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THE CONTRIBUTION OF THE FRONTAL LOBES TO PROPOSITIONAL LANGUAGE

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December 2005

A thesis submitted to the Institute of Neurology of the University of London for the degree of Doctor of Philosophy

ACKNOWLEDGEMENTS

There would be no study without the generosity of the patients. I continue to be amazed at the will of each patient to be part of research at perhaps the most difficult time in their life. First, thank you to CH whose enthusiasm and professionalism was outstanding and to KAS who introduced me to the acting world. Second, thank you to all of the patients in the group study who wanted to be part of this research in the hope that further understanding of the brain may help other patients in the future. I will do my best to justify your efforts and hopes.

I am truly appreciative of the continued support and overall guidance I have received from my main supervisor, Lisa Cipolotti, and for the timely and focussed guidance given by Tim Shallice. I am also thankful for the detailed lesion analyses provided by Dr Peter Rudge for the single case study patients and Dr Marco Bozzali for the group study patients.

As this PhD has been part-time over the last 5 plus years, while I have been a full-time Clinical Neuropsychologist, I need to acknowledge my work colleagues for their understanding of competing demands on my time. Particular thanks go to my colleagues in the Department of Neuropsychology for their support, especially in the last 6 months, and my clinical colleagues on the Acute Brain Injury Unit.

A project like this would never be possible without the unfailing support of my family and friends, from overseas and in London. The coffees and chats have been an integral part, as have been the encouragement you gave me and the faith you had in me. Thank you.

ABSTRACT

A single case and group study methodology was adopted to investigate the cognitive mechanisms involved in propositional language and the underlying anatomical substrates. Patients with dynamic aphasia and patients with unselected focal frontal and posterior lesions have been investigated. Dynamic aphasia is characterised by a severe propositional language impairment despite well-preserved nominal language. The results obtained in three patients with dynamic aphasia (ANG, CH and KAS) suggest two functionally and anatomically distinct cognitive mechanisms. One set of cognitive mechanisms is responsible for *high-level selection among competing verbal response options.* This mechanism is specific to the language domain and is implemented by the left inferior frontal region. Evidence for this first mechanism comes from the dynamic aphasic patients ANG and CH and frontal patients with left inferior frontal gyrus lesions. These patients were severely impaired on word and sentence generation tasks <u>only</u> when a stimulus activated many competing verbal response options. By contrast, they were unimpaired when a stimulus activated a dominant response. The second set of cognitive mechanisms is responsible for *generating a fluent sequence of novel thought.* This mechanism encompasses novel verbal and non-verbal generation and is supported by bilateral frontal region. Evidence for this second set of mechanisms comes from the dynamic aphasic KAS and patients with frontal lesions. These patients were severely impaired in generating multiple connected sentences. These patients were also impaired in the voluntary generation of novel verbal and non-verbal responses. The convergence of findings from dynamic aphasia, patients with focal frontal lesions and neuroimaging are discussed. These data confirm a role of the frontal lobes in propositional language generation and specify at least two sets of cognitive mechanisms involved in this process.

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CHAPTER ONE: INTRODUCTION

The ability to express our thoughts verbally is one of the distinctive aspects of being a human being. For a long time the relationship between language and thought has been of great interest; namely, can thought exist without language or does thought depend on language (see for example Weiskrantz, 1988). This issue has been discussed in many disciplines including philosophy, neurology, psychology and neuropsychology. The aim of this thesis is to explore the contribution of the frontal lobes to propositional language and investigate the cognitive mechanisms involved in the generation of language within a neuropsychological framework.

What is propositional language? Historically, this question was addressed in the 19th Century when the neurologist Hughlings Jackson wrote "to speak is not simply to utter words, it is to propositionise" (1879, reprint edited by Taylor, Holmes, & Walshe, 1932, p. 159). Further,

> a proposition is such a relation of words that it makes one new meaning; not by a mere addition of what we call the separate meanings of several words. The same proposition is *new* or [the] *latest* speech ... if the words ... are not ... *kept ready made up* in that particular combination, ... [but] when specially applied at a particular time to indicate then occurring relations of things which *are not fully organised*; it is then, otherwise stated, a voluntary use of words ... voluntary implies clear preconception... as distinguished from automatic, operations..." (Hughlings Jackson, 1879; reprint edited by Taylor et al., 1932, p. 188).

