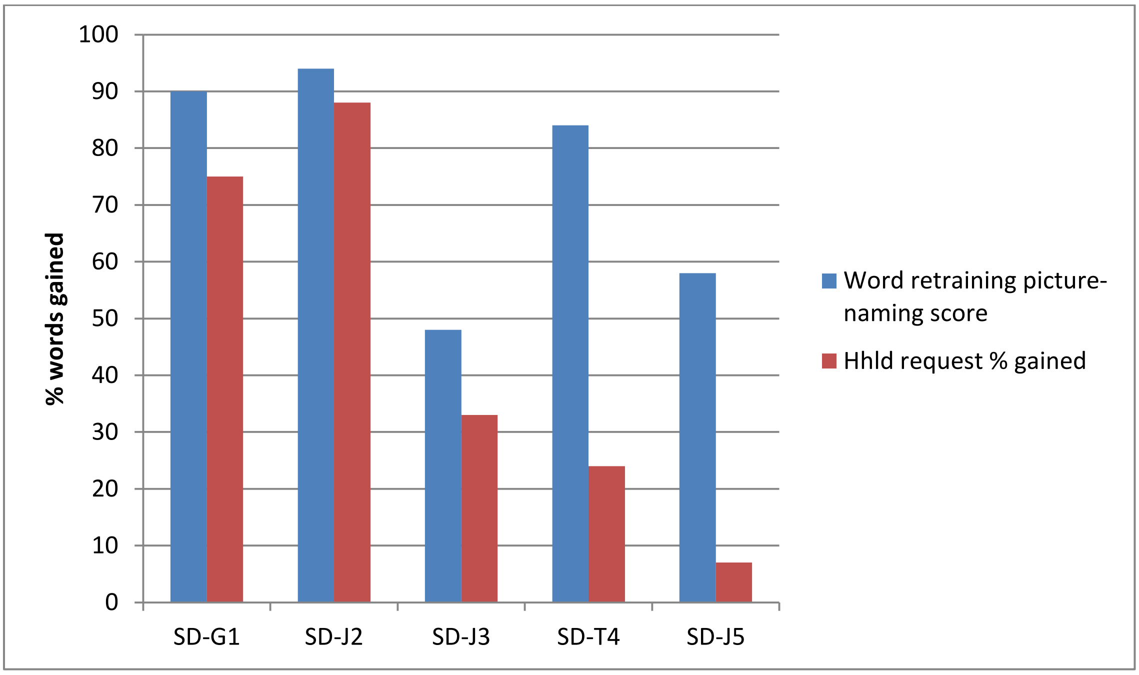

Figure 5.5: Comparison of gains made from pre- to post-intervention on the word retraining stimuli versus those made pre- to post-intervention on the household request task

When picture cues were provided, however, using word-picture matching, significant gains were observed for two of the severely impaired participants (SD-J3 and SD-T4). For SD-J3, the proportion of improvement was similar in magnitude to the overall word training effects (approximately 50% of possible gains). While the improvements seen for the mild SD patients did not reach significance, both patients were already performing well on this task at baseline (at approximately 80% correct) (see Figure 5.6). Again, when analysed at a group level, only the accuracy in trained items was significantly improved, z = 2.02, r = 0.64, p = .031, one-tailed, with no significant change in the untrained items, z = .365, p = .438, one-tailed.

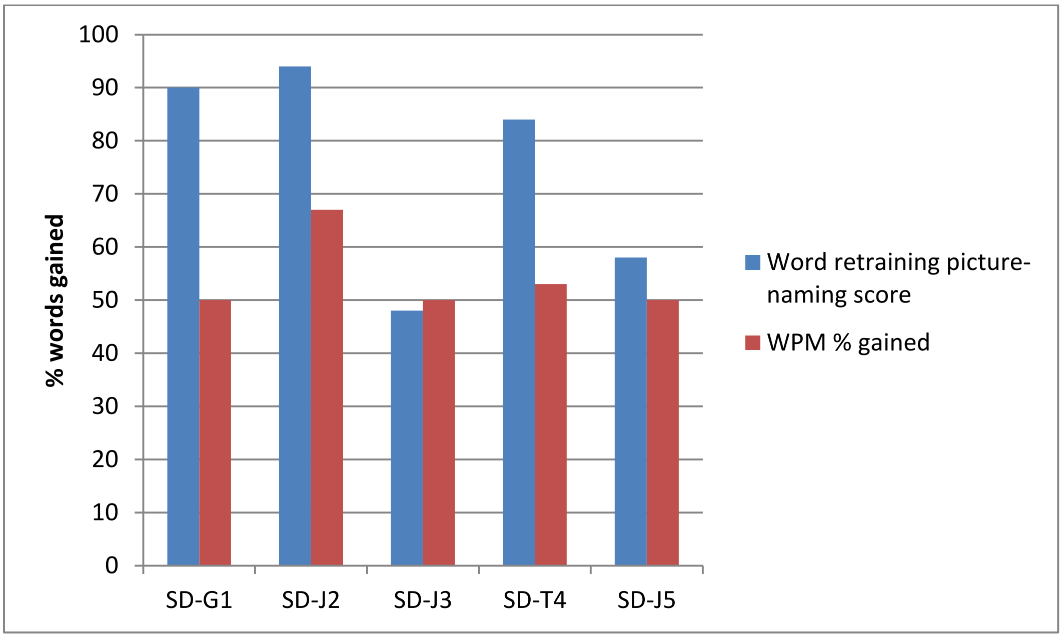

Figure 5.6: Comparison of gains made from pre- to post-intervention on the word retraining stimuli versus those made pre- to post-intervention on the word picture matching task

5.4. DISCUSSION

Overall summary

This study is the first systematic investigation of generalisation of therapy gains employing a range of expressive and receptive tasks to examine transfer of learning in SD patients with varying disease severity. Clear evidence for generalisation was found, with improvements made on word retraining transferred into other contexts, although the level of success varied both by task and disease severity. Patients with milder semantic impairments were able to make use of the words gained from training over a range of tasks, whereas patients with severe semantic deficits showed limited cross-task transfer. Over the same time period, no improvements were seen for untrained words, indicating that these gains for trained items were not due to practice effects from repeated assessment. Objects familiar and meaningful to the participants were selected for training, and measures with ecological validity were employed to provide the best possible evidence that treatment gains could be of real value to patients.

Discussion of findings

As predicted, the most consistent evidence of generalisation was seen on the task that most closely resembled the training situation: the video description task. Here, significant gains were achieved post-intervention in all but one participant. In two individuals (SD-G1 and SD-J3), this result mirrored the degree of naming improvement observed when tested on the actual training stimuli, despite the different format in testing and different exemplars used. For the other participants, the use of different versions of the target likely accounts for the tendency towards lower scores than when naming their own version of the item, given the effects of visual similarity and personal familiarity shown in previous studies (Bozeat et al., 2002). This effect, however, may have been partially offset by showing objects within the context of a scene, thereby supporting the existing conceptual representations.

The video task encouraged participants to use target words within sentences, providing evidence of their ability to access and apply the trained words into conversation. As illustrated by the examples in Appendix 7, patients were generally successful in integrating the words into a narrative. Only patients very severely impaired tended only to list items rather than form clear sentences. Arguably still a proxy measure of patient speech, the format of the task resembles real life situations where a patient may be asked questions about what they or others have been doing at home during the day. The significant improvements seen here are important in providing the clearest indication to date that word training interventions may assist everyday speech.

In addition to benefitting expressive language, improvements on tests of verbal comprehension were also found, although these varied according to disease severity. On the word-picture matching task, patients with milder semantic impairments showed little improvement given their high performance at baseline. This is unsurprising, given that naming is more severely affected than word comprehension in the earlier stages of SD (Lambon Ralph, McClelland, Patterson, Galton, & Hodges, 2001). For severely impaired patients, however, word recognition was considerably reduced at baseline (typically 50% correct or below), allowing for significant improvements to be found for two out of the three patients. For SD-J3, the improvement mirrored the level of gain from the program. Despite these positive results, participants' verbal comprehension did not improve for all items where the name was recalled post-intervention. This finding most likely reflects the use of different exemplars in training and testing, which were presented without any other contextual cues, and the added difficulty of having to distinguish targets from semantically related foils.

On the household requests task, which removed picture cues entirely thereby measuring the greatest degree of "far transfer", improvements were found in milder SD patients only. In these two individuals, the degree of improvement on this task was similar in magnitude to the improvements observed for picture naming using the training stimuli. As the requests used in the task were modelled on questions which may be asked around the home (e.g., "Can you put the kettle on?"), this result provides strong evidence that gains achieved through word training programs can translate directly into real world benefits.

Despite the general success of the group in demonstrating generalisation of retrained words, one severely impaired SD patient, SD-J5, who presented with the greatest general cognitive and executive function deficits, was unable to demonstrate significant improvements on the generalisation tasks compared to baseline. This participant showed one of the lowest gains in word retrieval and was assessed on a smaller number of items. Qualitatively, however, small improvements were still found across tasks for trained items, exceeding changes observed for untrained items, suggesting that some of the content gained could extend to other contexts.

While this highlights the potential mediating role of other cognitive impairments, the failure to find significant results here may have also arisen in part due to reduced statistical power.

Other factors such as mood may also play an important role and may explain some of the variability in the current results. SD-J3 was observed to make negative comments about his performance during the intervention, while SD-T4 remained positive and enthusiastic throughout. Future studies should aim to further refine predictors of success in word retraining to help identify those patients most likely to benefit.

Conclusions

In addition to providing rapid improvements in picture-naming, words gains through basic word retraining practices can be applied to a variety of contexts which relate to everyday living. For patients with milder semantic impairments, these include the ability to integrate object labels into a narrative describing everyday activities in the house, and respond correctly to verbal requests, which rely upon understanding trained words. For patients with significant impairments, expressive abilities may show the greatest level of improvement, although with visual cues, comprehension of verbal labels may also be enhanced through word retraining.

CHAPTER 6. Word over time - *maintenance of retraining gains in SD*

Following the results of the previous studies which demonstrate the success of word retraining in restoring word retrieval in the short-term (Chapter 4), and the ability to apply such gains in a variety of contexts (Chapter 5), the aim of this study was to measure longer-term maintenance of word retraining gains in a series of SD patients. Further, the study sought to identify schedules of revision that may extend retention, particularly for patients with greater disease severity. Understanding the level of ongoing commitment required to support word retrieval is an important variable when considering undertaking training, but has received little attention in the current literature. This study provides an important first step in exploring the amount of training that may be required at different levels of semantic impairment. Also, in recruiting the largest sample of SD patients to date, a secondary aim was to explore potential relationships between treatment outcome and patient characteristics.

6.1. INTRODUCTION

While the results of Chapter 4 and other studies have demonstrated the ability of SD patients to improve their naming ability through word retraining, these improvements often fade with varying levels of decline reported beyond the first 1-2 months post-intervention. In some cases, as seen in Chapter 4 with patient SD4, substantial declines may even be observed within the first 4 weeks. As cognitive interventions do not halt the continuing degeneration of the temporal lobes associated with the disease (Brambati et al., 2009; Krueger et al., 2010), decline over time is expected. In addition, models of learning, such as the Complementary Learning

Systems Theory (McClelland et al., 1995) would predict declines of any relearnt words, given increasing degradation to the temporal neocortex, which supports the slower process of consolidation of learning into long-term semantic storage. Therefore, it is likely that to sustain benefits, some level of ongoing training may be required. Despite this, no study as yet has focused specifically on the maintenance period to explore how this differs among patients, and to investigate whether introducing less intense forms of revision training may help sustain words over time.

In addition, while the majority of studies have focused on restoring forgotten vocabulary, it has also been suggested that word training may delay the onset of decline in current vocabulary (Jokel et al., 2010, 2006). In these two case studies, it was shown that words known at the beginning of the study which were left unpractised declined in contrast to known words that were trained. While this finding requires further replication, it also suggests that revision plays an important role in maximising the retention of words in the medium term for SD patients.

Study design and hypotheses

The key aims of this study were thus to train and monitor retention of words in a series of SD patients, by studying performance over two specific time periods:

1. the initial 2 months following treatment end where maintenance is usually reported,
2. a further 4 month period, during which revision training could be supplied, if necessary.

It was hypothesised that:

- The majority of patients would show significant declines in a 2-month period after ceasing practice;

- With revision (at a frequency less intense than the original training), patients would show ongoing benefit, with performance significantly above baseline, if not commensurate with immediate post-therapy;
- Training of words known at baseline would lead to superior maintenance of these words 8 months later, compared with words known at baseline that were not practised.

Given the expected range of individual differences across patients, a secondary aim was to identify pre-treatment clinical variables associated with intervention outcomes (both for the degree of learning achieved and the maintenance performance). Identifying such variables could assist in predicting the approach required for patient success in future studies.

6.2. METHOD

Participants

Nine patients, who had completed a word training program and were available for follow up over 6 months, were recruited to the study. This included four of the participants described in Chapter 5, together with a further five who were recruited following the Generalisation study. Participants ranged in age from 50 to 71 years, with symptom duration from 4 to 9 years (Table 6.1). All showed asymmetric anterior temporal lobe atrophy, with left greater than right atrophy with the exception of two participants (SD-P1 and SD-C1) who showed greater right than left volume loss at presentation. Disease severity, as measured by the Frontotemporal Dementia Rating Scale - which measures carer reported functional skills in daily living as well as behavioural disturbance - ranged from Mild through to Severe.

Table 6.1: Demographic characteristics and clinical profile of study participants

	SD-J1	SD-S1	SD-P1	SD-B1	SD-G1	SD-J2	SD-C1	SD-C2	SD-T4
Sex	M	F	F	M	M	F	M	M	M
Age	69	62	63	62	63	71	50	61	63
Education (years)	15	15	11	13	16	16	12	14	11.5
Disease duration (years)	5.5	6.0	6.5	5.0	6.5	9.0	8.0	4.0	6.5
Temporal lobe atrophy [a]	L > R	L > R	R > L	L > R	L > R	L > R	R > L	L > R	L > R
FRS	0.16	1.68	2.19	N/A	1.47	3.35	-0.80	1.26	-1.84
FRS stage	Moderate	Moderate	Mild	N/A	Moderate	Mild	Severe	Moderate	Severe
FTLD-CDR – Sum of boxes	5.5	3	1.5	N/A	2	6	6.5	5.5	15.5
Severity category	Mild	Mild	Mild	Mild	Moderate	Moderate	Moderate	Severe	Severe

Abbreviations: FRS = Frontotemporal Dementia Rating Scale; FTLD-CDR = FTLD-modified Clinical Dementia Rating; N/A = not available for this participant; [a] "L > R" indicates left greater than right atrophy; "R > L" indicates right greater than left atrophy

Table 6.2: Neuropsychological and language profile of study participants, ordered by severity of anomia

	SD-J1	SD-S1	SD-P1	SD-B1	SD-G1	SD-J2	SD-C1	SD-C2	SD-T4
ACE-R (100)	86	80	79	84	68	56	57	45	49
Digit Span (Age Scaled Score)	18	7	14	15	10	8	8	9	7
RCFT - Copy (36)	34	28	32	35	36	35	30	35	34
RCFT - 3 min recall (36)	23	19.5	11.5	17	22.5	25.5	9	6	12
Trail Making Test - A (seconds)	29	39	31	39	34	35	39	39	31
Trail Making Test - B (seconds)	61	73	58	41	80	111	78	198	88
Category fluency - Animals	15	10	15	12	7	13	10	2	3
SYDBAT Naming (30)	16	16	14	10	8	8	4	2	2
SYDBAT Repetition (30)	29	30	29	30	29	28	29	29	25
SYDBAT Word Comprehension (30)	27	26	21	19	17	17	14	9	12
SYDBAT Semantic (30)	25	26	21	19	17	15	15	13	7
SYDBAT Total (120)	97	98	85	78	71	68	62	53	46

Note: maximum scores in brackets where relevant; Abbreviations: ACE-R = Addenbrooke's Cognitive Examination Revised; RCFT = Rey Complex Figure Test; SYDBAT= Sydney Language Battery (cut-offs for 2StDs below control mean: Naming = 22; Repetition = 29; Comprehension =26, Semantic = 24)

Participants completed the standard neuropsychological and language assessment, as described in Chapter 2. Cognitive testing showed relative preservation of visuospatial skills, basic attention and executive function (although with disease progression some impairments were observed for SD-C2). In two participants, overall cognitive performance, as measured by the ACE-R, fell within normal limits (> 82). For all participants, word repetition skills remained well above the significant impairments in confrontational naming. Other measures of language revealed a range of performances on semantic tasks, from mild to severe impairments – as assessed using category fluency and subtests from the Sydney Language Battery (Naming, Word Comprehension, and Semantic Association), although the majority of performances fell at or below the first percentile (Table 6.2).

Based on a combination of overall cognitive testing, language testing and carer report, 4 participants were rated as mild, 3 as moderate and 2 as severe.

Experimental study: Research design

As in the previous chapters (4 and 5), a 'multiple-baseline-across-behaviours' (3 word lists) single subject experimental design was conducted for each participant. Baseline naming performance was established over a 3-4-week period, after which participants were trained on their first word list for 4 weeks. Training was then applied to a second list for 4 weeks, with practice withdrawn at the end of week 8. During the same period of time, a separate control list remained untreated. Participants were re-assessed at the end of each therapy week and performance was monitored over a further 6 months, firstly at weekly intervals (for the first 1-3 months), and then at monthly intervals, if performance remained steady. Following the 2-month post-assessment, training was re-introduced when evidence of decay was observed and participants were keen to re-commence practice.

Materials and training program

The training program was individually tailored with approximately 75-100 items selected for each person, divided into 3 word lists: two of which received training and one that remained untrained. For each participant, lists were matched on word frequency and category and included everyday items, such as clothing, food, and appliances. Additional categories, such as birds, flowers, and musical instruments, were also included for participants with milder disease severity (Table 6.3). Within each list, an attempt was made to include approximately 15 words that could be named correctly at the final baseline assessment, to assess the benefit of training on the maintenance of known words. In one case (SD-C2), however, it was not possible to identify more than 1 word per list.

Table 6.3: Word categories included for each study participant

Participant	Categories included in each list
SD-J1	Food, plants, insects, birds, marine and other animals, musical instruments
SD-S1	Food, kitchen items, clothing, musical instruments, insects
SD-P1	Food, kitchen items, plants, insects, birds, musical instruments
SD-B1	Food, household appliances, kitchen items, insects
SD-G1	Food, household appliances, kitchen items, gardening tools
SD-J2	Food, household appliances, clothing, sewing items
SD-C1	Food, household appliances, kitchen items, bathroom items, clothing, stationery
SD-C2	Food, household appliances, kitchen items, bathroom items, clothing, furniture
SD-T4	Food, household appliances, kitchen items, bathroom items, clothing

The training method was identical to the approach described in Chapter 5, and involved the Look, Listen, Repeat approach, in which a photograph of the object is paired with a visual and audio presentation of the word, presented on the participant's home computer via the internet using custom built software.

Participants logged on 5 days a week during the initial 8-week period. Following the initial 8 weeks of practice, training was re-introduced when evidence of decay was observed and/or participants requested to re-commence practice. Sensitive to patients' requests and needs, revision was tailored at an individual level rather than testing one specific approach or level of practice across all participants. In general, however, practice was reinstated once performance on trained lists dropped below 80% accuracy, and involved up to two training sessions of each word per week (specific details regarding the revision sessions per participant are provided in the Results section).