Thus, according to Hughlings Jackson "the proposition is the basic unit of living speech and the primary function of speech is the formulation of thoughts into propositions. A proposition ... always says something about something. Thus behind every proposition lies a thought" (cited in Luria, 1970, p. 188). The early work of Hughlings Jackson highlighted two specific aspects of propositional language: it is voluntary and novel. That is, a proposition lies within the realm of *voluntary* thoughts and is expressed in relation to a current context such that it is new or *novel.* Propositional speech differs from automatic (or nonpropositional) speech in terms of these two aspects. According to Hughlings Jackson (1879, reprint edited by Taylor et al., 1932, p. 189), automatic speech consists of producing overlearned sequences that are recurring utterances as well as being ready made up and not novel.

Is propositional language distinct from thought? The dominant view in the 1860s, according to Head (1926), was that we think in words, so thought and propositional language are very much linked. In contrast, Head (1926) held the view that thought can be expressed in words, which allows for a more independent non-language component. Head referred to propositioning as *symbolic formulation and expressing*, and focussed on two components of language: the formulation of thought and the skilful expression of it. Head argued that "acts of thinking cannot be expressed completely in words; the whole process is inherently illogical, intuitive and punctuated by irrelevancies… as soon as we attempt to express our thoughts even to ourselves, we re-arrange them and drastically prune away redundant and incoherent features… the results of unrestricted thinking are refined in accordance with logical canons" (p. 514). Other theorists implied a non-language early stage in the process of translating thought into speech. For example, Pick referred to the first process as being 'prior to linguistic formulation' (1931; cited in Brown, 1972), whereas, Brown discussed "imageless thought [in which] there is little more than a vague intuition of the idea to be expressed... [and] this may be a feeling of the presentation of the thought rather than an apprehension of its nature" (1972, p. 6). Although these ideas lack detail, they do assume a non-language component that precedes propositional language.

Head (1926) also considered the anatomical implications of the relationship between propositional language and thought. Unilateral lesions can disturb language processes requiring symbolic formulation and expressing. Head emphasised that this disruption should not exclude other mental behaviours that demand a symbolic aspect, implying that a similar process may occur for non-verbal information, but a lesion that is not necessarily unilateral may cause the disturbance.

Within these historical views, there is no clear consensus as to whether propositional language generation involves, or is related to, only verbal generative processes and unilateral left lesions, or if it also involves non-verbal generative processes and other lesions. Nevertheless, from the early writings it is clear that propositional language generation involves novel and voluntary expression. In this thesis, I will explore the voluntary generation of novel verbal and non-verbal responses and of propositional language, with the aim of expanding our understanding of the contribution of the frontal lobes to these processes.

1.1 THE ROLE OF THE FRONTAL LOBES IN VOLUNTARY GENERATION PROCESSES

The functions of the frontal lobe of the brain have been viewed as responsible for higher-level control operations (Shallice, 1988). This is not surprising given the human frontal lobes comprise approximately 25-33% of the total mass of the cerebral hemispheres and are what distinguish humans from animals (Luria, 1973; Walsh, 1987). Through the study of patients with frontal lobe damage, Luria (1973) proposed that the functions of the frontal lobe were involved in the programming, regulation and verification of human activity. For instance, control of conscious behaviour was postulated to require the regulation of activity level such that the formation and activation of plans and intentions was possible.

One of the higher order functions of the frontal lobe is *generation*. Nearly all types of overlearned and non-routine behaviours require a type of generation. Within neuropsychology, fluency tasks are used to tap voluntary *generation* of novel responses. In itself, *generation* of a response may involve a number of processes. For example, a sentence completion test (Hayling) was devised to investigate response initiation, response suppression and strategy use in patients with frontal lesions (Burgess & Shallice, 1996b). Patients with frontal lesions were poorer than patients with posterior lesions to both initiate a response (i.e., generate a connected word) and to suppress the habitual response (i.e., connected word). Frontal patients were also less likely to use a strategy to generate an unrelated word. On the surface this task involves generation of a single word to complete a sentence; however, the authors identified three executive processes involved in performing this task and it could be argued to also involve selection from a pool of possible words. With regard to response inhibition (or suppression), a failure in this process results in generation. This can be measured by perseverative or rule-break errors on fluency generation tasks. Inhibition processes have been investigated for various types of responses including imitative actions and overlearned associations such as reading in the Stroop Test (for recent review see Aron, Robbins, & Poldrack, 2004). A further example of the complexity of generative processes can be illustrated with the design fluency test that involves the generation of abstract drawings (i.e., designs that cannot be recognised or named;

Jones-Gotman & Milner, 1977). This task involves generation of novel responses, strategy formation and use for creating new drawings, suppression of familiar drawings, monitoring so that drawings are not repeated, and motivation (or perhaps maintenance of activation or energising) to continue generating novel drawings. In propositional language generation, tasks involve creation of a novel thought. This also involves retrieval of components of the thought (both language elements such as words and non-language ideas) and possibly selection if many potential elements or components are available. The latter has been suggested to fail in patients with damage to the left inferior frontal lobe (Thompson-Schill et al., 1998). The process of forming and using a strategy to retrieve and generate words in fluency tasks has been viewed as critical for a good performance (Gold et al., 1997; Reverberi, Laiacona, & Capitani, 2005a). Finally, continuing to generate items on fluency tasks involves some form of maintained activation in order to sustain the generation of output. This would seem to be different from a more psychological construct of motivation. Recently, reduced generation on a semantic fluency task has been attributed to a deficit in activation (Reverberi et al., 2005a). In a slightly different context of responding (cf. voluntary generation of novel responses), insufficient energizing of attention was found to affect concentrated responding (Alexander, Stuss, Shallice, Picton, & Gillingham, 2005). This energizing involves arousal and activation of cognitive systems.

A number of other higher-order frontal lobe functions operate on a given set of information, which less directly involve voluntary generation of novel responses. These functions include planning, organisation, concept formation, abstraction, decision-making, switching, monitoring, judgement and reasoning, all of which have been associated with damage to the frontal lobes (e.g., Benton, 1968; Burgess & Shallice, 1996a; Cicerone, Lazar, & Shapiro, 1983; Goel & Grafman, 1995; Manes et al., 2002; Owen, Downes, Sahakian, Polkey, & Robbins, 1990; Reverberi, Lavaroni, Gigli, Skrap, & Shallice, 2005b; Reverberi, Toraldo, D'Agostini, & Skrap, 2005; Rogers et al., 1998; Shallice & Evans, 1978; Shallice, 1982; Zalla, Plassiart, Pillon, Grafman, & Sirigu, 2001). It can be argued that all of these frontal lobe functions, to a more or less degree, involve generation. For example, planning is generally viewed as being more of an 'executive' task although it implicitly involves a generation component (i.e., generate or create a plan based on given information and constraints). On the other hand, some clinical features that more obviously relate to generation processes only manifest with a failure of non-generation processes (e.g., impulsiveness and disinhibition can result from faulty checking or monitoring). The story is more complex when one examines cognitive tests developed to assess these frontal lobe functions. For example, the Trail Making Test (Army Individual Test Battery, 1944) has been widely used in clinical settings as a test sensitive to frontal lobe dysfunction. It is viewed as a test of visual search, visual attention, monitoring and switching between concepts (Lezak, Howieson, & Loring, 2004; Olivera-Souza et al., 2000). Generation of a strategy could also be argued to be important for this task in order to be able to carry out all 4 processes, highlighting the difficulty one has in disentangling the processes involved in task performance.

A further question arises when considering whether the same generation process underlies one type or multiple types of information (e.g., actions, words, drawings, sentences, discourse). Moreover, is the voluntary generation of a novel response internally-generated or externally-cued and are these associated with the frontal lobes? This distinction has been made in reference to 'willed' action that has been defined as involving attention, conscious awareness, choice, control and intentionality (Jahanshahi & Frith, 1998a). This is in contrast to routine, or stereotyped, and externally-cued actions. Although willed action has been associated with the prefrontal cortex and frontostriatal circuits, it is not clear what level of control is needed for externally-cued actions and whether the same anatomical substrates supports this (Frith, Friston, Liddle, & Frackowiak, 1991a; Frith, Friston, Liddle, & Frackowiak, 1991b; Jahanshahi et al., 1998a). Further, does an impairment of willed action result in a state of no action or only stereotyped or repetitive movements?