Assessment

Naming performance was assessed via computer, with items from all three lists tested in a randomised order. Participants were presented with each photograph, one at a time, and given 10 seconds to say the correct name, after which they were asked to type their answer (untimed). Responses were audio recorded and reviewed later by the researcher (SS). To be credited with a score of 1 per item, participants were required to produce the target word accurately. Approximations were scored as incorrect (e.g., if shown an iron, "ironing" would get a score of 0). The following scores were then generated based on the total performance of the trained items (i.e., combining the results of lists 1 and 2):

- **% accuracy** = (total correct responses divided by total trained words) x 100. This score shows the pattern of performance for each individual over time from baseline to the final follow up.

- **ability to improve (% gain)** = (immediate post-intervention score minus baseline score)/ (total number of words trained minus baseline score) x 100. Given differences in the number of items per participant, this measure provides an equivalent metric to compare performance across individuals.
- **2-month independent maintenance** = proportion of trained words correct at immediate-post that remained correct at the 2-month follow up without further training. Given differences in level of learning achieved by training, this measure provides an equivalent metric to compare maintenance performance across individuals.
- **6-month maintenance** = proportion of trained words correct at immediate-post that remained correct at the 6-month follow up, assisted where necessary by a less intense revision practice.

Data analysis

Results for each individual were assessed using McNemar's Test for related samples. Ongoing training benefit was tested by comparing baseline performance with three time points: immediate post-training, 2 months post (independent maintenance) and 6 months post original treatment end (assisted maintenance, where necessary). P values were Bonferonni corrected for multiple comparison per data set (p = .05/3; p < .016 to indicate statistical significance). Degree of change following intervention was then evaluated by comparing immediate post-treatment results with both the 2-month and 6-month scores (using p < .025 to indicate statistical significance).

To evaluate effects over time specifically for words known prior to training, separate sub-analyses were run on the words that were correct at the final baseline assessment. Individual performance was tested using a one-tailed McNemar's Test to investigate decline in accuracy from baseline to the 6-month post assessment, firstly for trained words, and then for untrained words that were correct at the final baseline. Group level analyses were conducted using Wilcoxon paired rank test, comparing % accuracy across the two time points.

Lastly, Spearman's rho was used to investigate associations among either ability to improve or independent maintenance scores and the following cognitive measures: ACE-R (general cognitive ability), SYDBAT Total (semantic impairment), Rey Complex Figure Test recall (episodic memory), and Trail Making Test - B (executive function). To correct for multiple comparisons, $p < .013$ was used to denote significant findings. Relationships between demographic variables (age, education) and treatment outcomes were also explored in a separate analysis.

6.3. RESULTS

All participants showed significant improvement on trained words from the final baseline to the immediate post-intervention assessment (McNemar Test, all $p \leq .001$). Word retrieval gains ranged from 58% to 100% of possible gains, with majority of participants recalling at least 90% of the words that could not be correctly produced at baseline (Table 6.4).

2-month independent maintenance

Two months after training completion, all participants continued to name a significantly higher proportion of words than at baseline ($p < .005$), indicating a clear ongoing benefit of the earlier training. Despite this, statistically significant declines were evident in four participants (2 mild: SD-S1, SD-P1, 2 severe: SD-T4, SD-C2; all $p < .025$) when comparing immediate post-intervention performance with 2-month post performance. On average, however, 80% of the words named correctly at immediate post-intervention were still correctly provided at the 2-month post assessment (Table 6.4).

Table 6.4: Learning and maintenance outcomes by participant

Participant	Number of words trained	Ability to Improve (% gain)	2-month Independent Maintenance[a]	6-month Maintenance[b]
Mild				
SD-J1	60	100%	98%	86%
SD-S1	64	96%	76%	81%
SD-P1	64	97%	83%	84%
SD-B1	64	97%	97%	89%
Moderate				
SD-G1	64	90%	84%	90%
SD-J2	63	94%	83%	85%
SD-C1	65	87%	83%	93%
Severe				
SD-C2	50	58%	57%	86%
SD-T4	66	84%	62%	95%
Group mean		**89%**	**80%**	**88%**

[a] Proportion of trained words correct at immediate post-assessment that were maintained at 2 months post (with no further practice); [b] Proportion of trained words correct at immediate post-assessment that were maintained at 6 months (including revision).

6-month maintenance

Over the next 4 months, participant performance was monitored, with additional training sessions introduced where necessary, to avoid substantial declines (Table 6.5).

Table 6.5: Number and frequency of revision sessions provided during the post-intervention period

Participant	Total times revised	Frequency of list revision
SD-J1	0	0 /week
SD-S1	5	1 /week (initiated 3 months post)
SD-P1	3	2 /week for one week (initiated after 5 months post)
SD-B1	0	0 /week
SD-G1	4[a]	1-2 /week for 2 weeks (at 4 months post)
SD-J2	0	0 /week
SD-C1	8	1 /week for 3 weeks (at 4 months post); then 1 /fortnight
SD-C2	14	1 /week continuously (initiated after 2.5 months post)
SD-T4	23	2 /week continuously (initiated after 2 months post)

[a] *revision based on a subset of n = 15 trained words only, rather than the full training lists*

Three distinct patterns of performance emerged (Figure 6.1). For three participants (Group 1: SD-B1, SD-J1, SD-J2), little to no change was observed over the first 4 months post-intervention. While some decreases began to emerge at 5 months post, performance remained above 80% correct. As a result, revision sessions were not completed by these individuals. In four participants (Group 2: SD-G1, SD-C1, SD-P1, SD-S1), declines in performance were more apparent over the first 3 months post-intervention. A small level of revision was introduced (each list revised less than 10 times), with performances tending to improve and remain at or above 80%. In the remaining participants (Group 3: SD-T4, SD-C2), rapid declines in performance were evident within 2 months of ceasing practice. With the introduction of weekly or biweekly revision of words on a continuing basis, naming performance was restored to post-training level.

Regardless of the need for further training, all participants demonstrated significantly better naming 6 months post initial training compared to baseline (all p values < .005). In four participants who conducted revision (SD-G1, SD-C1, SD-C2, SD-T4), performance was equivalent or better than the immediate post-therapy result, confirming that even with less intense revision benefits of training could persist over this period. Declines were noted in four participants (SD-P1, SD-S1, SD-J1, SD-J2) who either had not revised or had minimal revision, although each continued to achieve at least 80% naming accuracy (Table 6.4). Only one participant (SD-B1) maintained a statistically equivalent performance over this length of time without further training.

Trained versus untrained words

Known words that had been trained appeared to be well maintained over the 6-month period, with little to no loss observed in all participants, with the exception of SD-S1. With one exception (patient SD-T4), individual case analyses indicated only non-significant losses for untrained known words over the same period (Table 6.6). Group analyses, however, revealed that while known trained words were maintained at 6 months (z = 1.83, p = .063, one tailed), an overall reduction in naming performance was observed at 6 months for untrained words known at baseline (z = 2.37, p = .008, one tailed).

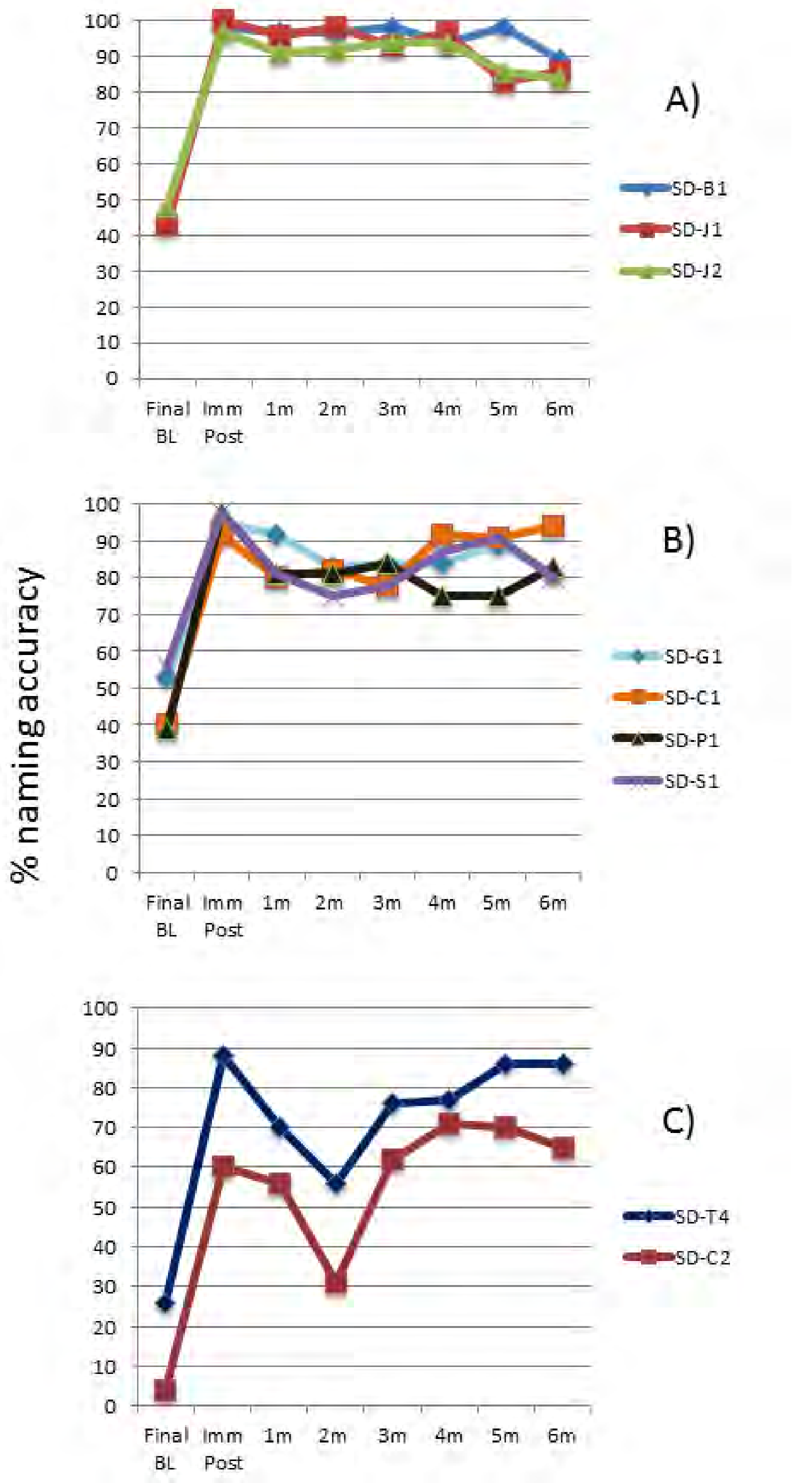

Figure 6.1: Patterns of naming performance over time for trained items

Figure A) Group 1: Independent maintenance (no revision); B) Group 2: Minimal revision after 2 months; C) Group 3: Continuous revision after 2 months. 'BL' = baseline performance; 'Imm Post' = performances immediately post-intervention; 'm' denotes month post intervention

Table 6.6: Effect of training on performance over time for words known at final baseline

Participant[a]		**Total items correct at Baseline**	**Total items correct 6-months (% retained)**	**p value (one tailed)**
SD-J1	Trained words	26	24[b](100%)	+
	Untrained words	17	15 (88%)	.500
SD-S1	Trained words	36	31 (86%)	.032
	Untrained words	20	19 (95%)	.500
SD-P1	Trained words	25	25 (100%)	+
	Untrained words	14	10 (71%)	.063
SD-B1	Trained words	29	29 (100%)	+
	Untrained words	16	14 (88%)	.500
SD-G1	Trained words	34	34 (100%)	+
	Untrained words	15	13 (87%)	.250
SD-J2	Trained words	29	28 (97%)	.500
	Untrained words	20	19 (95%)	.500
SD-C1	Trained words	26	25 (96%)	.500
	Untrained words	19	17 (89%)	.250
SD-T4	Trained words	17	16 (94%)	.500
	Untrained words	14	9 (64%)	.032

Note: p values derived from McNemar comparisons of baseline performance to the 6-month follow up assessment for each set of words; + McNemar test not possible due to identical values ; [a] Participant SD-C2 was excluded from this analysis given insufficient words available (only 2 trained words and 1 untrained word were correct at baseline); [b] 2 items were not administered at this assessment

Relationship between intervention outcome and clinical profile

The three patterns of performance over time appeared to relate to a general estimate of disease severity. Ability to improve was associated with overall cognitive ability (ACE-R: r_s = .745, p =.011), semantic impairment (SYDBAT Total: r_s = .874, p = .001), and executive function (Trail Making Test - B: r_s = -.828, p = .003). No significant correlations were found, however, between any of the measures of cognitive functioning and the degree of independent maintenance at 2 months post-intervention (ACE-R: r_s = .268, p =.243; SYDBAT Total: r_s = .496, p = .087; Rey Complex Figure Test recall: r_s = -.025, p = .474; Trail Making Test – B: r_s = -.527, p = .072). A significant relationship was found however between independent maintenance and word retrieval gains (r_s = .761, p = 009), indicating that those who showed a greater ability to recall words following retraining also showed greater ability to maintain these gains independently. No significant relationships were observed between the demographic variables of age at training start (Ability to improve: r_s = .169, p = .332; 2-month independent maintenance: r_s = .148, p = .352) or years of education (Ability to improve: r_s = -.198, p = .305; 2-month independent maintenance: r_s = -.376, p = .160).

6.4. DISCUSSION

Overall summary

Previous research has highlighted the tendency for naming improvements in SD to erode over time, but has not investigated how such losses may be minimised. This is the first study to focus specifically upon the maintenance period and demonstrate that less intense forms of revision can help SD patients sustain words over a 6-month period. As expected, reductions in naming performance were observed in the majority of patients when practice was withdrawn. Despite these initial declines, at least 80% of words correctly retrieved at the immediate post-assessment were still maintained 6 months later, regardless of the participant's disease severity (mild, moderate or severe). This level of performance over time was achieved using a variety of approaches, ranging from independent maintenance through to continuous revision. Importantly, while intense practice assisted in fast initial improvement of words, less intense schedules of revision were able to sustain the majority of words over time.

With respect to factors that may be associated with intervention outcome, the degree of naming improvement was correlated with neuropsychological measurements, but it did not relate to demographic variables such as age at training or years of education. No specific cognitive or demographic variables related to independent maintenance at two months, however, maintenance was associated with the level of gain in word retrieval post-intervention.

Additionally, although it is important to retrain words which can no longer be retrieved, evidence was also found to support the claim that practising words correctly recalled at the commencement of therapy may help these words persist over time, thereby delaying onset of vocabulary loss.

Discussion of findings

The range of performance declines observed during the immediate post-training period were similar to those reported previously in SD patients. Short-term maintenance was relatively well maintained by most participants, with five out of the current nine cases showing only non-significant declines after 2 months without practice. With increasing time, however, only three individuals could sustain 80% or more of their performance without some formal revision, with only one, mild SD case (SD-B1) able to perform at an equivalent level when tested 6 months later without practice.

The relative success of individuals with milder impairments to maintain word retrieval gains over time may reflect two key processes. Firstly, the training may strengthen existing links between concepts and the words stored in the lexicon, allowing greater ability to retrieve the correct label from memory. In such cases, the trained words initially difficult to recall on demand, became more easily accessible with practice. Alternatively, with respect to learning theories, the success over time for individuals with mild disease (such as SD-B1) suggests a preserved capacity to consolidate words to long-term storage. At earlier stages of the disease, even when words may no longer exist in the lexicon, patients may be able to draw upon a richer, existing semantic network to form strong links between the relearnt word and corresponding object. Indeed, in the current study, level of semantic memory impairment was strongly correlated with improvements in naming, which in turn was associated with maintenance success. As the conceptual reference point degrades, however, due to increasing anterior temporal lobe atrophy, the ability to hold the association between the verbal label and object may weaken or fail to be consolidated effectively, resulting in word retrieval failures. In other words, as the disease progresses, an over-reliance on transitory memory systems may mean that naming performance can only be maintained through some level of revision. Previous research has shown that naming improvements can persist with ongoing, intense practice (Graham et al., 2001). This study now demonstrates that continued practice need not be as intense as the original training, even for cases with severe impairments. Compared with 5 sessions of training per week offered during the initial program, only 1-2 sessions of revision per week were necessary to sustain performance. Further, performance at 2 months post-intervention appeared to be a crucial indicator of the degree of revision required to sustain word gains, with rapid drops towards baseline signalling the need for more regular revision.

To date, studies have concentrated predominantly on training words that cannot be correctly recalled at baseline. The current findings show some benefit in also practising words known at the beginning of the intervention, as previously reported (Jokel et al., 2010, 2006). For all but one individual enrolled in this study, the decline in naming performance on untrained items was relatively subtle, and similar to the small declines reported in a mild SD patient (Dressel et al., 2010). Group analyses, however, supported the claim that practicing words known at the commencement of therapy also helps maintain these words. The fact that larger declines in the known but untrained words were not observed may reflect that these words are particularly salient to the person, and are already being reinforced informally through everyday use, strengthening their semantic link. It is also plausible that in this group of patients, mostly with mild to moderate disease severity, the repeated reassessment of the words may have provided a level of reinforcement to memory or assisted in the ease by which to retrieve words successfully from the lexicon. Studies in aphasia following stroke suggest that improvements could be observed simply through repeated attempts to name, even without feedback (Nickels, 2002). To exclude this last possibility, future studies will need to measure levels of decline in matched words that are only tested at baseline and at 6 months.

From a practical perspective, the results of this study have important implications for clinicians and families considering cognitive intervention. Recognising these different patterns of maintenance will assist with anticipating the likely time commitments required. For patients with mild semantic impairments, intense training may restore words quickly, with a small number of revision sessions recommended every few months to support performance. For patients rated in the severe range, however, continued weekly revision may need to follow the initial intense retraining, requiring a greater commitment to sustain benefit. This difference in continuing schedules also has implications for the total number of word lists that can be retrained and supported. With ongoing decline expected over time, consideration must also be given for training words still able to be retrieved correctly if they are important in supporting the everyday functioning of the individual.

Conclusion

Despite the neurodegenerative nature of the disease, this study demonstrates that not only can patients with Semantic Dementia undertake cognitive interventions that help restore word memory and retrieval, but that with appropriate monitoring and revision schedules, significant ongoing benefits can be achieved. This occurs over a time period where declines would otherwise be reported, and extends not only to patients with mild disease severity, but also to those who present with severe semantic impairments at the beginning of training. Reinforcing known words may also assist with better retention over time. While declines are an expected consequence of this disease, involvement in ongoing word retraining can help combat this.

CHAPTER 7. Language awareness in SD

As a final component of the project, the aim of this study was to investigate patient awareness regarding the nature and severity of their language impairment. Awareness of deficits can impact both rehabilitation planning and outcomes, influencing the extent to which patients can be self-directed and make decisions regarding the content of their therapy, as well as impacting their motivation to commence and comply with interventions. While it is generally believed that patients with Semantic Dementia demonstrate good awareness of their difficulties, little empirical investigation has been conducted to verify this.

7.1. INTRODUCTION

Loss of insight (or 'anosognosia') refers to a compromise in awareness of one's own functioning. As a complex phenomenon, impairments may vary in severity (from mild to profound), and in the domain affected, such that a person may be aware of declines in one area of functioning (e.g., memory), but not in another (e.g., personality change) (Aalten et al., 2005; Hannesdottir & Morris, 2007). As a disorder of metacognition, it suggests a breakdown in the storage and updating of self-knowledge and/or processes of self-monitoring and self-regulation (Eslinger et al., 2005), resulting in a diminished ability to accurately appraise one's skills. As noted in Chapter 1, impairments in self-awareness arise in dementia syndromes (Rosen, 2011), and may result from disturbances in a range of cognitive systems including perceptual, memory, and executive processes (Agnew & Morris, 1998; Hannesdottir & Morris, 2007). This may be conceptualised into four different levels of awareness, ranging from impairments in sensory registration, through to disturbances in monitoring and evaluating performance, and lastly in the meta-representation of oneself - the ability to reflect on one's situation and the changes experienced (Clare, Marková, Roth, & Morris, 2011).

Although little investigation of awareness has been conducted specifically in patients with Semantic Dementia, some level of impairment is likely. Firstly, the cognitive models recently described include a role for semantic memory, in the storing and updating of knowledge regarding one's abilities (Hannesdottir and Morris, 2007). Thus semantic memory may be important in making evaluative judgements of language performance. A link between semantic memory and anosognosia has also been supported in a study of LPA patients, where scores on a semantic association task and reduced information content in speech were predictive of larger discrepancies between patients and carers when rating the patients' current behaviour . In addition, results from two questionnaire-based evaluations have suggested some impairments regarding awareness of changes in apathy, empathy (Eslinger et al., 2005) or social interaction (Hornberger et al., 2014).

Against this hypothesis, however, some limited evidence suggests that SD patients are preserved in their awareness of diagnosis, language problems (Hornberger et al., 2014) and functioning in other broad cognitive domains (Eslinger et al., 2005). This may suggest preservation of evaluative judgements or the meta-representations of self with respect to language skills. In these studies, awareness is measured by relying upon subjective ratings alone, with impairments to awareness defined by a significant difference between a patient's self-rating of functioning and the caregiver's rating of the patient's functioning. Further support for awareness of cognitive ability in relation to intact evaluative judgement has also been reported in one study, when comparing patient self-assessment with objective measures of performance. In this study, strong correlations were found between how eight SD patients rated their performance on word generativity and word list learning tasks and their actual test scores (Eslinger et al., 2005), suggesting accurate appraisal of their verbal skills.

Considering the domain of language, the ability evaluate one's functioning accurately likely reflects a complex interplay of knowledge of past linguistic skills, knowledge of current linguistic skills, the ability to evaluate oneself generally, and the ability to judge or have knowledge of language. While SD patients report difficulties with remembering or understanding the meaning of words, it seems likely that awareness regarding the extent of their difficulty may be compromised, as this store of knowledge about words is degraded. Previous studies have illustrated how declines in semantic knowledge affect patients' language ability, resulting in an over-reliance on both higher ordinate words to describe objects (e.g., "peanut" becomes "nut", becomes "food")(Hodges et al., 1995), and on general rules of language which are not always correct (e.g., rejecting low frequency words that are atypical in spelling in preference for non-words which appear more typical) (Patterson et al., 2006). Patient awareness of these errors and how this may impact upon perception of their changing language ability, however, has not been directly measured.

Anecdotal observations suggest that this aspect of language awareness may be compromised, therefore affecting performance monitoring and evaluation. For example, when shown the object "coaster" and asked for the name, one patient enrolled in word retraining (SD-B1) remarked with surprise "oh, is there a word for that? I just thought that was a little cup plate" and claimed to never have heard the word "coaster" before. This raises two possible impediments to language awareness. Firstly, if a patient is unaware that a specific word even exists for an object, then he/she cannot be aware of the failure to recall it. Secondly, if an accurate sense of having once known the word does not exist, it is not possible to acknowledge a decline in naming ability in these instances.

As questionnaire-based methods of investigating awareness often use broad scales (e.g., "yes/no" or 3-point scales) asking about the presence rather than degree of problem (e.g., "Does s/he ask what words mean?"), they may be insensitive to capturing subtle reductions.

The use of specific, objective measures may allow a close examination of awareness in this population.

Study design and hypotheses

The current study aimed to assess language awareness in SD by creating novel, experimental tasks to measure accuracy in evaluating language, as well as beliefs regarding one's past knowledge of words. It was hypothesised that while SD patients may rate their performance on language tasks as impoverished by virtue of knowing they have a disorder affecting language, the severity of deficit would be under-stated. Further, the ability to identify poor language performance in others would be reduced. Finally, some decline in awareness of past knowledge was anticipated. For comparison, the study also included a disease-control group of nonfluent PPA patients, as these patients also experience language related problems, but have preserved semantic memory by which to judge language performance.

7.2. METHOD

Participants

Consecutive patients, with a diagnosis of primary progressive aphasia (Gorno-Tempini et al., 2011), attending the FRONTIER Research Clinic in 2013 for an initial or review assessment, were recruited to the study. Clinical diagnoses were established following a comprehensive multi-disciplinary assessment including neurological, neuropsychological, and language testing in conjunction with MR imaging (as described in Chapter 2). To qualify for entry into this study, patients needed to demonstrate sufficient attention and comprehension skills to engage in the study tasks. Exclusion criteria were: (a) mutism; (b) limited or no formal education in English; or (c) the presence of additional neurological disorders, including motor neuron disease or other movement disorders. This resulted in 22 SD patients and 9 nonfluent PPA patients.

Patient groups were similar with respect to age, years of education and time since diagnosis; however, SD patients had experienced a longer history of symptoms. In both groups, roughly half the participants had been assessed the previous year, as part of a longitudinal study in Frontotemporal dementia, with the other half newly presenting to the clinic. Participant characteristics are provided in Table 7.1.

Participants completed a short battery of standardised cognitive assessments to profile their current skill levels. These included: the Addenbrooke's Cognitive Examination-Revised (Mioshi et al., 2006), which includes a separate language subscale as a broad screen of language skills encompassing reading, writing, verbal comprehension, naming, repetition, and semantic knowledge; Animal fluency to measure word generativity under time pressure; as well as two subtests from the Sydney Language Battery (SYDBAT) to assess single word processing skills: Naming and Word Comprehension. To indicate normal performance on each of these language measures, results from 15 age- and education-matched healthy controls from the FRONTIER database are also presented as a reference.

Table 7.1: Demographic details by group

	SD	Nonfluent	Group comparisons
Males / Females (n)	12 / 10	3 / 6	X^2 (1) = 1.15, *p* = .28
New cases / Review (n)	9 / 13	4 / 5	X^2 (1) = .03, *p* = .86
Age	65.2 ± 6.8	67.8 ± 9.6	*t* (29) = .87, *p* = .39
Education (years)	12.5 ± 2.6	13.9 ± 3.0	*t* (29) = 1.29, *p* = .21
Time since diagnosis (years)	1.8 ± 2.0	1.0 ± 0.8	*t* (28.9) = -1.40, *p* =.17[a]
Disease duration (years)	5.8 ± 2.0	3.0 ± 1.1	*t* (26.5) = -4.98, *p* < .001 [a]

Values are Mean ± Standard Deviation; [a] degrees of freedom adjusted given equal variances were not assumed

Experimental study: Stimuli and design

To examine language awareness, three different experimental tasks were used. Each task was structured so that it was simple to understand and required minimal language skills in order to respond. These tasks were designed to assess awareness at the levels of performance monitoring and evaluative judgement (as described by Clare et al., 2011).

1. **Cookie Theft performance evaluations** – participants were asked to rate the quality of responses given to the Cookie Theft picture description task (Figure 7.1) - a widely used measure of expressive language ability wherein patients describe in as much detail as possible what is happening in a black and white line drawing of a kitchen scene (Goodglass & Kaplan, 1983).

Figure has been removed due to Copyright restrictions

Figure 7.1: Cookie Theft picture

In the first condition (Rating of Self), participants were asked to complete the description task, which was audio recorded, and immediately following this, rate their performance out of 100, using the following visual analogue scale:

0 100

Very low score Very high score

☹ 😐 ☺

To guide their rating, participants were told that a zero score meant that no elements of the picture had been described, whereas a score of 100 would mean that all aspects of the picture had been clearly described.

The descriptions provided by the participants were then transcribed and re-recorded in the researcher's (SS) voice, to mimic the performance provided by the patient. The purpose of this was to provide an identical level of content, but remove any bias in ratings introduced by attitudes or beliefs about oneself. Thus in the second condition, participants were asked to rate the performance of this re-recorded description (Rating of re-recorded Self). Thirdly, four other recordings of Cookie theft descriptions, each approximately 1 minute in length, were played to the participant. These were samples previously collected by the FRONTIER research group, selected to represent a range of performance from very poor to good descriptions (see Appendix 8 for transcripts of these). Participants were asked to listen to each description, and consider if the person speaking had any problems with words. Participants were encouraged to indicate what sorts of problems, if any, they noticed. They were then asked to provide a rating of the performance using the visual analogue scale. A copy of the Cookie Theft picture was provided throughout the task and patients were directed to look at the picture while listening to the descriptions.

2. **Word identification task** – To investigate participant knowledge regarding their past exposure or use of words, 25 single-syllable items were presented both orally and visually, one at a time, and the participant was asked whether they had heard or used the word before, and whether they had a sense or feeling of knowing the word. Participants were informed that some words were not real words, but had been made up and did not mean anything. Items included five high frequency words familiar to all participants (e.g., dog, room, food), as a check that the task was understood. Ten items were lower frequency words, which would have been known to the participant in the past but may not be known now (e.g., eel, crumb, bead), and 10 items were non-words (e.g., prad, jart, blane), which the participant had not encountered before.

3. **Word awareness task** – As a measure of word knowledge, participants were presented with images depicting four everyday objects (tree, car, computer, and face) for which an overall word could be used to describe the object (e.g., "a tree"), but 4-6 specific words could also be provided per picture when targeting various components (e.g., "branches", "leaves", "roots", "trunk" – see Figure 7.2). Overall, 20 words were tested and three scores of word knowledge were generated (Word Exists, Word Known Now, Word Known in the Past). The task began by confirming the overall word for each of the four items (e.g., "This is a picture of a tree."), and then probing knowledge for the specific words within each picture. Firstly, participants were asked whether a specific word existed for each of the components (e.g., "is there a name for this particular part of the tree *[pointing to the trunk]*?"). If the participant indicated that a word existed, the participant received a score of 1 (Word Exists), responses of "no" or "don't know" were scored as 0. A separate point was then awarded for each correctly named component (Word Known Now). If no word was provided or an incorrect label was given, the response was scored as 0. Lastly, if the participant believed the word existed but could not recall the name, the participant was asked "do you think you would have known the word in the past (e.g., 10 years ago) and you just can't think of it now, or do you think

you might never have known it?". If the participant confirmed either past or current knowledge of a word for that component then an additional point was awarded (Word Known in the Past).

Figure 7.2: Word Awareness pictures

Data analysis

IBM SPSS Statistics 22.0 was used for analysis of the results. Comparisons on demographic and clinical variables were conducted using independent samples t-tests for continuous variables, and chi-squared tests for categorical variables. For the experimental measures, Kruskal-Wallis and Mann Whitney U tests were used to compare groups, given non-normality.

Objective scoring of the Cookie Theft descriptions was conducted by two raters, where the second rater was blind to the diagnosis of the participant. Each transcript was given a score out of 23, according to the classification of semantic or content units as described by Croisile and colleagues (1996). See Appendix 9 for full details. Inter-rater reliability was assessed using a two-way mixed, absolute average-measures intra-class correlation based on each rater's total score of each participant (McGraw & Wong, 1996). Resulting inter-rater reliability was excellent, ICC = 0.99, indicating a high degree of agreement between the two raters. Scores were then converted by dividing the total by 23 and multiplying by 100, to allow direct comparison with participant ratings.

7.3. RESULTS

Language profile

As expected, SD patients showed significant impairments across each of the language related tasks compared with age-matched controls (all $p < .001$), while nonfluent patients were impaired on Animal fluency (t (22) = -6.16, $p < .001$) and the ACE-R Language scale (t (22) = -7.00, $p < .001$), but otherwise performed relatively well (Table 7.2). Examining patterns of performance on the word comprehension test, it was apparent that approximately half of the SD patients performed very poorly (scoring less than 50% correct), while nonfluent patients performed consistently at a high level. Given this wide range of performance, together with the prediction that greater semantic impairment would result in poorer language awareness, results from the experimental measures for the SD group were also divided into those scoring above (mild-moderate SD) and those scoring below 15/30 correct (severe SD) on this measure (Table 7.2).

Table 7.2: Language profile by group (Means and Standard Deviations)

	Controls (n = 15)	Nonfluent (n = 9)	SD all (n = 22)	mild-mod SD (n = 11)	severe SD (n = 11)
ACE-R (100)	94.4 ± 3.4	83.3 ± 7.4[a]	57.4 ± 18.3[a]	72.0 ± 12.0[a]	42.8 ± 9.7[a]
ACE-R Language (26)	25.1 ± 0.9	21.4 ± 1.7[a]	11.45 ± 5.8[a]	15.7 ± 4.7[a]	7.2 ± 2.8[a]
Animal fluency	20.7 ± 4.6	10.3 ± 2.6[a]	6.5 ± 4.8[a]	10.1 ± 3.5[a]	2.9 ± 2.8[a]
SYDBAT Naming (30)	27.4 ± 2.1	25.0 ± 6.2	7.6 ± 7.2[a]	12.0 ± 6.9[a]	2.2 ± 1.6[a]
SYDBAT Comprehension (30)	29.2 ± 0.7	29.2 ± 1.2	16.1 ± 7.9[a]	22.0 ± 4.4[a]	8.8 ± 3.9[a]

Note: maximum scores in brackets where relevant; values are Mean ± Standard Deviation; Abbreviations: ACE-R = Addenbrooke's Cognitive Examination-Revised; SYDBAT = Sydney Language Battery; [a] p < .005 compared with Controls

Cookie theft performance evaluation

Objective scoring of the Cookie Theft picture descriptions confirmed significant group differences in the quality of responses provided ($H(2) = 16.09$, $p < .001$) with severe SD patients performing more poorly than both the mild-moderate SD patients ($U = 10.5$, $z = -3.29$, $p = .001$) and the nonfluent patients ($U = 4.5$, $z = -3.42$, $p < .001$), capturing a median of only 17% of the picture content in comparison to approximately 50% of the content covered by the other groups.

To examine individuals' ability to judge their own performance accurately, discrepancy scores were calculated by subtracting the objective performance score of each individual from their own rating, where a positive score indicates an overestimation of performance. As shown in Figure 7.3, immediately following the task, the difference between actual and perceived ability varied to include both over-estimations as well as under-estimations of performance in all three groups. While the majority of nonfluent patients appeared to show either small or negative discrepancy scores, no significant group differences in discrepancy scores emerged either when

SD patients were considered as a whole (U = 50, z = -1.59, p = .111), or when dividing groups based on severity of semantic impairment ($H(2)$ = 2.68, p = .262). In contrast, when the descriptions were re-recorded in the examiner's voice and presented back to patients later, clear group differences in the discrepancy scores now emerged ($H(2)$ = 7.54, p = .023). While median discrepancy scores for nonfluent patients remained close to zero, signalling maintained accuracy in rating performance, severe SD patients were now significantly poorer than nonfluent patients at rating performance (U = 10, z = -2.5, p = .012), producing large overestimations despite the content of the description remaining the same. Increases in median discrepancy scores were also observed in mild-moderate SD patients, however, the difference in discrepancy scores compared with nonfluent patients failed to reach significance (U = 19, z = -1.90, p = .058).

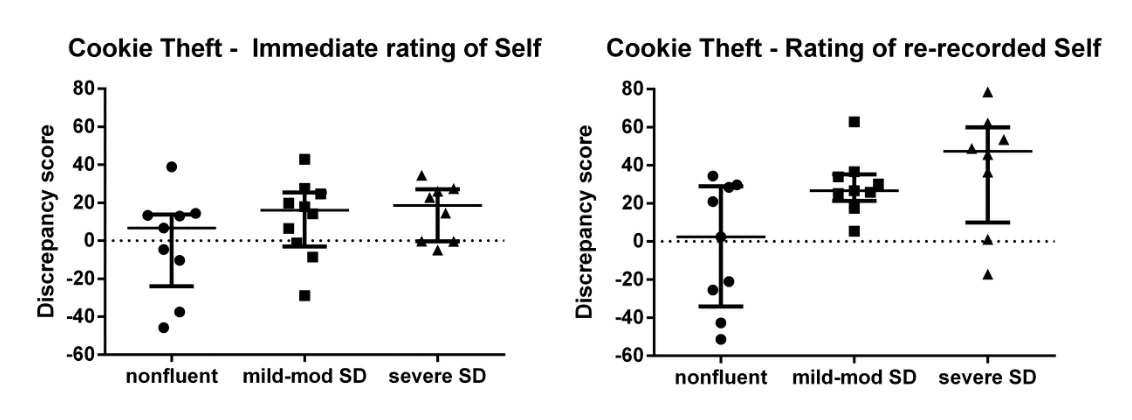

Figure 7.3: Cookie Theft Discrepancy self-ratings by group

Discrepancy scores = (Actual Performance – Rated Performance). Bars indicate median and interquartile range.

Ratings of other example Cookie Theft descriptions indicated a general appreciation of performance by participant groups: each group rated the very poor example (Sample 1) with the lowest median scores and the control example (Sample 4) with the highest median scores (see Table 7.3).

Table 7.3: Median (IQR) Cookie Theft ratings for example descriptions

	n	Sample 1- Very Poor	Sample 2 – Poor (semantic)	Sample 3 – Poor (word finding difficulty)	Sample 4 – Good
Actual score		*13*	*28.2*	*34.8*	*56.5*
Rated score					
nonfluent	9	8 (7.5)	27 (23.5)	34 (26)	80 (26)
mild-mod SD	9	12 (6)	51 (24.5)	51 (33.5)	91 (8.5)
severe SD	8	24.5 (25.8)	53 (33)	51 (1.8)	89.5 (12.3)

Once again, however, group differences on discrepancy scores emerged, with the SD group as a whole significantly poorer than nonfluent patients at evaluating descriptions (Sample 1: U = 32.5, z = -2.10, p = .036; Sample 2: U = 24.0, z = -2.83, p = .005; Sample 3: U = 33.5, z = -2.33, p = .02; Sample 4: U = 34.5, z = -2.27, p = .023). As seen in Figure 7.4, this was particularly evident for severe SD patients, who showed a tendency toward rating poor examples of Cookie theft descriptions more generously than nonfluent patients (Sample 1: U = 10.5, z = -2.46, p = .014; Sample 2: U = 6.5, z = -2.84, p = .004; Sample 3: U = 13.0, z = -2.23, p = .026), with no significant differences in discrepancy scores found between mild-moderate and severe SD patients (all p values > .19).