An associated question is how generation relates to initiation, activation and drive? The literature reports that patients with these impairments may present with apathy, abulia and decreased motivation (for an overview see Stuss & Benson, 1986). First, the term initiation is often used interchangeably with generation. With regard to activation and drive, one could speculate that a deficit in activation and an overall lack of drive would affect the generation of any response, and particularly voluntary and novel responses. Thus, are voluntary generation processes part of the same processes responsible for initiation, activation and drive? Or are these functionally and possibly anatomically separable? One report stated that British neurologists and psychiatrists identified a lack of voluntary activity and decreased initiation of spontaneous speech as characteristics of abulia (Vijayaraghavan, Krishnamoorthy, Brown, & Trimble, 2002). Abulia has been associated with frontal lobe dysfunction (Vijayaraghavan et al., 2002) and basal ganglia lesions (Bhatia & Marsden, 1994). Another study implicated initiation in apathy, which was defined by the absence of responsiveness to stimuli or as the absence of self-initiated action (van Reekum, Stuss, & Ostrander, 2005). Thus, despite some confusion surrounding the terms abulia and apathy, it appears that both responsiveness to stimuli and voluntary generation of novel responses require a base level of activation but that responsiveness to stimuli may involve a lower level of executive control compared to voluntary generation of novel responses.

The Supervisory Attentional System (SAS) model developed by Norman and Shallice (1986) addresses the different levels of activation. The SAS model was based on two main premises; namely, that routine selection of routine operations is decentralised and that non-routine selection is qualitatively different and involves a general-purpose Supervisory System that modulates rather than dictates the operation of the rest of the system[1]. In the SAS model, the process of routine selection between routine actions is termed contention scheduling. The Supervisory component operates by modulating the lower level contention-scheduling system by activating or inhibiting particular schemas. It is required in situations where the routine selection of actions is unsatisfactory, "for instance, in coping with novelty, in decision making, in overcoming temptation, or in dealing with danger" (Shallice, 1988; p. 335). The carrying out of routine actions implicitly involves action initiation. Shallice (1988) interpreted a failure to initiate action as being due to a disconnection between the Supervisory System and contention-scheduling system.

Overall, it seems that within the large number of subprocesses ascribed to the frontal lobes, a division can be made between those processes that involve the voluntary generation of novel responses (i.e., a primary generative component) and those tasks that involve the initiation of a supervisory, higher-order, control process (e.g., planning). Despite great interest in the frontal lobes, its functions remain little understood. Nevertheless, the last decade has seen a rise in popularity of the view that there is a fractionation of frontal lobe functions. For example, Stuss and Alexander have stated that there is " no unitary executive function... there are distinct processes that do converge on a general concept of control functions" (2000a, p. 291). The focus of this thesis is the role of the frontal lobes in the process of primary voluntary generation of novel responses.

[1] This has been referred to as regulation of behaviour rather than behaviour per se (Perceman, 1987).

1.1.1 Verbal and Non-Verbal Fluency Tasks

Traditionally, fluency tasks are used to tap the ability to voluntarily *generate* novel responses. The classic verbal generation task is word fluency, with the two most widely used tasks being phonemic (also known as letter or phonological) and semantic (also known as category) fluency. Although both require the production of words within a given time, phonemic fluency is constrained by the initial sound of words (e.g., words beginning with S) whilst semantic fluency is constrained by semantics (e.g., items from the category of 'animals').

Since the seminal study of Milner (1964), there has been a multitude of lesion data demonstrating reduced word fluency performance in patients with frontal lobe lesions (Baldo & Shimamura, 1998; Rogers et al., 1998; Schwartz & Baldo, 2001; Stuss et al., 1998). Specifically, phonemic fluency impairments have been documented in frontal patients compared to both posterior patients (Miceli, Caltagirone, Gainotti, Masullo, & Silveri, 1981; Milner, 1964; Pendleton, Heaton, Lehman, & Hulihan, 1982; Perret, 1974) and controls (Benton, 1968; Coslett, Bowers, Verfaellie, & Heilman, 1991; Owen et al., 1990; Pendleton et al., 1982; Perret, 1974; Stuss et al., 1998). However, a selective frontal impairment for phonemic fluency has not always been found as some studies documented impairments in both frontal and posterior patients (Stuss et al., 1998; Vilkki & Holst, 1994). For semantic fluency, impairments have been found in frontal patients (Pendleton et al., 1982; Stuss et al., 1998; Vilkki et al., 1994), although other studies have not documented this (Martin, Loring, Meador, & Lee, 1990; Newcombe, 1969; Vilkki et al., 1994), and some studies report equivalent frontal and posterior impairments (Coslett et al., 1991; Newcombe, 1969). A recent meta-analysis revealed that frontal patients had large and comparable deficits for phonemic and semantic fluency; whereas, temporal patients showed a larger deficit for semantic fluency and a lesser deficit for phonemic fluency (Henry & Crawford, 2004a). The latter has also been reported in patients with semantic dementia that have focal temporal pathology (Hodges, Patterson, Oxbury, & Funnell, 1992).