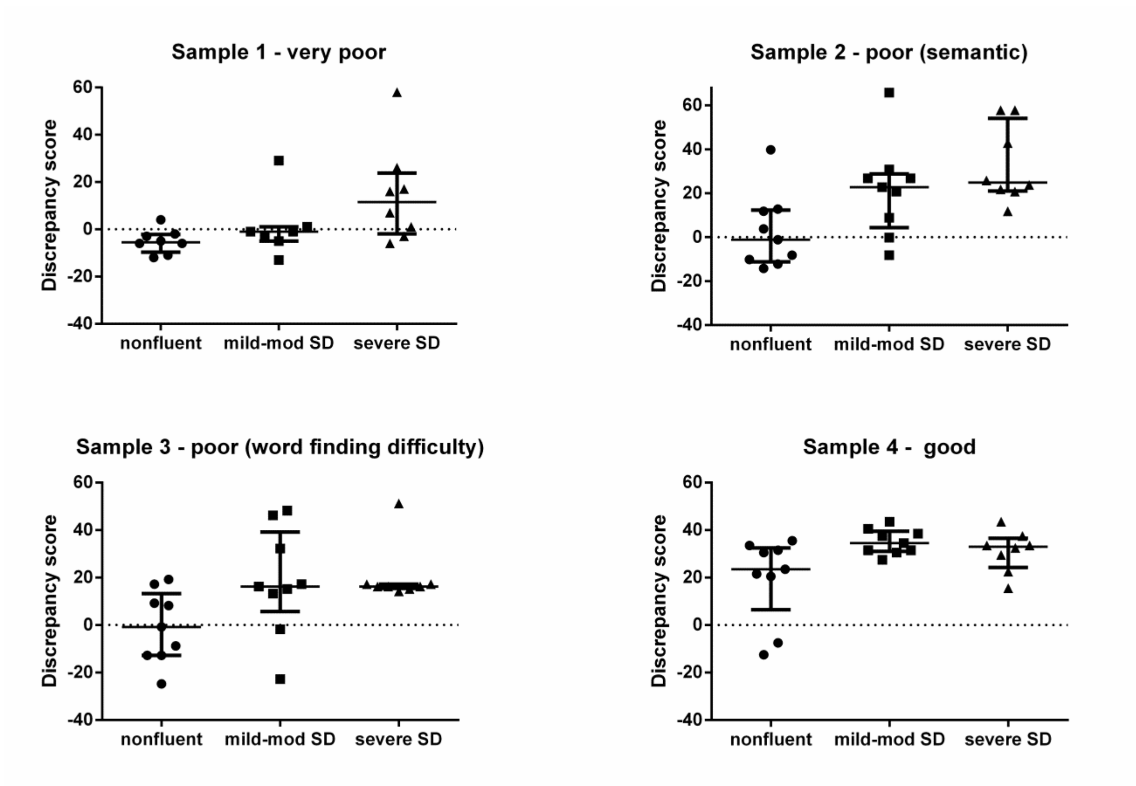

Figure 7.4: Cookie Theft discrepancy ratings for example descriptions by group

Discrepancy scores = (Actual Performance – Rated Performance). Bars indicate median and interquartile range.

Examining response patterns within individuals, four participants (3 with severe SD and 1 with mild-moderate SD) rated "Sample 2 – poor (semantic)" and "Sample 4 – good" as equally well described. This pattern was never observed in the nonfluent group. From descriptive comments made when conducting ratings, some SD patients believed Sample 2 to have been completed very well ("his speech was perfect"; "he talked about lots of aspects"). While some mild-moderate SD patients did at times detect word finding difficulty (e.g., saying that the person "forgot some words" or that descriptions may have had "bits missing"), only one appeared to notice the use of unusual vocabulary (such as the use of the word "equipment" for "dishes"). Interestingly, one severe SD patient was hesitant about providing ratings, as he acknowledged having difficulty comprehending the content of the descriptions provided. By contrast, more nonfluent patients identified the use of vague language (e.g., "food" instead of "cookie") or errors in word choice (e.g., "a problem finding the *right* words").

Word identification

When word knowledge was tested using the word identification task, all participants correctly responded to the five high frequency words, indicating good task comprehension. For low frequency words, however, group differences emerged (H (2) = 10.52, p = .005), with severe SD patients no longer able to recognise all the words as previously familiar, in contrast to the nonfluent (U = 9, z = -3.17, p = .002) and mild-moderate SD patients (U = 14, z = -2.23, p = .026) (Table 7.4). Compared to both mild-moderate SD and nonfluent patients, these patients had little confidence in knowing their meaning (mild-moderate SD vs severe SD: U = 7.5, z = -2.78, p = .005; nonfluent vs severe SD: U = 4.5, z = -3.50, p <. 001). While nonfluent patients were also good at discerning the non-words, the SD group as a whole was significantly poorer on this task (U = 28, z = -2.70, p = .007), mistakenly identifying some of these words as familiar, although they did not confabulate a meaning for these words (Table 7.4).

Table 7.4: Word identification performance by patient group (Median and IQR)

		Word recognition		**Feeling of Knowing**	
	n	**Low Frequency**	**Nonword**	**Low Frequency**	**Nonword**
nonfluent	9	10 (0)	10 (1.0)	10 (0)	10 (1.0)
mild-mod SD	9	10 (1.0)	8 (8.5)	9 (1.0)	10 (1.0)
severe SD	8	8 (2.5)	8 (1.5)	3.5 (2.0)	9.5 (1.8)

Scores are out of 10

Word awareness

When asked about specific words relating to components of common objects, group differences emerged for all three subscores of this test (Figure 7.5). As expected, all patient groups showed some difficulty retrieving these words, with fewer words produced by severe SD than mild-moderate SD patients ($U = 3$, $z = -3.59$, $p < .001$), who in turn produced fewer words than the nonfluent patients ($U = 11.5$, $z = -2.75$, $p = .006$). Only SD patients were prone to believing either that a word did not exist for that component ($U = 36$, $z = -2.85$, $p = .004$) or that they would not have known it in the past ($U = 24$, $z = -3.18$, $p = .001$), with greater uncertainty for patients with more severe impairments (Word Exists - mild-moderate SD vs severe SD: $U = 15$, $z = -2.74$, $p = .006$; Word Known Past - mild-moderate SD vs severe SD: $U = 11$, $z = -2.97$, $p = .003$).

This tendency to make errors in word knowledge rather than simply in word retrieval was further illustrated by comments made by severe SD patients while completing the task. When asked about a steering wheel, one person with severe SD confirmed there was a word for it, but when asked if he'd ever known it, said "I can't tell you". When asked about "chin" he did not know if he'd ever known the word. Another individual with severe SD indicated that the "forehead" was just "the top of your head" and another agreed that in the case of the computer there were not separate words for each component and it simply was "all just a computer".

In milder SD patients, errors in labelling were often observed. In some cases, a lack of awareness that the words provided were erroneous was apparent. One participant, for example, claimed that "forehead" was a "head-face-top" and that this was the word he had always used. Similarly, this individual indicated that he had always called nostrils "nose vents".

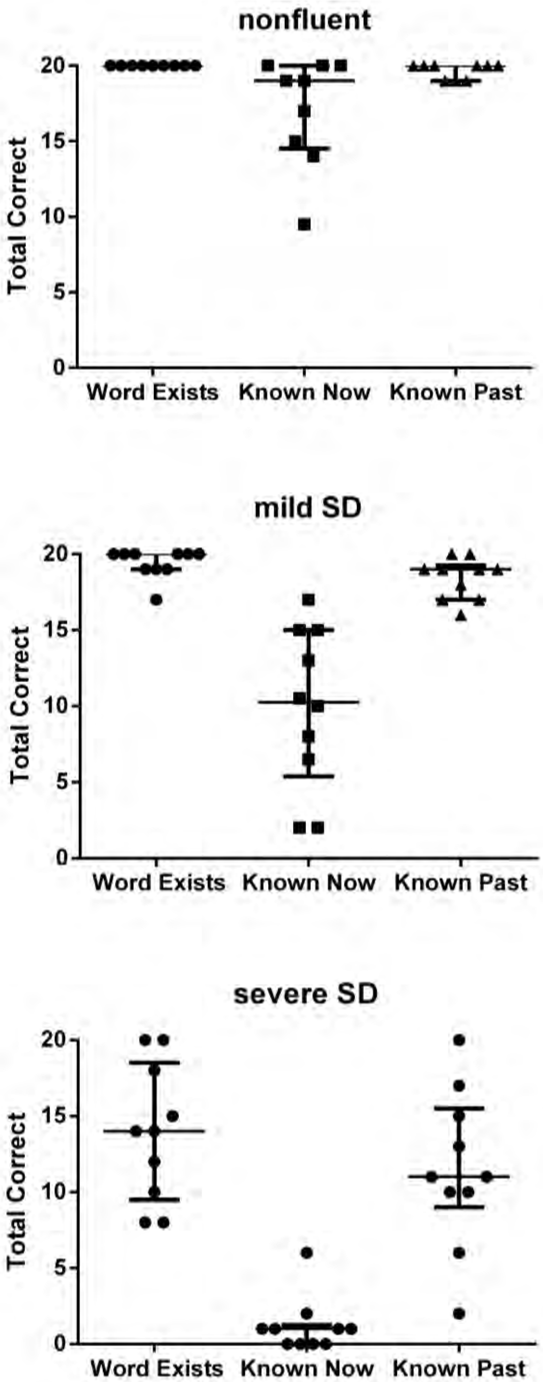

Figure 7.5: Word Awareness scores by group

Bars indicate median and interquartile range.

7.4. DISCUSSION

Overall summary

The current study investigated language awareness using experimental measures of both accuracy in evaluating language and knowledge of words. This allowed examination of two of the levels of awareness outlined by Clare and colleagues (2011), regarding the ability to identify errors (relevant for performance monitoring aspects of awareness) and to make evaluative judgements (specifically relating to changes in functioning and quality of one's performance). While both nonfluent and SD patients acknowledged a reduction in their performance on a language task (Cookie Theft), the ability to distinguish good language from poor language production was compromised in SD only. This deficit was observed in this group on different tasks. Firstly, when asked to rate the content of their own language production re-recorded in a different voice (i.e., when the reference to themselves was removed), SD patients were more likely to over-estimate the quality of the performance (particularly for more severe patients). In contrast, nonfluent patients showed little change in their ratings between conditions. Further evidence of the SD difficulty in assessing language samples was provided by the sample Cookie Theft descriptions. Again, SD patients showed a greater discrepancy in ratings from objective scores than nonfluent patients. Lastly, the impact of language impairment on judgements of past knowledge was demonstrated by the increased errors made by severe SD patients in recognising low frequency words, and in judging whether a word even exists when discussing components of an object. Such errors were never made by nonfluent patients. Collectively, these results indicate that despite a general awareness of language problems, SD patients have difficulty assessing specific impairments and relating their current knowledge of words to their past ability.

Discussion of findings

The reduced language performance reported by SD patients following the completion of the Cookie Theft task is consistent with previous findings showing that these patients are aware of their diagnosis and do report experiencing language problems (Hornberger et al., 2014). Corresponding to their actual task performance, severe SD patients provided the lowest median ratings of performance, followed by the milder SD patients. Although the median discrepancy between perceived and actual performance was closer to zero for the nonfluent patients, no statistically significant difference was found between the diagnostic groups. Thus, contrary to expectation, SD patients appeared to rate their performance with an overall level of accuracy similar to nonfluent patients. In part, this reflects the variability found in both patient groups, with some rating performance either more positively or more negatively than objective scoring would suggest. It does indicate, however, some SD patients rate their level of impairment accurately, regardless of disease severity.

When the reference to self was removed by using another voice, however, SD patients increased their ratings, compared with nonfluent patients, suggesting that SD patient perceptions of quality were influenced by the knowledge of who has completed the task versus the actual content of the description. While self-evaluation can be affected by factors relating to mood and personality (Grut et al., 1993; Jorm et al., 1994), it is interesting here that SD patients performed well under this condition. The method of asking patients to evaluate re-recorded samples of their performance has also been used in studies of jargon aphasia, where language awareness may be affected post-stroke. In this population, however, the reverse pattern is found, where patients rate their own immediate performance positively but are critical of the same poor content when it is presented back again in someone else's voice (Maher, Rothi, & Heilman, 1994; Shuren, Hammond, Maher, Rothi, & Heilman, 1995). In these cases, reduced awareness of functioning is thought to relate to attentional difficulties in monitoring performance while completing a task. In the current study, it appears that these inaccurate ratings arise from an inability to judge language based on content alone (i.e. to detect errors). This position is supported by the rating discrepancies found when SD patients evaluated other language samples. Although milder SD patients performed similarly to nonfluent patients when evaluating very poor language performance (where very few words are produced), samples that included word finding difficulty and semantic substitutions were generally rated more favourably by SD patients. Thus, SD patients were able to judge performance appropriately only when descriptions were provided by someone known to have a problem with words (i.e., themselves) or when obvious cues of impairment were present (such as reduced quantity of speech). When fine discriminations in language quality were required based on the clarity of content, the accuracy in evaluating language was reduced. Median performance of nonfluent patients, however, remained close to zero for all three impoverished descriptions.

Further evidence of the impact of semantic impairments on the ability to evaluate language was found by the results of the word identification and word awareness tasks. When assessed on beliefs regarding past knowledge, SD patients with milder impairments recognised that the reductions in current ability were in contrast to previous knowledge. This awareness was seen both on the Word Identification test where mild-moderate SD patients still showed good recognition of previously encountered low frequency words, but a reduced sense of currently knowing the word, and on the Word Awareness test in correctly identifying that different components of everyday items had a label, even if they were unable to produce it correctly. Severe SD patients, however, showed reduced performance on both tasks, with failures to appreciate where past word knowledge may have differed to current performance. This finding suggests that the benchmarks with which to judge performance degrade with increased disease severity, affecting levels of awareness through impairments to both performance monitoring and evaluative judgements. While such impairments may be more evident with disease progression, it is important to note that evidence of reduced awareness was present even in milder disease stages – with instances of gross mislabelling of object components without awareness of these errors (which did not occur in the nonfluent patients). This suggests some early reductions to performance monitoring skills in SD.

Overall, the results indicate that subtle changes to language awareness arise in SD as a result of semantic impairments impeding the ability to evaluate or realise deficiencies in language performance. While comprehension impairments have been ruled out as the main factor leading to unawareness in post-stroke patients (Cocchini, Gregg, Beschin, Dean, & Della Sala, 2010), such impairments may be of greater importance in SD. With respect to the Cognitive Awareness Model of anosognosia (Hannesdottir & Morris, 2007), diminished cognitive awareness may arise from a compromised semantic system reducing the sensitivity of the comparator mechanisms in detecting specific language problems, due to both reduced knowledge of language and a degraded sense of past performance in the Personal Knowledge Base (Agnew & Morris, 1998). Given episodic memory is relatively well preserved in SD, the knowledge of having a progressive language disorder may allow for an updated general sense of deteriorating language to be incorporated in the self-representation, potentially explaining why semantic impairment does not appear to affect the accuracy of self-rating immediately following a task, but does affect other judgements of language. Although this provides one explanation, further empirical studies testing the Cognitive Awareness Model are, however, still required.

While semantic memory appears to be a contributing factor to language awareness in SD, anosognosia is a complex construct and includes not only cognitive variables but also psychological and social factors (Ownsworth, Clare, & Morris, 2006). As observed in other studies of awareness in people with dementia or mild cognitive impairment, considerable variability can be seen among individuals (Agnew & Morris, 1998; Ries et al., 2007), and not all SD patients were poor at evaluating language. Future studies may wish to explore language awareness in larger samples, and measure performance over time to verify how self-perceptions of language ability change with disease progression.

Conclusions

Given that SD patients possess a broad awareness of language functioning, but a reduction in appreciation of specific deficits, this perhaps equates to an “underawareness” or “underappreciation” of the severity or extent of their deficits (Kaszniak & Edmonds, 2010) rather than *un*awareness. Results do, however, support a role for semantic memory in anosognosia. On a practical level, while broad awareness may help motivate SD patients to seek treatment, awareness of the exact nature of their difficulties may be lacking. While Chapters 4, 5 and 6 have shown that both mild and severe SD patients benefit from undertaking tailored word retraining programs, careful selection of words is important given treatment effects are only found for those words specifically trained. While patients in the early stages of the disease may be able to provide greater input regarding which words to train, severe patients are likely to require guidance.

CHAPTER 8. Summary and General Discussion

The objectives of this thesis were to evaluate the language functioning of patients with a rare but debilitating progressive condition, Semantic Dementia, and investigate how improvements in functioning may be made using a simple cognitive intervention. The main findings of each experimental section are summarised here, followed by a discussion of the implications of the work. In addition limitations and future directions are considered.

8.1. LANGUAGE ASSESSMENT IN PPA

Summary of results

The study presented in Chapter 3 addressed the need for a simple assessment tool for diagnosing and characterising single word processing in patients with progressive language disorders. Despite the rarity of these conditions, the study was able to include over 50 patients with PPA, including 22 cases with SD. Results demonstrated that each PPA subtype could be distinguished through the pattern of performance across subtests of a newly designed language test, the SYDBAT, with the expected impairments found for each subtype. Overall, 80% of participants were correctly classified on the basis of three SYDBAT tests alone. Diagnostic accuracy was particularly high for SD and PNFA cases where false positives were less than 10% of cases. Reliability and validity measures indicated excellent correspondence with existing language instruments for naming, repetition and semantic association.

Implications for language assessment and rehabilitation

Although the distinction among subtypes of PPA can be difficult and time consuming, the high classification accuracy achieved using the SYDBAT, together with its strong psychometric properties, demonstrates how this battery can provide a simple and useful tool to improve accuracy in diagnostic assessments. This in turn can assist in identifying PPA patients most likely to benefit from intervention. Using the SYDBAT, relative strengths and weaknesses within single-word processing can be identified and considered when developing rehabilitation approaches. For example, verifying the differential ability of repeating words versus retrieving words from memory is important when considering word retraining approaches that assume intact phonological processing; PPA patients who show significant difficulties in word repetition are likely to require alternative or modified approaches to assist word retrieval difficulties.

The SYDBAT also provides an efficient assessment of semantic memory to characterise impairment levels. To date, various clinical measures have been used to profile the language skills of SD patients undertaking retraining, using different stimuli to assess key aspects such as naming and semantic association. As a result, the relative impairments of skills within a patient, and differences in impairment levels among patients, have been difficult to determine. In the current series, the SYDBAT provided a method to measure and compare the disease severity of SD patients undertaking word retraining, and in doing so, investigate relationships between semantic impairment and therapy outcomes of learning, generalisation (Chapter 5) and maintenance (Chapter 6).

Limitations and future directions

Although the SYDBAT was highly successful in identifying and characterising the majority of PPA patients, a false positive rate of over 10% was found in LPA cases, emphasising the need for other methods to detect deficits specific for this syndrome. Future studies identifying other tests or methods for analysing subtle aspects of speech are therefore required. A study aimed at distinguishing PNFA and LPA patients using an automated acoustic analysis of SYDBAT Repetition words has already shown promising results. Using this method alone, 88% of PNFA patients were identified from LPA and healthy control participants (Ballard et al., 2014). Importantly, however, not all PNFA patients demonstrate apraxia of speech. Therefore, identifying effective measures of receptive and expressive grammar to incorporate into assessments is also recommended. In distinguishing LPA cases from mild SD patients, results of another recent investigation suggest that the use of SYDBAT naming and repetition subtests together with tests of auditory short-term memory (such as sentence repetition and digit or word span) assists in distinguishing PPA subtypes (Leyton et al., 2014).

As a newly created instrument focused on language profiles seen close in time to diagnosis, the current study was limited in its ability to consider changes in language skills over time. The sensitivity of the SYDBAT to capture this across each of the PPA groups thus requires longitudinal study. Additional normative and psychometric evaluation in a larger sample of patients and healthy controls will also assist clinical practice.

At present, the SYDBAT is freely available from the FRONTIER website (http://www.neura.edu.au/frontier) for use by clinicians and researchers, and has been downloaded across more than 20 countries.

8.2. WORD RETRAINING IN SD

Previous studies have demonstrated the ability for SD patients to improve their picture naming ability in response to repeated practice. Few studies, however, have focused on refining training methodology or demonstrating whether such improvements provide a real benefit to everyday living. Evidence of real benefits may include either demonstrating the translation of these naming improvements into other contexts or the sustainability of results over time. The studies presented in Chapters 4, 5 and 6 addressed these key issues, across participants ranging in disease severity from mild to severe semantic deficits.