Word fluency performance has been compared in patients with unilateral left and right lesions with the consensus that left lesions are more impaired than right lesions (Loring, Meador, & Lee, 1994; Miceli et al., 1981; Martin et al., 1990; Milner, 1964; Newcombe, 1969; Pendleton et al., 1982; Perret, 1974; Vilkki et al., 1994). Although some studies document impairments in right unilateral lesions (Loring et al., 1994; Martin et al., 1990; Perret, 1974), some studies report these patients to be comparable with controls (Milner, 1964; Newcombe, 1969). More specifically, left frontal lesions have been reported as resulting in reduced phonemic fluency (Benton, 1968; Milner, 1964; Perret, 1974; Stuss et al., 1998). For example, Stuss and colleagues (1998) found phonemic fluency was most severely impaired following left dorsolateral lesions although moderate impairment followed superior medial lesions.

Word fluency impairments have not only been documented in patients with focal cortical lesions, but also in patients with subcortical lesions (Laplane et al., 1989) or pathologies resulting in widespread damage (e.g., traumatic brain injury - Henry & Crawford, 2004b; Alzheimer's disease - Henry, Crawford, & Phillips, 2004). Thus, phonemic and semantic fluency impairments have been documented in various patient groups with pathology that either involves the frontal lobe or disrupts the fronto-striatal connections; namely, Parkinson's Disease (Henry & Crawford, 2004c), multiple system atrophy (Bak, Crawford, Hearn, Mathuranath, & Hodges, 2005), progressive supranuclear palsy (Lange et al., 2003; Bak & Hodges, 1998; Bak et al., 2005), amyotrophic lateral sclerosis (Abrahams et al., 1997; Abrahams et al., 2000), Huntington's Disease (Henry, Crawford, & Phillips, 2005; Rosser & Hodges, 1994) and corticobasal degeneration (Graham, Bak, Patterson, & Hodges, 2003).

Do word fluency tests involve only generation? Perret (1974) suggested that phonemic fluency involves both generation and suppression of responses. He argued that generation of words beginning with a letter requires suppression of the automatic or habitual use of words according to meaning, inevitably leading to a conflict between the habitual and less automatic use of words[2]. This contrasts sharply with semantic fluency that does not involve conflict as generation of words from categories uses the "well-established associative habits of word-finding" (Perret, 1974, p.324). This implies that resolving conflicts amongst competing responses to generate a word may be required only for phonemic rather than semantic fluency. It could be argued, however, that response suppression is also a component of semantic fluency as semantically related words from a different category must be suppressed (e.g., for the category of *Animals ... lion* is correct but *safari gun etc* are incorrect).

Response suppression, as referred to by Perret (1974), would only apply to tasks that tap stored responses. If one does not agree with Perret that word generation is somehow automatic (at least for semantic fluency), it would seem that word fluency

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[2] Perret drew similarities between this and the conflict condition of the Stroop Test (Stroop, 1935) that involves suppression of an automatic response (reading) in favour of a less habitual response (colour naming).

tasks involve active retrieval from a lexical/semantic store. In this case, a strategy would need to be developed and implemented, the lack of which has been held responsible for impaired word generation performance (Gold et al., 1997). Recently, Reverberi and colleagues (2005a) examined strategy, initiation, switching and monitoring in the semantic fluency performance of patients with frontal lobe lesions. They found that all frontal patients had a primary generation deficit, as evidenced by a reduced number of words. They argued that lateral frontal patients had a defective search strategy, as evidenced by a disorganised word sequence, whereas mesial frontal patients had an activation deficit, as evidenced by a reduced but otherwise normal performance.

The number of words produced in a word fluency task can provide a measure of the primary generation aspect. Word fluency performance has also been investigated by measuring features such as clustering, the average number of words within semantic or phonemic subcategories in a sequence, and switching, the ability to shift between clusters (Troyer, Moscovitch, & Winocur, 1997; Troyer, 2000). These investigators have argued that an optimal fluency performance, in terms of number generated, involves clusters of semantically or phonologically related words and then switching to a new subcategory when the current one is exhausted (Troyer, Moscovitch, Winocur, Alexander, & Stuss, 1998). Troyer and colleagues (1997) found both switching and clustering were highly correlated with semantic fluency, whereas switching was more highly correlated than clustering with phonemic fluency. This study also demonstrated that switching decreased by divided attention. Indeed, frontal patients have been shown to have a switching but not clustering deficit for phonemic and semantic fluency (Troyer et al., 1998). This impairment was only found in patients with left dorsolateral and superior medial frontal lesions. Temporal patients were not impaired for phonemic fluency but they did show a clustering deficit for semantic fluency. The authors interpreted this as clustering and switching being dissociable fluency components with only switching related to frontal lobe functioning. In contrast to this finding, however, Reverberi and colleagues (Reverberi et al., 2005a) recently found that lateral frontal patients (no lateralisation) did not have a switching deficit on a semantic fluency task, despite producing a less organised word sequence.