Summary of results

Prior studies have suggested that effective methods in word retraining combine semantic and phonological processing, focus on personally relevant items, and can be completed either in the clinic or at home. The study in Chapter 4 further refined these methods, finding that a simple but intense home practice, which pairs the picture and word using the Look, Listen, Repeat (LLR) approach, produced significant naming improvements in SD patients with a range of semantic deficits. While 3 weeks appeared sufficient for significant improvements to occur, longer practice (6 weeks) assisted maintenance over time. The use of more elaborate combinations of pictures, words and autobiographical descriptions of items, with or without the addition of an active practice of sentence generation, while also effective, did not clearly produce superior results at follow up. SD patients with severe semantic impairments exhibited the largest effect sizes.

The online version of the program, developed for the studies in Chapters 5 and 6, used the same simple LLR practice but was modified to promote active retrieval during training. Sessions included two passive repetitions of the picture-word pairs, with the third exposure requiring participants to produce the word when shown the picture alone. This method proved highly effective, with significant improvements in naming demonstrated by each of the 11 participants involved across these two studies. The majority of participants gained more than 80% of the words unable to be correctly retrieved at baseline, regardless of having mild, moderate or severe semantic deficits.

Having established simple yet effective methods in Chapter 4, the study in Chapter 5 showed significant improvements can extend beyond the direct training context, when recalling and understanding trained words in other language tasks, . As expected, this transfer of performance gains was greatest on tasks which more closely resembled the training format (i.e., producing the name of items in the video description task). Transfer, however, was not limited to this, with increased ability also to comprehend the words, requiring knowledge to be adapted (i.e., from naming a picture) to different situations (following verbal instructions or matching a spoken word to the correct picture). Although generalisation of improvements for trained words was not demonstrated for every word, impressively, the degree of improvement on the generalisation measures was similar in magnitude to improvements on the direct training measures for some patients. With increasing severity of disease this level of transfer was reduced. As expected, a repeated finding across the studies (Chapters 4-6) was that untrained words did not significantly improve.

Finally, the longevity of training benefits was examined. As observed in previous studies, maintenance of trained words over time varied across participants. In Chapter 4, both patients in Study 1 and SD4 from Study 2 suffered significant losses within the first month for words trained for 3 weeks only. Non-significant declines were observed however if longer periods of practice were provided. In Chapter 6, the maintenance of training improvements was monitored for 9 participants following a 4-week program. Importantly, this study identified levels of revision that allowed a high level of naming accuracy to be maintained, with three different patterns of performance emerging over a 6-month period. For milder SD participants, picture naming accuracy generally remained at or above 80% in the absence of any additional training. For moderate SD participants, within 2 months significant declines appeared but performance could be raised back to at least 80% accuracy by undertaking a small number (less than 10) of revision training sessions. Finally, for severe SD participants, without regular, weekly practice, sharp declines in accuracy were observed within a few weeks of ceasing the initial intense training. Over the 6-month period at a group level, words initially retrieved at baseline that were not practised suffered mild declines. At an individual level, significant declines in these words occurred when semantic impairments were severe.

Implications for word retraining methods

The results of Chapters 4, 5 and 6 have important and direct implications for the development of cost effective, practical therapy programs which may be delivered to a wide range of SD patients. Significant improvements were obtained by a program run within the patients' home, thereby maximising accessibility for patients and minimising travel requirements, clinician time and expense.

The repeated finding that the simple combination of presenting the picture and word was sufficient for highly significant improvements is important. While previous studies have similarly shown that these elements assist in the ability to later recall these words, the relative benefit of including additional components, such as personalised descriptions which draw upon autobiographical memory or allude to a variety of properties of the object (as described by Snowden and Neary, 2002; Jokel et al., 2006 or Heredia et al., 2009) has not previously been tested across participants. The current results indicate that when at least some semantic knowledge of the object remains, accompanying descriptions are not required in order to improve the recall of object names. This is important as the incorporation of these descriptions can be time consuming for the clinician setting up the program, and in some cases difficult to achieve when selected vocabulary does not carry unique, memorable associations (e.g., describing a fork). If retraining is required for objects where the underlying concept is significantly eroded, then alternative approaches may be preferable, as suggested in a recent case study (Suárez-González et al., 2014). Prior to commencing retraining, an assessment of conceptual knowledge for each item should be undertaken, to identify items where sufficient residual knowledge exists to support basic retraining versus items where intense clinician-based conceptual enriched practice may be needed.

With regard to length of training, the results suggest that implementing intense programs of 3-4 weeks should allow significant naming improvements to occur in a wide range of SD patients. For participants with milder disease (e.g., SD3 from Chapter 4, and 4 participants from Chapter 6), a 3-4 week period allowed words to be fully acquired and potentially 'over-learned'; for patients with more severe deficits, 3 weeks resulted in significant improvements in naming but extending this period up to 6 weeks provided further opportunity to maximise the number of words recalled. Reviewing progress at 3 weeks may prove a useful time point for clinicians to determine whether patients should continue practice on the current list or commence a new list of words.

The current series also provided results that contribute to the methodological debate regarding errorless and effortful learning. Both the sentence generation activity in Chapter 4 (where the word and a model sentence were provided, but the participant was still required to generate another example) and the short quizzes of trained items immediately following the two presentations of items in Chapters 5 and 6, afforded the opportunity for active learning while still minimising errors. Even for patients with severe impairments both types of active practice were possible and high levels of attainment were observed. When comparing LLR only with LLR plus sentence generation, participants demonstrated slightly higher learning with the combined practice. However, similar to other studies investigating active methods, while initial learning may have been enhanced, no clear evidence was found that the use of effortful, active methods resulted in greater maintenance. Despite this, additional advantages to incorporating these methods may exist, particularly in the case of milder SD patients, where the frequent, repeated passive exposure of words already relearned may be unstimulating.

From a theoretical perspective, the improvements in naming observed in this patient group may arise as a result of two key mechanisms. Firstly, for those patients in a milder stage of the disease, words may still be recognised when read or spoken by another person, but are not successfully accessed when the person attempts to recall the name themselves. For these patients, the difficulties experienced in retrieving object names on demand may primarily reflect weakened links between degrading conceptual knowledge of the object and the word form which still exists within the person's lexicon. Word retraining in this context provides reinforcement to this existing knowledge through the facilitation effect of repetition in reducing the threshold required to access the word next time.

With disease progression, however, the further degradation of semantics impacts upon the integrity of word forms such that the vocabulary of the person is eroded. In this case the restoration of object names within a short timeframe remains consistent with the Complementary Learning Systems model of memory (McClelland et al., 1995), which predicts that initial learning of arbitrary associations (word label and object) can occur rapidly due to relative preservation of the hippocampus. This model also predicts the need for continued rehearsal of information over time, given that consolidation is weakened by the progressive temporal neocortical atrophy. This could explain the finding of relatively equivalent retention rates at follow up when comparing LLR only with LLR plus sentence generation methods (as decay in learning may occur under both methods in the absence of practice). The importance of ongoing practice is discussed within the next section.

Practical benefits of word retraining – can SD patients 'use it' and 'not lose it'?

The results of Chapters 5 and 6 provide important assurance that the words re-gained through word retraining can be used and that benefits may be retained over time. This was in the context of a training method that varied the order of item presentation, and focused on items where some conceptual knowledge remained (thereby stimulating existing representations).

Firstly, with respect to generalisation of training effects, it was noteworthy that participants were able to apply their knowledge of retrained words not only across different kinds of task but also associate the word with a version of the item that did not always closely resemble the picture used in training (or in the case of Household Requests, did not involve a picture at all). Importantly, tasks used in this study approximated everyday living scenarios, in describing or completing everyday actions in the home, thereby providing for the first time empirical support for the anecdotal observations made that participants make use of trained words in daily life (e.g., recalling flower names in the garden - Jokel & Anderson, 2012; ordering a muffin by name at the coffee shop - Jokel et al., 2010). These finding therefore provide an important foundation to support the continued development of remediation approaches in SD in light of the positive, and functionally relevant implications.

Generalisation of training was not, however, complete, and was demonstrated in different ways according to disease severity. These results corroborate current theoretical debate regarding generalisation and the role of the anterior temporal lobes. The integrity of these structures is thought to play a significant role in successful generalisation (Lambon Ralph & Patterson, 2008), acting as a "hub" for integrating information (Patterson et al., 2007). In Chapter 5, a closer correspondence of treatment and generalisation effects was seen for patients with unilateral, left ATL atrophy (i.e., SD-G1, SD-J2), than for those with pronounced bilateral atrophy (i.e., SD-T4, SD-J5). This suggests that earlier on patients may show a greater ability to generalise but that as the disease progresses to encompass more of the anterior temporal lobes bilaterally generalisation may become restricted.

The results from Chapter 6 provide important evidence that the improvements in naming achieved through word retraining can be sustained by SD patients over time. Further, while the majority of participants required some level of revision practice to accomplish this, the process never involved the same level of intensity as during the training period. These results have direct implications for clinical practice, providing necessary evidence to support the value of undertaking such therapies in the context of a progressive condition. In addition, results provide guidance regarding the crucial time points at which to review and recommence retraining programs, and give an indication of the time commitments required by patients and clinicians to maintain performance at various severity levels. In particular, performance at 2 months post-intervention appears to be a useful indicator of the frequency of revision that will be required for sustained maintenance - implying that this is a key time point for clinicians to monitor and then formulate the revision program for patients with mild to moderate semantic impairment. For patients already identified as having severe semantic impairments, however, continued weekly intervention is recommended after the initial 3-4 week practice given the likelihood of fast declines. For milder patients, explicit retraining of words may not be required for up to 6 months or more, although regular retrieval practice in the form of short quizzes may be assistive.

The finding that known words left unpractised may decay also has important implications for practice. This was first demonstrated in Chapter 5 for two participants where declines in performing the generalisation tasks were found for untrained items, but was clearly shown in Chapter 6. Overall, these results indicate a benefit of practising words that can still successfully be retrieved to protect these words from degrading, particularly in more severe patients. As a result, key words in everyday living that can still be named should be considered both when initially selecting words to include in the program, and at subsequent review points where additional items may be added. Words which are seasonal in nature (e.g., specific types of fresh food, types of clothing) may be particularly good candidates as there may be periods of time when everyday life experience does not provide additional support for the ongoing maintenance of these words.

Individual variables influencing word retraining outcomes

Given the rarity of the disease, a continuing difficulty in all studies of word retraining in SD is the relatively small number of participants involved, limiting the ability to identify and investigate differences among subgroups of patients. As the largest series of patients investigated to date, this thesis began exploring some potentially contributing factors for treatment success.

Disease severity - Across the three word retraining studies in this thesis (Chapters 4-6), 14 different participants each demonstrated significant improvements in naming as a result of training. This most likely reflects the similar level of preservation in other supporting cognitive skills such as everyday memory and attention. While significant improvements in naming were consistently achieved, as discussed in the previous sections, the degree of semantic deficit did impact upon how flexibly the words could be generalised and how quickly improvements faded without additional practice to support retention. As a result, it is important for prospective patients and families looking to undertake retraining to understand both how this intervention may assist and be limited by disease stage. The results, however, provide a convincing argument that word retraining should be considered for SD patients with mild through to severe semantic impairments.

Other demographic and clinical factors – Although demographic variables such as age and education are commonly associated with performance on cognitive measures, no significant relationships among treatment outcomes (ability to improve and independent maintenance) and age, education level or gender were found when results of nine participants were analysed (Chapter 6). A strong and significant relationship did, however, emerge between ability to improve and executive function, in keeping with the theory that successful word retrieval depends upon both semantic memory and semantic control (Jefferies & Lambon Ralph, 2006). While replication in a larger group of patients is required, these results suggest that executive function may prove a useful predictor of patients most likely to benefit and deserves further exploration.

Although not systematically examined in the current thesis, other variables relating to psychological distress may also play a role in degree of treatment success. As noted in Chapter 5, some variability in performance of severe SD patients may have arisen as a result of mood disturbances (e.g., SD-J3). Unlike behavioural variant FTD patients, those with SD can be prone to depression (Medina & Weintraub, 2007; Thompson, Patterson, & Hodges, 2003). Although other participants in the program also suffered from low mood or anxiety and continued to perform well (e.g., SD-J2, SD-S1), future studies should aim to investigate this further.

8.3. LANGUAGE INSIGHT AWARENESS IN PPA

Summary of results

Finally, the study in Chapter 7 investigated levels of awareness regarding language deficits in patients with SD as compared to other patients with progressive language disorders. Although awareness of deficits can impact rehabilitation outcomes in other groups, such as in Alzheimer's Disease (Clare et al., 2004), no detailed studies have investigated how aware SD patients are regarding their language problems. Using novel, experimental tasks, results of this thesis showed that while SD patients could correctly identify that their language performance was impoverished, they had difficulty evaluating language content, and made errors regarding their past knowledge of words. Patients with mild to moderate semantic impairments showed a tendency to make gross mislabelling errors when naming components of objects, for which they showed no awareness. The errors made by patients with more severe semantic impairments extended to include poor recognition of words known in the past and a failure to realise that certain specific words even existed. Nonfluent PPA patients, by comparison, did not show these difficulties in judgement.

Implications of level of language awareness on word retraining

Although previous research has suggested that SD patients are aware of their language difficulties, such investigations have relied on questionnaires asking broad questions ill-suited to detecting subtle reductions in awareness. From the results of the current study it was possible to demonstrate for the first time both the broad awareness SD patients hold regarding their difficulties with words, but also the limitations of this – with examples of impaired judgement of language content and errors regarding past ability. This confirms the generally held perception that patients with SD recognise that they are having problems with their language, which can be an important motivating factor in seeking help. Due to the degrading semantic store, however, it can be difficult for patients with SD to identify specific problems in their language, which has implications regarding their role and input into rehabilitation planning. While SD patients should contribute to the process of selecting words for retraining, to ensure a full range of appropriate words are selected, programs should not be based on patient judgement alone, but ideally involve family members or other informants familiar with the range of vocabulary that would be important for the individual with SD. It is important to note, however, that while at a group level these impairments in judgement were evident, not all SD patients were poor at evaluating language performance.

Limitations and future directions for investigating language awareness

Given the variability in responses in both patient groups, larger sample sizes are needed in future studies to explore language awareness. Severe SD patients showed a greater range of impairments in language awareness than mild to moderate SD patients. As the study was cross-sectional, however, longitudinal studies will be required to understand how self-perceptions of language ability may change with disease progression. Finally, while comparisons in insight were made between SD patients and nonfluent PPA patients, as LPA patients can develop semantic impairments over time, future studies wishing to examine the relationship between semantic memory and anosognosia may need to include all three groups.

8.4. CONCLUDING REMARKS

Currently no cures exist for progressive language diseases such as Semantic Dementia. The results of this thesis, however, provide clinicians with tools to both efficiently diagnose and treat language impairments in this patient group. By engaging in a simple word training program, SD patients with various levels of semantic impairment were able to improve their word production. Importantly, the results of this work show clearly for the first time that not only can improvements in word retrieval and recall occur within a few weeks, but that these improvements in naming can extend and be demonstrated on tasks resembling everyday living scenarios. Moreover, the improvements can be retained, even for patients with severe semantic impairments if regular but less intense practice is continued. These results have direct relevance for clinical practice and highlight that patients with severe semantic impairments should not be overlooked when considering word retraining programs. The results also bring some hope to patients and families of dementia sufferers, by demonstrating that positive change is still possible. Overall, this thesis contributes to improved methods and understanding of word retraining. Future research will be important in both refining techniques and expanding the range of materials that can be retrained in this debilitating disorder.

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APPENDICES

APPENDIX 1 – LITERATURE REVIEW SUMMARY TABLE

Table A. 1: Word retrieval intervention studies in SD (ordered chronologically)

Authors	Patients	Training Method	Stimuli	Length of treatment	Outcome measures	Results
Funnell, 1995	Mrs P	Location: Home-based Procedure: Repeated presentation of vegetables with spoken word. Selected reminding for unknown items, repeated up to 10 times in different orders. Self-practice by studying names and descriptions of items with the vegetables	6 vegetables (partial knowledge retained) 13 other vegetables untrained (7 known, common, 6 unknown and uncommon) Self-study materials with the written names and descriptions of items	1 session with the clinician, then self-study for 1 week	Accuracy in naming objects Generalisation measure of naming untrained items	Immediate: named all 6 treated items. Maintenance: Good retention over 2-3 months. 8 months post could only name 3 vegetables (50% retention). Generalisation: No improvement on untrained items and forgot 5 of the previously known, untrained items.
Graham et al., 1999; Graham et al., 2001	DM	Location: Home-based Procedure: Repeated study of pictures with the written word, rehearsal with actual objects, and study of self-generated lists of items recorded in a notebook. Items usually grouped within semantic categories.	Colour pictures in the Oxford Picture Dictionary or actual objects. 2 training sets of 100 items across 6 categories (4 target categories of interest and 2 foil categories). Training stimuli also included a notebook of self-generated lists	30 mins/ day for 4 weeks in total Each set of 6 categories practised for 2 weeks	Category fluency Generalisation measured by Pyramids and Palm trees Test (PPT) and category fluency for untrained categories	Immediate: Clear improvement (e.g., for Set 1: >30 extra words) Maintenance: significant drops 2 weeks later for Set 1 (approx. 33% of new items lost); after 8 weeks 56% retained. Some benefit compared with baseline. Improvements re-appear once practice is resumed. Generalisation: No change on PPT. Evidence of rote learning and DM did not understand meaning of all words produced.

Author	Patient	Training Method	Stimuli	Length of treatment	Outcome measures	Results
Snowden & Neary, 2002	KB	Location: Clinic-based. Procedure: Repeated exposure of picture and written word. Patient told to concentrate on each picture and read aloud the word. The name was then repeated to her. Errorless learning approach	20 line drawings in a training booklet, with the picture on one side and the word on the adjacent page. Includes n = 10 partially known items & n = 10 unknown items (all unable to be named prior to training)	2 therapy sessions involving 3 trials each, 14 days apart	Accuracy in naming pictures	Immediate: 30% accuracy after initial 3 trials, up to 60% accuracy after a further 3 trials (12 words gained) Maintenance: good over a 2-week interval but 4 months post performance dropped to 10% accuracy (2 words maintained). Better learning for items where there was residual knowledge.
Snowden & Neary, 2002	CR	Location: Home-based, following an initial session with the clinician. Procedure: Initial session - picture is presented, patient reads the word aloud, then listens to personalised autobiographical cues. At home, repeated exposure of picture and written word. Patient concentrates on each picture and reads aloud the word. Descriptive information re-provided on request. Errorless learning approach	20 line drawings in a training booklet (all items unable to be named prior to training and all where no semantic knowledge) Autobiographic cues for items provided by her husband	1 session with the clinician, then self-study 20 mins/day for 19 days. Some self-initiated revision of materials 2 days prior to 6 week follow-up, and the day before the 6-month follow up	Accuracy in naming pictures. Generalisation of trained items tested by assessing the material in the reverse order used in training and then in random order on a blue background. Also tested definition to pictures and to spoken words	Immediate: At 20 days, all 20 items correct without cueing. Maintenance: 100% retained at 60 days if same or reverse order, 65% accuracy (13 words) at 6 months post if same order (100% if cued). Generalisation: 75% accuracy (15 words) when pictures randomised with blue background 6-weeks post; (40% accuracy- 8 words- at 6-month post). Definitions to pictures improved (0% to > 60% at immediate post, approx. 50% at 6 months post); Definitions to spoken words 60% accuracy at immediate-post.

Author	Patient	Training Method	Stimuli	Length of treatment	Outcome measures	Results
Jokel, Rochon, & Leonard, 2002, 2006	AK	Location: Home-based. Procedure: Repeated exposure of picture with the written word and a written personalised item description. Patient looks at the picture then reads the word and description aloud. Errorless learning approach	90 pictures trained, with label on back (n=30 could name and comprehend, n=30 unable to name but could comprehend, n=30 unable to name or comprehend) 90 pictures untrained (with same division as above)	30 mins x 6 days for each treatment set Total training = 3 weeks	Accuracy in naming pictures. Testing in different order to presentation Generalisation measured by naming untrained items	Immediate: Significant improvements (29 words learned; 48% available to learn). Maintenance: trained words retained better than untrained words (1 and 6 months post-treatment), but declines (45% of learned words maintained). Greater maintenance of words originally known and trained vs known but not trained (87% vs 73%; at 6 months: 80% vs 60%). Generalisation: no significant improvements on untrained words.
Frattali, 2004	1 case with SD	Location: Clinic-based. Procedure: Interactional discourse, errorless learning approach – conversational exchange with researcher to analyse features. Compare, associate, categorical sorting/grouping, reasoning, spatial and temporal analysis	40 photos: 20 nouns (2 categories), 20 verbs (2 categories) Another set of n=40 as control. Randomised order of presentation within categories and for order of category	12 x 2hr weekly sessions over 3 months (8 sessions for nouns, 4 sessions verbs)	Accuracy in naming Generalisation measured by naming untrained nouns and verbs	Immediate: some improvements for trained nouns during first intervention period (appeared to gain 8/20 items). For verbs, appeared to gain approx. 6 items out of 11 available to learn. Maintenance: largely lost after 3 month (approx. 5/14 items learned overall were maintained). Generalisation: No improvement on untrained words.

Author	Patient	Training Method	Stimuli	Length of treatment	Outcome measures	Results
Jokel, Cupit, Rochon, & Graham, 2007; Jokel, Rochon, & Anderson, 2010	CS	Location: Clinic-based. Procedure: Errorless learning using computer program. Presentation of the picture, a spoken and written description of the object, and the written word. Patient instructed to "Look, Listen, Repeat" (LLR). Each training item displayed for 20-25 seconds and presented twice within each treatment session	90 colour pictures from the MossTalk Words computer therapy programme. Trained on 3 lists of 30 items each (n=10 words already able to name, n=10 can't name but can comprehend, n=10 can't name or comprehend).	3 sessions/week Each list is trained for 12 sessions or until 80% accuracy achieved.	Accuracy in naming pictures Generalisation measures including Philadelphia Naming Test (PNT), category fluency, oral Sentence Production	Immediate: Improvements on all 3 lists (learned 41 words). Maintenance: good (80% of learned words retained at 1 month; 73% at 3 months). Maintenance better for words verbally comprehended, & for trained words known at baseline (100%) vs words originally known but not practised (9 words forgotten). Generalisation: improved verbal fluency (4 word increase) and naming of alternate pictures of trained items (PNT).
Henry et al., 2008a	PA2	Location: Clinic-based, with homework Procedure: Semantic treatment for strategic retrieval. Tasks of picture sorting, generating semantic attributes to exemplars, comparing/contrasting exemplars. Spoken production of target words also required.	3 categories of living things, 3 categories of nonliving things. Matched with control categories for the above	90 mins / day for 12 sessions over 16 days. Each category trained for 2 sessions before starting a new one.	Verbal fluency for treated categories Generalisation measures included verbal fluency of untreated categories, Boston Naming Test and Pyramid and Palm trees Test (PPT)	Immediate: significant ($p < .025$) but small effect ($d = 2.00$; average 3 words/category). A medium effect ($d = 7.00$) for the specific category of Dogs (improved by 7 words). Maintenance: poor (1 week post-treatment effect size = .25). Generalisation: No significant improvements, although a small change on PPT (score now within normal range).

Author	Patient	Training Method	Stimuli	Length of treatment	Outcome measures	Results
Bier et al., 2009	TBo	<u>Location</u>: Clinic-based. <u>Procedure:</u> Semantic feedback and graded cueing. Patient presented with the picture, spoken name, a specific attribute and written category name, then asked to recall the name and attribute. If incorrect, given feedback and cues (category name, specific attribute, phonemic cue, then full answer). Simple repetition (for n=4 words) and spaced retrieval methods (for n=4 words)	8 line drawings (parrot, owl, guitar, mushroom, peach, saxophone, bee, caterpillar) - name unknown and poor semantic knowledge Also 8 items untrained from same categories; 8 items untrained from other categories	6 intervention sessions 2 sessions/week	Accuracy in naming pictures and generation of verbal attributes. Tested in random order Generalisation measured by assessing untrained items and through letter fluency (where some treated words began with the same letter used in the letter fluency test)	<u>Immediate</u>: 3/8 correct by the end of intervention (vs 0 learned from untrained sets). Spaced retrieval not significantly better than repetition approach, although fewer errors were made with spaced retrieval. <u>Maintenance</u>: retained for 5 weeks. <u>Generalisation</u>: No improvement on untrained list. No trained words were produced either pre- or post-intervention on letter fluency.
Heredia et al., 2009	CUB	<u>Location</u>: Home-based <u>Procedure</u>: "Look and say" method. Computer presentation of picture and then picture and the written word. Patient instructed to read the word aloud. Same order of pictures used each day. Errorless learning approach	28 pictures from the Western Aphasia Battery and the EPLA/PALPA using Microsoft Powerpoint. A further 28 pictures used as a control, untrained set.	Daily for 4 weeks	Accuracy in naming pictures Generalisation measured by assessing naming of alternative versions of the trained items	<u>Immediate</u>: 100% accuracy for trained items (28 words learned) <u>Maintenance</u>: At 6-months, 82% (23 words) retained; trained words significantly better than untrained words. <u>Generalisation:</u> good naming of alternative versions of trained items (92% correct), but influenced by typicality of the image. Some rote learning effects observed.

Author	Patient	Training Method	Stimuli	Length of treatment	Outcome measures	Results
Newhart et al., 2009	1 case with SD	Location: Clinic-based. Procedure: 5 step cueing technique: spontaneous naming, written naming, notebook search, reading, repetition (and cued in reverse order)	80 pictured objects over 2 personally relevant categories – fruit and vegetables and clothing (20 typical, 20 atypical exemplars from each category) & a notebook provided with the written names or the objects, organised by category	30-60 min therapy session over 29 non-consecutive days (8-9 weeks not including weekends)	Accuracy in naming pictures Generalisation assessed using additional pre-post measures in oral naming, written naming, spelling, reading, reading comprehension, and repetition. These measures included untrained items from both trained and untrained categories	Immediate: Fruit and vegetable category improved from 55% to 95% accuracy for typical exemplars (8 words gained) and 0% to 60% for atypical exemplars (12 words gained); less clear for clothing category (from 0% to 20% accuracy). No statistical analysis. Maintenance: No follow up data. Generalisation: Declines in untrained categories. Less decline for untrained words in trained categories. A non-significant improvement in reading comprehension for the trained category fruit & vegetables.
Robinson et al., 2009	HD	Location: Clinic-based, with homework. Procedure: Errorless learning. Researcher models name, definition and use, and patient repeats. Presented 3 times / session. For daily self-practice, patient watches a DVD	17 household objects (kitchen utensils, stationery, tools) were trained 16 household objects as a control set	6 sessions with clinician (2/week x 3 weeks) Independent practice (10 minutes/day)	Accuracy in object naming, definition, and object use Generalisation measured by untrained items	Immediate: small, significant improvement in naming (6 words gained); qualitative improvements in object definition (more specific nouns used); significant improvement in the movement scale of object use. Maintenance: retained 1 month later Generalisation: No improvements.

Author	Patient	Technique	Stimuli	Length of treatment	Outcome measure	Results
Robinson et al., 2009	VH	Location: Clinic-based, with homework. Procedure: Errorless learning. Researcher models name, definition and use, and patient repeats. Presented 3 times / session. For daily self-practice, patient watches a DVD	17 household objects were trained 16 household objects as a control set	6 sessions with clinician (2/week x 3 weeks) Independent practice (10 minutes/day)	Accuracy in object naming, description of object function, and demonstration of object use Generalisation measured by untrained items	Immediate: No improvement in naming. Some improvement in definitions found for both trained and untrained objects. Significant improvements in holding and orienting the objects. Maintenance: no improvement at immediate-post to maintain. Generalisation: No improvement on untrained items.
Dressel et al., 2010	BF	Location: Clinic-based. Procedure: Cued by therapist List 1: lexical-phonological approach - cues involve clapping syllables, first sound, providing the word List 2: lexical-semantic access approach - cues involve superordinate label, definition, semantic phrase, then providing the word	60 line drawings of nouns, divided into 2 training lists (n=30); An addition 30 line drawings as a control list	Daily for 4 weeks. 5 sessions (20 mins), each block for 1 wk. Each item trained in 2 sessions; presented 6 times/session (i.e. 12 treatments /item)	Accuracy in naming pictures Generalisation measured by naming of untrained items	Immediate: significant improvements from baseline for both approaches (15-17 words gained); trained words significantly better than control list. Some evidence of greater effect for semantic access training. Maintenance: after 2 months: trained items significantly better than at baseline (by 7-8 words) but no advantage of approach; not significantly better than control items. Generalisation: no improvement on untreated items.

Author	Patient	Technique	Stimuli	Length of treatment	Outcome measure	Results
Senaha et al., 2010	Case 1	Location: Clinic-based, with homework. Procedure: Errorless learning using vanishing cues, conducted with the researcher. Also daily self-training with study cards	119 study cards constructed for personally relevant items Study cards comprise photos, descriptions or figures on one side, and cues on the other side	Session with researcher 1-2 times/week over 14 months Daily self-training.	Accuracy in naming pictures (with phonemic cueing if needed). Generalisation measured using Boston Naming Test	Immediate: Performance on treated items increased, but only modestly without cueing (29% accuracy; approx.. 34 words gained). No statistical analysis reported. Maintenance: Not measured. Generalisation: Declines observed in non-treated items from pre- to post-intervention.
Senaha et al., 2010	Case 2	Location: Clinic-based, with homework. Procedure: Errorless learning using vanishing cues, conducted with the researcher.	87 study cards constructed for personally relevant items Study cards comprise photos, descriptions or figures on one side, and cues on the other side	Session with researcher 1-2 times/week over 18 months.	Accuracy in naming pictures (with phonemic cueing if needed). Generalisation measured using Boston Naming Test	Immediate: improvements on treated items (53% accuracy without cueing; approx. 46 words gained) at the post-intervention assessment. No statistical analysis reported. Maintenance: Not measured. Generalisation: Declines observed in non-treated items from pre- to post-intervention.

Author	Patient	Technique	Stimuli	Length of treatment	Outcome measure	Results
Senaha et al., 2010	Case 3	<u>Location</u>: Clinic-based, with homework. <u>Procedure:</u> Errorless learning using vanishing cues, conducted with the researcher. Also daily self-training with study cards	65 study cards constructed for personally relevant items Study cards comprise photos, descriptions or figures on one side, and cues on the other side	Session with researcher 1-2 times/week over 6 months Daily self-training.	Accuracy in naming pictures (with phonemic cueing if needed). Generalisation measured using Boston Naming Test	<u>Immediate</u> Treated items increased up to 100% accuracy without cueing (65 words gained). <u>Maintenance</u>: Not measured. <u>Generalisation</u>: Declines observed in non-treated items from pre- to post-intervention.
Mayberry et al., 2011	NH	<u>Location:</u> Home-based but under the direction of the researcher each session. <u>Procedure:</u> Repeated exposure of photograph and written word. Patient told to look at the photograph, try to name it, then turn the page to view both the photograph and written word and read aloud the answer.	30 colour photographs arranged in a training booklet.	15 sessions (5 days/week for 3 weeks) Initial session face to face by the researcher, with subsequent sessions conducted over the phone	Accuracy in naming pictures. Generalisation measures of naming alternative photographs of trained items, and naming associated items	<u>Immediate</u>: Significant improvements (100% correct, 19 words gained). <u>Maintenance:</u> full retention at 1-month follow up (100% correct). <u>Generalisation</u>: No significant improvement in naming alternative photographs of trained items, or associated items.

Author	Patient	Technique	Stimuli	Length of treatment	Outcome measure	Results
Mayberry et al., 2011	GE	Location: Home-based but under the direction of the researcher each session. Procedure: Repeated exposure of photograph and written word. Patient told to look at the photograph, try to name it, then turn the page to view both the photograph and written word and read aloud the answer.	30 colour photographs arranged in a training booklet.	15 sessions (5 days /week for 3 weeks) Initial session face to face by the researcher, with subsequent sessions conducted over the phone	Accuracy in naming pictures. Generalisation measures of naming alternative photographs of trained items, and naming associated items	Immediate: Significant improvements (97% correct; 24 words gained). Maintenance: maintained performance (97% correct) after 1 month; also maintained performance on naming the alternative photograph. Generalisation: Significant improvements naming alternative photographs of trained items, but at reduced level (43% correct).
Villanelli et al., 2011	Marian	Location: Clinic-based. Procedure: Phase 1 - Phonemic and semantic cues, verbal description of the object, multi-sensory stimulation, implicit memory techniques (vanishing cues forward and spaced retrieval). Phase 2 - 14 photos of relatives and their names, using the same techniques as in Phase 1. Home practice also included	Phase 1 - n = 10 images of vegetables and fruit trained; n= 10 images untrained Phase 2 - n=14 photographs of relatives	Phase 1 - 2 x 45 min session/ week for 2 months Phase 2 - 2 x 45 min session/ week for 2 months plus daily home practice	Accuracy in picture naming (performance of trained items vs untrained items) Generalisation not measured – untrained set used for the purpose of measuring against the trained items to indicate treatment effect	Immediate: Phase 1 - from a baseline of zero, a slight improvement for trained items (3/10 correct without cueing), but same level of improvement seen for untrained items. Phase 2 - improvement at the end of treatment (8/14 relatives named). Maintenance: Phase 1 - not maintained at 6 months (1/10 trained now correct); Phase 2 - maintenance reported (11/14 relatives named).

Author	Patient	Technique	Stimuli	Length of treatment	Outcome measure	Results
Jokel & Anderson, 2012	P1 P2 P3 P4 P5 P6 P7	Location: Clinic-based. Procedure: Presentation of a picture with a cueing hierarchy, and repetition of the target word. 4 methods: • EL-P: errorless passive – all cues and name provided by the researcher • EL-A: errorless, active – successive Y/N questions asked by researcher • EF-P: errorful passive - researcher provides erroneous names and cues. • EF-A: errorful active – researcher asks open-ended questions as cues.	120 pictures from Peabody Pictures set. Each training approach n=30 words (divided to include 15 items where auditory recognition of the word is spared and 15 where it is not)	12 x 30 minute sessions with the researcher for each training set of 15 items 2 sessions/day, 2-3 times per week. Completed over 24 different days, within a 8-12 week period	Accuracy in naming pictures, accuracy in auditory comprehension/recognition. Generalisation measures included Philadelphia Naming Test, Oral Sentence Production test, connected speech measure, Peabody Picture Vocabulary Test-III, verbal fluency and semantic association tests	Immediate: Significant improvements in naming across the 12 sessions. Best results using the errorless learning approach (up to 70% correct; approx. 21 words gained) vs errorful approach (up to 50% correct; approx. 15 words gained). Better learning if auditory recognition intact (up to 70% correct vs 40% correct). At a group level, recognition/comprehension of treated items improved to a similar extent across all four treatment methods. Maintenance: significant retention reported at 1 and 3 months, although declines evident (performance halved by 3 months). At a group level, maintenance at 1-month appeared to be greater for errorless learning, but did not remain more effective after 3 months. Generalisation: Marginal evidence of improvements in picture naming (in PNT) at a group level. A small improvement in semantic fluency (for an untrained category).

Author	Patient	Technique	Stimuli	Length of treatment	Outcome measure	Results
Farrajota et al., 2012	2 patients with SD (as part of a group of n=10 PPA patients)	Location: Clinic-based. Procedure: Individualised multimodality stimulation approach with speech therapist (picture naming, description of picture actions, reading & writing, verbal comprehension, description & organisation of sequences). Homework includes 5–10 exercises	Adapted to each case. Not described in detail	1hr/week therapy for 11 months	Accuracy in naming pictures - Snodgrass and Vanderwart test (128 black and white picture drawings)	Immediate: No separate results provided for the SD patients. A significant overall group effect was reported, indicating better naming performance for the treated group versus an untreated group.
Henry et al., 2013	SV	Location: Clinic-based, with homework Procedure: Lexical Retrieval Cascade (LRC): Picture presented with self-cueing hierarchy: semantic, orthographic, phonemic. If needed, written word shown & spoken model provided Generative naming (GN): as above + identifying semantic features and recounting personal experiences. Homework includes sorting, creating semantic "maps"	LRC: 20 imageable, low frequency items, named incorrectly prior to treatment (but semantic knowledge remained). Divided into 4 training sets of n=5 items GN: photos of items in trained semantic categories	LRC: 1 hr x 2/week for 4 weeks with the clinician 30 min x 5 days/week in homework GN: 2hrs x 5/week for 2.5 weeks 1 x 12 hrs homework	LRC: Accuracy in naming pictures Generalisation measures included Boston Naming Test (BNT) and object naming from the Western Aphasia Battery GN: category fluency Generalisation measures fluency for untrained categories	Immediate: LRC - significant improvements with moderate effect size d = 7.22. GN – significant increase in items generated from trained categories (approx. 4 extra words) Maintenance: LRC - well maintained at 1-month (90%) and 4 months (100%). GN – well maintained 1 and 3 months later. Generalisation: some improvements on untrained items/categories; improvement on BNT after GN treatment. Now within normal range on Pyramids & Palm trees Test.

Author	Patient	Technique	Stimuli	Length of treatment	Outcome measure	Results
Suárez-González et al., 2014	VC	Location: Home-based, with researcher available for clarification over the phone. Procedure: Standard retrieval therapy – "look and say" method. Patient looks at each picture, is asked to give the word, turns the page to see the word. Brief description of item provided at first session Conceptual Enrichment Therapy (COEN)- Patient looks at target picture, then training slide with additional pictures and written label. Brief description of the training slide explaining the items provided at first session	Standard treatment: 101 simple line drawings and label (104 additional line drawings left untrained) COEN: 88 training slides each containing a target picture with associated pictures, and label (90 additional pictures left untrained) All items unable to name or comprehend prior to treatment	Each therapy: 30 mins/day for 3 months	Accuracy in naming pictures Generalisation measures of naming alternative pictures, description to naming and naming to description tasks	Immediate: Significant improvements in naming were found for both therapy approaches (84% improvement for Standard treatment –85 words gained; 82% improvement for COEN –73 words gained). Maintenance: not measured. Generalisation: No improvements for untrained items. Good ability to name visually dissimilar pictures (79%, 90%). Some evidence of greater generalisation for trained items across tasks under COEN therapy for all three generalisation tasks.

Author	Patient	Technique	Stimuli	Length of treatment	Outcome measure	Results
Macoir et al., 2014	NG	Location: Clinic-based Procedure: Patient watches video and is asked to name the verb. Feedback and cues given: sentence where verb would be the last word, phonological cue, spoken word to repeat	37 x 5 second videos depicting actions presented on a laptop computer for cued therapy Additional 37 videos for uncued exposure; 37 videos completely untrained	12 sessions 2/week x 5 weeks then 1/week x 2 weeks	Accuracy in naming actions in videos Generalisation measured by naming of untrained items	Immediate: Significant improvements in verb naming - improved by 40% on cued list, small-medium effect size: d = 4.74 (approx. 15 words gained). Maintenance: good retention 2 and 4 weeks later (97% accuracy). Generalisation: no significant improvement for uncued or control verbs.

APPENDIX 2 – LIST OF SYDBAT ITEMS

Table A. 2: SYDBAT item list and mean word frequency per block

	Block 1 - Easy	**Block 2 - Medium**	**Block 3 - Hard**
Item	Banana	Caterpillar	Rhinoceros
	Butterfly	Cauliflower	Stethoscope
	Computer	Screwdriver	Hippopotamus
	Potato	Dinosaur	Chandelier
	Bicycle	Thermometer	Tiara
	Cigarette	Escalator	Secateurs
	Elephant	Shuttlecock	Hieroglyphics
	Radio	Asparagus	Balaclava
	Envelope	Leotard	Orangutan
	Battery	Dandelion	Pagoda
Mean SMH occurrences (per million words)*	905.9	35.5	9.2

** The Sydney Morning Herald Word Database. Noetica: Open Forum 1, 1995 (http://psy.uq.edu.au/CogPsych/Noetica)*

APPENDIX 3 – SYDBAT REPETITION SCORING

Score correct if:

- all syllables are correctly pronounced and are done so without pauses between syllables/uneven delivery of syllables in a word, distortion in phonemes or clusters (e.g., “fl” or “gl”), restarting due to articulation problems (indicating laboured speech e.g., stuttering on the first sound, self-corrected sounds);
- the examinee adds an “-s” to the end of the word or leaves off an “-s” at the end of the word;
- the examinee’s response is another common pronunciation of the word, as long as the response still conforms to the above rules;
- there are minor variations due to accent in examinees who have English as a second language (e.g., hippopotamus = ‘ippopotamus).

Score incorrect if:

- the examinee cannot say the word;
- the examinee must re-start the word in order to say it correctly (e.g., stuttering over first phoneme);
- the examinee uses the wrong phoneme in the word (e.g., “dande-iron” for dandelion);
- the examinee clearly segments the word or says some syllables slowly and others in a rush (e.g., “hip-po-pot-a-mus”; or “hip-po-potamus”).

APPENDIX 4 – EXAMPLE WORD RETRAINING ITEMS

Table A. 3: Items included in the word retraining program for SD-G1

List allocation	Category	Word
1	Food or Drink	avocado
1	Food or Drink	lettuce
1	Food or Drink	apple
1	Food or Drink	butter
1	Food or Drink	cucumber
1	Food or Drink	onion
1	Food or Drink	peppers
1	Food or Drink	parsley
1	Food or Drink	potatoes
1	Food or Drink	tomato sauce
1	Food or Drink	eggs
1	Food or Drink	silver beet
1	Food or Drink	salt
1	Household appliances	dishwasher
1	Household appliances	remote control
1	Household appliances	television
1	Household appliances	toaster
1	Household appliances	oven
1	Kitchen items	chopping board
1	Kitchen items	fork
1	Kitchen items	gladwrap
1	Kitchen items	paper towel
1	Kitchen items	placemats
1	Kitchen items	teapot
1	Kitchen items	grater
1	Kitchen items	tongs
1	Kitchen items	potato masher
1	Outdoor items/ Tools	broom
1	Outdoor items/ Tools	lawn mower
1	Outdoor items/ Tools	leaf blower
1	Outdoor items/ Tools	paintbrush
1	Outdoor items/ Tools	nail

List allocation	Category	Word
2	Food or Drink	bread
2	Food or Drink	teabag
2	Food or Drink	mayonnaise
2	Food or Drink	pear
2	Food or Drink	sausages
2	Food or Drink	tomatoes
2	Food or Drink	broccoli
2	Food or Drink	cheese
2	Food or Drink	orange
2	Food or Drink	grapes
2	Food or Drink	sugar
2	Food or Drink	jam
2	Household appliances	Heat pump
2	Household appliances	computer
2	Household appliances	cooktop or stove
2	Household appliances	sink
2	Household appliances	telephone
2	Household appliances	fan
2	Kitchen items	bowl
2	Kitchen items	dish cloth
2	Kitchen items	potato peeler
2	Kitchen items	saucepan
2	Kitchen items	wine glass
2	Kitchen items	aluminium foil
2	Kitchen items	casserole dish
2	Kitchen items	spatula
2	Kitchen items	colander
2	Outdoor items/ Tools	measuring tape
2	Outdoor items/ Tools	screwdriver
2	Outdoor items/ Tools	secateurs
2	Outdoor items/ Tools	pliers
2	Outdoor items/ Tools	shifting spanners

List allocation	Category	Word
3	Food or Drink	milk
3	Food or Drink	olive oil
3	Food or Drink	carrot
3	Food or Drink	raisins
3	Food or Drink	corn
3	Food or Drink	mandarin
3	Food or Drink	mint
3	Food or Drink	mushrooms
3	Food or Drink	strawberries
3	Food or Drink	juice
3	Food or Drink	steak
3	Food or Drink	leeks
3	Household appliances	jug
3	Household appliances	microwave
3	Household appliances	refrigerator or fridge
3	Household appliances	iron
3	Household appliances	washing machine
3	Household appliances	barbecue
3	Kitchen items	coasters
3	Kitchen items	coffee cup or mug
3	Kitchen items	knife
3	Kitchen items	plate
3	Kitchen items	spoon
3	Kitchen items	can opener
3	Kitchen items	tea towel
3	Kitchen items	kitchen scales
3	Kitchen items	serviettes
3	Outdoor items/ Tools	edge trimmer
3	Outdoor items/ Tools	leaf rake
3	Outdoor items/ Tools	hammer
3	Outdoor items/ Tools	loppers
3	Outdoor items/ Tools	electric drill

.

APPENDIX 5 - WORD LIST CHARACTERISTICS

Table A. 4: Word list characteristics per participant

	n	Mean Word frequency (SUBTL-WF)	Kruskal-Wallis p	Mean Frequency of Use[a]	Kruskal-Wallis p	Baseline - Known[b]	Chi Squared p	Cochran Q p[c]
SD-G1			.633		.906		1.00	
List 1	32	10.4		2.25		13		.564
List 2	32	11.7		2.44		13		.414
List 3	32	11.5		2.44		13		.564
SD-J2			.635		.923		.572	
List 1	32	13.1		2.00		12		.819
List 2	31	12.6		2.13		11		1.000
List 3	36	14.1		2.15		17		.223
SD-J3			.221		.636		.375	
List 1	32	11.21		2.03		3		.174
List 2	10[d]	13.78		1.80		0		.368
List 3	55	18.65		1.95		8		.307

Abbreviations: SUBTL-WF = is the SUBTLEX word frequency per million words (Brysbaert & New, 2009)

[a] *Frequency of use scales where 1 = daily; 2 = several times per week; 3 = weekly; 4 = fortnightly; 5 = monthly; 6 = seasonally/less often.*

[b] *"Baseline known" was determined by performance over a series of assessments prior to commencing practice. An item was considered "known" if the correct word could be produced at least 67% of the time during the baseline phase. Numbers here indicate the total number of words classified as known.*

[c] *Cochran Q is used to assess baseline stability (p >.05). Based on weekly test results during the baseline period.*

[d] *Original design was for 32 items in List 2. Given significant mood issues and slower learning, during the first month of intervention, the lists were modified so that only 10 new words were introduced for List 2.*

	n	Mean Word frequency (SUBTL-WF)	Kruskal-Wallis p	Mean Frequency of Use[a]	Kruskal-Wallis p	Baseline - Known[b]	Chi Squared p	Cochran Q p[c]
SD-T4			.964		.427		.953	
List 1	33	25.7		1.62		7		1.00
List 2	33	17.3		1.69		8		.199
List 3	41	16.2		1.94		9		.307
SD-J5			.210		.533		.928	
List 1	23	36.2		1.24		6		1.000
List 2	21	21.5		1.27		6		.157
List 3	25	28.8		1.42		5		.414

Abbreviations: SUBTL-WF = is the SUBTLEX word frequency per million words (Brysbaert & New, 2009)

[a] *Frequency of use scales where 1 = daily; 2 = several times per week; 3 = weekly; 4 = fortnightly; 5 = monthly; 6 = seasonally/less often.*

[b] *"Baseline known" was determined by performance over a series of assessments prior to commencing practice. An item was considered "known" if the correct word could be produced at least 67% of the time during the baseline phase. Numbers here indicate the total number of words classified as known.*

[c] *Cochran Q is used to assess baseline stability (p >.05). Based on weekly test results during the baseline period.*

APPENDIX 6 – FULL DATA SETS FOR ONLINE WORD RETRAINING PARTICIPANTS

Table A.5: SD-G1 raw baseline naming data (% correct) by word list

	BL1	BL2	BL3	BL4	BL5	BL6	BL7	BL8	BL9	BL10
List 1 (n=32)	28	31	50	53	47	44	41	50	44	47
List 2 (n=32)	28	41	44	53	44	44	41	50	47	53
List 3 (n=32)	31	34	44	50	50	44	44	47	50	47

BL = Baseline assessment

Table A. 6: SD-G1 raw naming data (% correct) during treatment phase by word list:

	T1	T2	T3	T4	T5	T6	T7	T8
List 1 (n=32)	**69**	**84**	**100**	**97**	94	91	81	94
List 2 (n=32)	47	47	47	56	**66**	**88**	**97**	**94**
List 3 (n=32)	50	56	56	41	56	56	53	59

T = Treatment assessment week; Bolded results indicate the period during which training occurred

Table A. 7: SD-G1 raw naming data (% correct) post initial treatment phase

	P1	P3	P4	P5	P6	P7	P8	P10	P12	P13	P14	P15	P16	P20	P24
List 1 (n=32)	88	81	88	88	84	88	81	78	81	88	84	84	88	88	75
List 2 (n=32)	94	75	91	84	84	84	78	91	88	75	72	84	88	69	91
List 3 (n=32)	44	44	56	50	59	59	59	56	59	56	63	63	56	53	53

P = Post-treatment assessment week (e.g. P1 = 1 week after treatment end)

Table A. 8: SD-J2 raw baseline naming data (% correct) by word list

	B1	B2	B3	B4	B5	B6	B7	B8
List 1 (n=32)	31	28	47	25	50	47	53	50
List 2 (n=31)	29	23	42	48	45	48	45	45
List 3 (n=36)	33	47	53	53	53	56	61	53

BL = Baseline assessment

Table A. 9: SD-J2 raw naming data (% correct) during treatment phase by word list

	T1	T2	T3	T4	T5	T6	T7	T8
List 1 (n=32)	**84**	**94**	**97**	**100**	94	94	91	88
List 2 (n=31)	42	39	45	42	**77**	**90**	**97**	**94**
List 3 (n=36)	50	50	42	58	56	61	61	69

T = Treatment assessment week; Bolded results indicate the period during which training occurred

Table A. 10: SD-J2 raw naming data (% correct) post initial treatment phase

	P1	P2	P3	P4	P5	P6	P7	P8	P10	P12	P16	P20	P24
List 1 (n=32)	97	88	94	88	88	81	94	97	91	91	91	91	97
List 2 (n=31)	97	81	77	94	87	94	90	97	90	90	97	81	77
List 3 (n=36)	58	56	58	64	53	61	64	56	53	56	67	61	61

P = Post-treatment assessment week (e.g. P1 = 1 week after treatment end)

Table A. 11: SD-J3 raw baseline naming data (% correct) by word list

	BL1	BL2	BL3	BL4	BL5	BL6	BL7	BL8	BL9	BL10
List 1 (n=32)	16	9	13	19	13	19	16	16	9	9
List 2 (n=11)	18	0	0	18	9	9	0	0	9	0
List 3 (n=54)	19	13	13	19	17	28	26	19	24	26

BL = Baseline assessment

Table A. 12: SD-J3 raw naming data (% correct) during treatment phase by word list

	T1	T2	T3	T4	T5	T6	T7	T8
List 1 (n=32)	**28**	**47**	**50**	**83**	n/c	79	n/c	n/c
List 2 (n=11)	9	0	9	0	**n/c**	**27**	**n/c**	**n/c**
List 3 (n=54)	20	22	24	20	n/c	26	n/c	n/c

T = Treatment assessment week; n/c = assessment not completed; Bolded results indicate the period during which training occurred

Table A. 13: SD-T4 raw baseline naming data (% correct) by word list

	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10	B11	B12	B13	B14
List 1 (n=33)	15	15	24	27	21	21	21	21	24	24	33	27	30	24
List 2 (n=33)	24	27	27	27	21	24	21	24	24	24	18	24	24	27
List 3 (n=41)	17	20	27	24	20	24	24	22	27	24	32	29	24	34

BL = Baseline assessment

Table A. 14: SD-T4 raw naming data (% correct) during treatment phase by word list

	T1	T2	T3	T4	T5	T6	T7	T8
List 1 (n=33)	**52**	**67**	**82**	**94**	76	61	58	70
List 2 (n=33)	27	21	24	27	**36**	**48**	**55**	**82**
List 3 (n=41)	27	29	37	29	27	32	45	24

T = Treatment assessment week; Bolded results indicate the period during which training occurred

Table A. 15: SD-T4 raw naming data (% correct) post initial treatment phase

	P1	P2	P3	P4	P5	P6	P7-R	P8-R	P9-R	P10-R	P11-R	P12-R	P13-R	P15-R	P16-R	P17-R	P19-R	P22-R	P24-R
List 1 (n=33)	55	67	64	58	58	64	**61**	**76**	**82**	**73**	**79**	**82**	**76**	**82**	**85**	**88**	**94**	**94**	**94**
List 2 (n=33)	76	76	70	70	58	55	**73**	**70**	**76**	**73**	**79**	**76**	**79**	**70**	**73**	**73**	**88**	**79**	**85**
List 3 (n=41)	27	32	27	32	22	29	27	29	24	27	34	32	24	29	32	29	27	24	22

P = Post-treatment assessment week (e.g. P1 = 1 week after treatment end); R = Assessment week in which revision training had been provided; Bolded results indicate the period during which training occurred

Table A. 16: SD-J5 raw baseline naming data (% correct) by word list

	BL1	BL2	BL3	BL4
List 1 (n=33)	8	19	15	12
List 2 (n=33)	14	19	19	12
List 3 (n=41)	16	19	19	8

BL = Baseline assessment

Table A. 17: SD-J5 raw naming data (% correct) during treatment phase by word list

	T1	T2	T3	T4	T5	T6	T7	T8
List 1 (n=33)	**58**	**65**	**n/c**	**69**	77	n/c	65	77
List 2 (n=33)	8	12	n/c	19	**19**	**n/c**	**69**	**62**
List 3 (n=41)	19	15	n/c	23	15	n/c	8	23

T = Treatment assessment week; n/c = assessment not completed; Bolded results indicate the period during which training occurred

Table A. 18: SD-J1 raw baseline naming data (% correct) by word list

	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10	B11	B12
List 1 (n=30)	40	43	40	43	37	40	37	40	43	43	40	47
List 2 (n=30)	43	40	40	37	47	43	43	43	47	43	43	40
List 3 (n=37)	38	41	41	43	38	43	43	46	46	46	46	43

BL = Baseline assessment

Table A. 19: SD-J1 raw naming data (% correct) during treatment phase by word list

	T1	T2	T3	T4	T5	T6	T7	T8
List 1 (n=30)	**100**	**100**	**100**	**100**	100	100	100	100
List 2 (n=30)	50	50	47	40	**93**	**100**	**100**	**100**
List 3 (n=37)	41	43	43	46	46	55	49	49

T = Treatment assessment week; Bolded results indicate the period during which training occurred

Table A. 20: SD-J1 raw naming data (% correct) post initial treatment phase

	P1	P2	P3	P4	P5	P6	P7	P8	P12	P20	P24
List 1 (n=30)	100	100	97	100	100	92	97	90	97	87	90
List 2 (n=30)	100	97	97	88	94	96	87	97	97	82	89
List 3 (n=37)	59	62	62	62	40	56	59	59	59	56	53

P = Post-treatment assessment week (e.g. P1 = 1 week after treatment end)

Table A. 21: SD-S1 raw baseline naming data (% correct) by word list

	BL1	BL2	BL3	BL4	BL5	BL6	BL7	BL8	BL9	BL10	BL11
List 1 (n=32)	33	37	52	45	41	34	44	44	58	61	56
List 2 (n=32)	20	44	32	36	47	42	41	41	53	48	56
List 3 (n=32)	29	56	36	50	42	42	52	52	42	52	55

BL = Baseline assessment

Table A. 22: SD-S1 raw naming data (% correct) during treatment phase by word list

	T1	T2	T3	T4	T5	T6	T7	T8
List 1 (n=32)	**91**	**97**	**n/c**	**100**	94	91	91	88
List 2 (n=32)	56	53	n/c	59	**91**	**100**	**100**	**97**
List 3 (n=32)	61	58	n/c	55	58	61	52	48

T = Treatment assessment week; n/c = assessment not completed; Bolded results indicate the period during which training occurred

Table A. 23: SD-S1 raw naming data (% correct) post initial treatment phase

	P2	P3	P4	P5	P7	P8	P10-R	P12-R	P13-R	P14	P15	P16	P17	P20	P22	P24
List 1 (n=32)	81	84	81	91	78	78	**97**	**90**	**97**	91	91	94	94	78	72	78
List 2 (n=32)	78	87	75	78	72	69	**97**	**n/c**	**78**	75	69	78	78	88	78	81
List 3 (n=32)	61	64	61	73	73	70	64	61	76	64	73	69	67	64	66	67

P = Post-treatment assessment week (e.g. P1 = 1 week after treatment end); R = Assessment week in which revision training had been provided; Bolded results indicate the period during which training occurred

Table A. 24: SD-P1 raw baseline naming data (% correct) by word list

	BL1	BL2	BL3	BL4	BL5	BL6	BL7	BL8	BL9
List 1 (n=32)	31	31	38	28	34	34	38	38	38
List 2 (n=32)	34	34	34	34	34	31	34	34	38
List 3 (n=32)	24	27	33	33	36	39	33	39	42

BL = Baseline assessment

Table A. 25: SD-P1 raw naming data (% correct) during treatment phase by word list

	T1	T2	T3	T4	T5	T6	T7	T8
List 1 (n=32)	91	97	97	100	94	88	88	81
List 2 (n=32)	38	34	34	41	94	97	100	97
List 3 (n=32)	36	36	36	39	36	36	36	36

T = Treatment assessment week; Bolded results indicate the period during which training occurred

Table A. 26: SD-P1 raw naming data (% correct) post initial treatment phase

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P12	P16	P24-R1
List 1 (n=32)	88	81	84	81	81	81	81	78	78	78	75	**94**
List 2 (n=32)	100	94	94	81	91	88	84	81	78	91	72	75
List 3 (n=32)	39	36	36	33	36	36	36	33	36	36	31	30

P = Post-treatment assessment week (e.g. P1 = 1 week after treatment end); R = Assessment week in which revision training had been provided; Bolded results indicate the period during which training occurred

Table A. 27: SD-B1 raw baseline naming data (% correct) by word list

	BL1	BL2	BL3	BL4	BL5	BL6	BL7
List 1 (n=32)	22	34	44	41	41	47	44
List 2 (n=32)	19	38	41	41	41	41	41
List 3 (n=33)	21	39	36	45	39	48	42

BL = Baseline assessment

Table A. 28: SD-B1 raw naming data (% correct) during treatment phase by word list

	T1	T2	T3	T4	T5	T6	T7	T8
List 1 (n=32)	**100**	**100**	**100**	**100**	97	91	91	100
List 2 (n=32)	34	41	41	44	**94**	**100**	**100**	**100**
List 3 (n=33)	42	39	52	45	45	42	48	45

T = Treatment assessment week; Bolded results indicate the period during which training occurred

Table A. 29: SD-B1 raw naming data (% correct) post initial treatment phase

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P29	P24
List 1 (n=32)	100	97	97	100	100	97	97	97	97	97	94	97	94	94	88	100	94	91
List 2 (n=32)	100	100	100	94	91	94	91	94	88	91	94	100	91	97	97	91	97	84
List 3 (n=33)	52	45	45	55	48	48	58	58	58	55	56	58	58	64	64	61	64	58

P = Post-treatment assessment week (e.g. P1 = 1 week after treatment end)

Table A. 30: SD-C1 raw baseline naming data (% correct) by word list

	BL1	BL2	BL3	BL4	BL5	BL6	BL7
List 1 (n=31)	34	45	30	41	38	45	42
List 2 (n=31)	39	33	41	44	44	42	42
List 3 (n=32)	43	45	47	48	52	45	42

BL = Baseline assessment

Table A. 31: SD-C1 raw naming data (% correct) during treatment phase by word list

	T1	T2	T3	T4	T5	T6	T7	T8
List 1 (n=31)	**64**	**100**	**n/c**	**85**	76	91	76	79
List 2 (n=31)	50	29	n/c	59	**94**	**91**	**97**	**100**
List 3 (n=32)	52	58	n/c	55	69	67	61	64

T = Treatment assessment week; Bolded results indicate the period during which training occurred

Table A. 32: SD-C1 raw naming data (% correct) post initial treatment phase

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P12	P14-R	P17-R	P18-R	P20-R	P21-R	P22-R	P24-R
List 1 (n=31)	79	73	70	69	63	71	73	73	87	73	**87**	**87**	**85**	**72**	**81**	**93**	**88**	**94**
List 2 (n=31)	100	94	93	90	91	90	94	94	84	94	**84**	**97**	**97**	**86**	**93**	**97**	**84**	**94**
List 3 (n=32)	73	64	67	53	64	58	61	64	55	64	55	61	70	66	61	67	61	67

P = Post-treatment assessment week (e.g. P1 = 1 week after treatment end); R = Assessment week in which revision training had been provided; Bolded results indicate the period during which training occurred

Table A. 33: SD-C2 raw baseline naming data (% correct) by word list

	BL1	BL2	BL3	BL4	BL5	BL6	BL7	BL8
List 1 - part 1 (n=16)	7	7	0	6	0	6	0	6
List 1 - part 2 (n=17)	23	15	19	19	19	24	18	18
List 2 - part 1 (n=17)	18	18	6	12	24	12	6	12
List 3 (n=49)	13	10	6	6	11	10	8	8

BL = Baseline assessment

Table A. 34: SD-C2 raw naming data (% correct) during treatment phase by word list

	T1	T2	T3	T4	T5	T6	T7	T8
List 1 - part 1 (n=16)	**6**	**31**	**44**	**75**	**81**	**93**	73	73
List 1 - part 2 (n=17)	0	n/c	0	n/c	n/c	**59**	**71**	41
List 2 - part 1 (n=17)	6	0	6	0	0	0	**18**	**35**
List 3 (n=49)	6	8	8	6	6	4	4	8

T = Treatment assessment week; Bolded results indicate the period during which training occurred

Table A. 35: SD-C2 raw naming data (% correct) post initial treatment phase

	P1	P2	P3	P4	P5	P6	P8	P9-R1	P10-R2	P11-R3	P12-R4	P13-R5	P14-R6	P15-R7	P16-R8	P20-R12	P24-R16
List 1 - part 1 (n=16)	81	88	81	75	81	88	53	**75**	**63**	**69**	**88**	**100**	**88**	**100**	**88**	**75**	**87**
List 1 - part 2 (n=17)	65	65	59	47	47	53	38	**29**	**41**	**47**	**53**	**59**	**47**	**65**	**65**	**71**	**53**
List 2 - part 1 (n=17)	35	41	35	47	47	29	24	**12***	**24**	**35**	**47**	**53**	**59**	**59**	**63**	**65**	**59**
List 3 (n=49)	3	6	4	2	6	2	12	9	9	9	6	6	6	3	3	3	3

P = Post-treatment assessment week (e.g. P1 = 1 week after treatment end); R = Assessment week in which revision training had been provided; Bolded results indicate the period during which training occurred; * Sample size reduced to n=33 for the remainder as a further n=17 words commenced training

APPENDIX 7 – EXAMPLE ASSESSMENT MATERIALS AND RESPONSES FOR THE VIDEO DESCRIPTION TASK

Administration instructions: "Watch the following short video, then describe in as much detail as you can what you saw happen in the video. It is important to be as detailed as you can, so make sure you describe what you see the person doing by mentioning the names of any of the objects and by saying exactly what they do with them (as if you are telling someone who is not able to see the picture)".

Allow the person to describe the scene. If responses are unclear or a whole section of the video is left undescribed, then general prompts may be given e.g., "you said she made a drink. Can you tell me about what was she using to make the drink?"

Scoring instructions: For each word correctly mentioned, score 1 point. The exact word or acceptable synonym must be provided. If additional, descriptive words are used in the naming of an item that would not normally be used, the answer is considered spoiled (e.g., dishwashing machine instead of "dishwasher"; bread toaster for "toaster").

Transcript – SD-G1 Baseline: Video- Making a hot drink: *Note: words required for a correct response are indicated in square brackets, responses scored as correct are shown in bold*

Participant: "The lady was there when it was .. when it started .. who was wearing shorts and she picked up a boiling jug [kettle or jug] and came across to the tap [sink] and filled it with water and set it up and then she turned to the right and opened a cupboard and took out a **cup**

and then she walked across to the, past her oven, to a cupboard door beside the **refrigerator** and she took out tea and a tea bag bee.. teabag, I suppose you call it a **teabag** and then brought that out and set that up and poured hot water into it. And she had also picked up **sugar** and then she went into the fridge and got **milk** and then she put that beside the cup of tea and then she poured the brewed tea into her tea cup, added about a **teaspoon** of sugar and then added milk and stirred it all together. But she didn't drink it!"

Examiner: "No! You said she poured the brewed tea into a cup, what did she pour it from? What was she using?"

Participant: "The boiling jug. She poured it from the boiling jug [teapot]."

Transcript – SD-G1 Follow up: Video- Making a hot drink

Participant: "Well the lady picked up a **jug** and filled it with water, and then she it took it back to her right and obviously plugged it in. Then she came back past the **sink** and opened a folded door and took out from that a **cup** and put that close to where the hot water was. Then she um.. went back and opened, pulled out a drawer and took out a **spoon**. Then she went back and opened the top of a… **teapot**.. she actually opened the side door first and took out tea and **sugar**, and brought that across and then opened out the teapot and then put in a couple of sheets of **teabags** into the teapot and put more hot water into it. Then she went across to the **fridge** and got out **milk** and then she put that across and then she poured the ah.. tea into the jug.. sorry the cup, and then added some milk and some **sugar**.. sorry it was the sugar first and then the milk and then she stirred it."

<u>Transcript – SD-J2 Baseline: Video- Making a hot drink:</u> *Note: words required for a correct response are indicated in square brackets, responses scored as correct are shown in bold*

Participant: Ok so she came in and she got the **kettle** and put the water in and went over to the **sink** and put water into the k.. and then plugged that in and had it going and then went over and ah got the little box that has the **teabags** in it and brought that over to get the teabag and she had the little, tea… box [teapot] or whatever you call it. Oh first of she went over and got a **mug**. It.. ah it wasn't a cup and saucer it was er a mug. And she put the tea bag in to .. and ah when, when the kettle had… she was able to pour that in. And she went into the **fridge** and got the um **milk** and brought the milk over and um got some **sugar** over in the … there. And ah so then, when she got all those, and she poured the water into the teabag ah she was then able to pour the ah .. the tea into the mug and ah put some milk in and put in one **spoon** of of **sugar**. Only one . And stirred it up.

Examiner: and what was she using to pour the tea into the cup?

Participant: yes, it's a tea.. um.. .I forget the name. It's not a cup. It's a tea.. and it's not a bag.. it's a tea…pot. **Teapot**.

<u>Transcript – SD-J2 Follow up: Video- Making a hot drink</u>

Participant: Ok so she um went over to the.. the… left hand side and got the **kettle** and brought it, filled it up with water and put the lid back on and put it over there and turned it on to heat it up. Then she walked over… inside for her … and she bent down into the cupboard and she got out a **mug**. And ah then she went into the next one and .. ah she got um.. a er… um.. a .. she.. got brought out and got .. a um.. **spoon**. Um and… yeah. And then um she put she went over into that one and she got um.. a box of **tea** and ah one of **sugar** and brought it out and put it down. And then she got a little um **teapot** and she put, took the tea with the water and put it into the teapot. Then she poured it in there but then she went to the um **fridge** and got the um **milk** and brought that out. Um… have the um.. ah… **sugar**. Sugar? And ah so then when she poured that in, she then put the milk in and one cup, one little spoon, spoon of sugar in there. Then she's ready to, she'll be able to…

Examiner: And in the beginning when she got the water for the kettle, where was she getting the water from?

Participant :Um in the ah the **sink**.

Transcript – SD-J3 Baseline: Video- Making toast: *Note: words required for a correct response are indicated in square brackets, responses scored as correct are shown in bold*

Participant: I know exactly what it is, but not the words. I'm sorry. The only thing.. the only word I know is the **bread**. Electricity

Examiner: Can you tell it as a bit of a story, even if you can't think of all the words?

Participant: She's cooking breakfast. And I know exactly what those things are but I can't think of the words. That's what I use but I never know the words. Now and again I come up with a word. I can't.

Examiner: What about some of the things here?

Participant: Apart from the meat, that's all I know. **Knife**. Is it knife? I can't believe it. I remembered! I was trying to think of it before.

Examiner: And these?

Participant: Yeah, but I don't know the name

Examiner: do you remember where she got this from?

Participant: The kitchen [fridge]

Transcript – SD-J3 Follow up: Video- Making toast:

Participant: Is it called a grater? No, toaster? Is it toaster? What do you call that machine?

Examiner: You keep going

Participant: Going to make something to eat. She's opened the **fridge**, got something out. Some meat [bread] and heat it up. Is it kettle? [toaster]

Examiner: Keep going

Participant: Fridge. She's got a **knife** and ….cheese [butter] and it looks like a **jam**. Pull it out, probably add the cheese and the jam. Not cheese, it's some **butter**.

Examiner: So if you can tell me everything about what you saw her do and all the things she's been using?

Participant: Oh well she's… she's just having breakfast and she put some **bread** into the… I know what it is, it's to heat it up but I can't think of the word. And once it was warm enough, hot enough, then she put some .. ah… jam on it and … some butter.

Examiner: What were some of the other things you can see here that she's been using?

Participant: Oh she had a knife and a **plate**.

Examiner: And if you had to decide what word this was, what is it? [pointing to toaster]

Participant: It's used for heating up bread. Um… can't think of it.

<u>Transcript – SD-T4 Baseline: Video – Making a hot drink</u> *Note: words required for a correct response are indicated in square brackets, responses scored as correct are shown in bold*

Participant: "Ok the first step was that she, she got some water and I thought it was cooking in the in the .. **kettle** but she then got this special thing.. oh and I've forgot that other thing, but then she also brought out the **milk** from the **fridge** and some **sugar**. So I'm not sure if she made a tea or a coffee, but probably a tea I think. Oh yeah, she put a special **tea** thing in their first. But yeah.. she hasn't drunk it yet!

Examiner: So what is she holding at the moment?

Participant: Oh well I thought she was just holding the the tea , tea thing that went in and then after a little while she might take the tea thing out and put more water in, I'm not sure

Examiner: What else is she holding?

Participant: Well she's holding a this, but I can't tell you that one!

<u>Transcript – SD-T4 Follow up: Video – Making a hot drink</u>

Participant: "well the first step was, I thought she she had a **kettle** to heat some water, but I'm sorry I don't know why she then went across there. That's not a coffee machine, I don't think. Anyway, then the next step, she did she she got some **sugar** out and she got the **milk** out and she put it all on the table but then she waited for that to get fixed in there and then she poured it in there and then she put some salt [sugar] and some milk in that **cup**. And then before she's eating that, she put the.. the milk back in the **fridge**.

Examiner: Ok, just going back a little bit. What else is she holding here?

Participant: oh just a special **spoon** to, to swing that in there because that's sugar I think.

Examiner: And if we go all the way back here. What's she doing here?

Participant She's just putting water in the kettle

Examiner: Where's she getting the water from?

Participant Oh, from the **sink** there.

Transcript – SD-J5 Baseline: Video – Making a hot drink *Note: words required for a correct response are indicated in square brackets, responses scored as correct are shown in bold*

Participant : She went in the house and she just went in the door and got stuff out. I thought it was coffee that she was putting in but it might be something different. Probably didn't see everything that she was putting in on that.

Examiner Were there other things that she was using or things that she took out?

Participant : Yeah she took a few things out to put in that that place. And put some back

Examiner Yeah, can you think of any of the names of any of things she was using or took out?

Participant : No, no, not by myself. What you put in there.

Examiner So if you had to say overall what she was doing, what was she doing?

Participant : Just going to eat herself a drink

Transcript – SD-J5 Follow up: Video – Making a hot drink

Participant: Got some sort of jam. Shirt. And coffee. Could be **tea**, I suppose. **Refrigerator,** refrigerator. Milks, **milk**. Milk in the coffee. She's got coffee. She's put the milk in the coffee. She's gone to the door.

Examiner Can you tell me a whole little story about that? What did you see happening?

Participant : Well she just, working, fixing the food stuff. Probably just doing a lot of things.

Examiner Can you tell a little story about it? What happened? What she did?

Participant Ah no, I can't do that.

Table A. 36: Video description sample scoresheet – SD-G1: Making a hot drink

Target Word	List*	Baseline Score	Follow up Score
Kettle or jug	1	0 (boiling jug)	1
Sink	2	0 (tap)	1
Cup	3	1	1
Spoon or teaspoon	2	1	1
Refrigerator	1	1	1
Milk	1	1	1
Sugar	3	1	1
Tea bag	1	1	1
Teapot	2	0 (boiling jug)	1

** List 1 and 2 = trained words; List 3 = untrained words. Incorrect responses are shown in parentheses*

APPENDIX 8 - COOKIE THEFT SAMPLE DESCRIPTIONS

Sample 1 - Very poor

There's a lady. Ah… this little, there's a little girl there. And … there …what else…. Um… and cooking? Um... happily! [laughs] Oh goodness! Little girl… There's something there I can't quite grasp..… um... a jar?

Sample 2 - Poor (semantic)

Right um well the water's overflowing…. which is going onto the floor and causing problems there. The lady is cleaning, you know, various equipment, you know, um there's a.. um… sh-shawls no… I'm always cleaning them! [laughs]… and the boys, you got a boy and a girl, and well they've got sh-shoes on etcetera. And he's on the ah… that is over at an angle and it's going to fall over and that's the trouble. Um.. and it's.. not a table um… I, I can't come at that, but he's going through the food for himself and also giving one to his… girl, ah which I presume is his s.. sister. [laughs]

Sample 3 - Poor (word finding difficulty)

Oh ok, the children, um… oh well the boy um has got the … cookie jar [laughs] um but he's going to go ..ah.. .off the… the… mmm what's it? Um.. anyway, that thing. Ah the little girl wants one too, but I don't know think she's going to do it.[laughs] The mother is doing the plates. But she's not doing anything else! [laughs] Looking out the window and it's the um, tap… is flowing over. [laughs] And um it's the table…. Tea towel.

Sample 4 - Good

The mother is wiping up the plate. The sink is flowing over with water and it's spilling onto the floor. Two children are getting into the cookie jar. The boy is up on a stool which is overbalancing. He's got one or two cookies in the … left hand. The girl has her …. Left hand up to take one, and she's got her finger, her index finger pointing to her mouth to keep, to keep them quiet so the mother won't hear.

APPENDIX 9 - COOKIE THEFT ANALYSIS

Each transcript was given a score out of 23, according to the classification of semantic units as described by Croisile and colleagues (1996), which includes reference to subjects (boy, girl, woman), places (kitchen, exterior through the window), objects (cookie or biscuit, jar, stool, sink, plate, dishcloth, water, window, cupboard, dishes, curtains) and actions (boy taking/stealing, boy or stool falling, woman drying or washing dishes/plate, water overflowing or spilling, action performed by the girl, woman unconcerned by the overflowing, woman indifferent to the children). A full point was awarded to a clear and precise reference to each semantic unit, with half a point assigned where units were described incompletely or with more generic language (e.g., use of the word “chair” instead of “stool”, “food” instead of “biscuit” – see below for detailed scoring rules). Zero points were given if there was no reference to the semantic unit, or if the information was unclear or incorrect.

Subjects

- 1 point: for each of the 3 people in the picture. For full credit the reference must be exact – boy/brother, girl/sister and woman/lady/mother. If there is mention of “2 children” then this must be followed by a clear reference to gender of each child through the use of pronouns in order to get full credit
- 0.5 point: mention of a child (non-specified gender); mention of “2 children” = 0.5x2
- 0 point: only generic words are provided e.g., “3 people”; “children” (without quantity), or pronouns without mentioning children or adults; incorrect information is given “e.g., 4 children” etc.

Places

- 1 point: for each of the two places. For credit, there must be the explicit use of the word "kitchen", and some reference to "outside" (also acceptable would be "out the window", "yard/front yard"). Where reference is given to the "kitchen sink" or "kitchen cupboards", then credit is awarded both for objects and places
- 0 point: references are not clear enough (e.g., "inside the house" or "there's a view out the window")

Objects

- 1 point assigned for each object named from the list of 11 objects
- 0.5 points assigned for generic substitutions (e.g., "food" instead of "cookie/biscuit", "chair/seat" instead of "stool")
- 0 points assigned if the object is not mentioned or for each object if semantic errors are made (e.g., "table" or "couch" for stool). Descriptions of objects are not accepted (e.g., "the place where you do washing up of things" instead of "sink")

Actions

- 1 point assigned for each action described from the list of 7 actions. To qualify for full credit it should be clear who is completing the action and the verb used should be specific to convey the full meaning of the semantic unit
- 0.5 points assigned for each action if using generic verbs (e.g., "get" instead of "take/steal"; "doing washing" for "washing up dishes"); or incomplete descriptions of the action (e.g., "doing washing" for "woman washing up dishes") or incomplete reference of who is

completing the action (e.g., “she is washing” instead of “woman” or “the children are getting the cookies from the jar”). Half point would also be given if the action and the object is split into adjoining statements “e.g., she is washing.. clean dishes now”.

- 0 points assigned for each action if the action is not mentioned or if it is incorrectly described (e.g., “the girl is falling”)

Note: here to score a point for “action by the girl” the action must include some reference to the intentions or communication of the little girl regarding the cookies or her brother. If the person says “girl is watching” or “girl is standing and watching”, this is insufficient. The action must relate to her gesturing or communicating to her brother.

Note: for the last two actions, the idea conveyed must be that the woman either does not care or does not notice what is happening with the water overflowing or with the children getting into the biscuits. The reference must be in relation to the action of the woman (vs what the children are doing “behind mother’s back”).