Non-verbal generation tests such as design fluency have been developed as analogues to word fluency tasks (Jones-Gotman et al., 1977). The original design fluency task contained two conditions: free and fixed. The free task required subjects to invent as many different drawings as possible that neither represented real objects nor were derived from such objects. The fixed task was similar, except that each drawing had to consist of four straight or curved lines. The fixed task is more constrained by the stimulus even though novel generation is still required. Jones-Gotman and Milner found that right frontal and right central patients were the most impaired for both tasks in terms of number of designs generated. For the fixed task, all patient groups, frontal and temporal, were reduced compared to controls. The right frontal group also made the most perseverative responses and nameable errors. Jones-Gotman and Milner concluded that the right frontal group's impaired performance on design fluency tasks was due to impoverished output (i.e., a primary generation deficit) as well as high perseveration. Although several subsequent studies have failed to associate the right frontal lobes with impaired design generation, most studies have implicated the frontal lobes with this non-verbal generation task (e.g., Baldo, Shimamura, Delis, Kramer, & Kaplan, 2001; Tucha, Smely, & Lange, 1999).

Three other fluency tasks have sporadically been used to assess voluntary and novel response generation: ideational fluency, gesture fluency, and motor movement generation. Ideational fluency[3] involves generating uses of objects (e.g., brick) under two conditions: conventional (e.g., build a house) or unconventional (e.g., paperweight). Patients with focal frontal lesions have been found to generate fewer unconventional uses of objects, compared to controls and posterior patients, which has been interpreted as a deficit of diverse novel uses generation (Eslinger & Grattan, 1993; Tomer, Fisher, Giladi, & Aharon-Peretz, 2002). Gesture fluency was developed to assess novel responding in frontal lobe patients (Jason, 1985). It involves generating as many different finger positions as possible under two conditions: meaningless and meaningful. Jason found that left frontal patients were impaired in both conditions as measured by number generated and perseverative errors; whereas, right frontal patients (specified as ventro-lateral or orbital lesions) were only impaired in the meaningful condition as measured by number generated. Motor movement generation involves making random movements with a joystick and was first used to investigate generation and selection of movements in the context of neuroimaging (Deiber et al., 1991). As these three fluency tasks have been rarely reported, little is understood about their verbal or non-verbal cognitive properties or anatomical correlates, except that they involve generative processes and are thought to tap frontal lobe functions.

[3] This is also referred to as the Alternate Uses Test and the Uses of Objects Test.

All fluency tasks involve voluntary generation of multiple single responses given a single cue or stimulus; however, the equivalence of different tasks has been questioned. For example, Turner (1999) argued that although word fluency is a generative task it places little demand on novelty as it does not require a subject to go beyond stored knowledge. By contrast, Turner suggested that ideational fluency tests tap the ability to generate new and imaginative (i.e., novel) responses in addition to stored responses. Turner also argued that design fluency tasks that require drawing of abstract designs (i.e., objects that cannot be recognised) place even more demands on generative skills as there is little use of stored knowledge in this task. If these criticisms are applied to gesture fluency, the demands are similar to ideational fluency because the meaningless condition requires novel gesture generation whilst the meaningful condition taps stored responses. A further consideration is that, presumably, tasks that tap stored knowledge place high demand on a search or retrieval strategy (possibly lexical/semantic); whereas, tasks that require a novel response place more demands on developing a new strategy to create and generate a novel or imaginative response. Moreover, suppression of automatic responses would vary depending on whether a task taps stored knowledge or not.

1.2 THE ROLE OF THE FRONTAL LOBES IN LANGUAGE GENERATION

An impairment of language generation processes resulting in reduced verbal output is frequently observed in patients with frontal lobe damage and the left frontal lobe has been implicated in the production and organisation of verbal output (Benton, 1968; Cappa & Vignolo, 1999; Luria, 1973; Milner, 1982). An inability to produce words in connected sequences that results in reduced and nonfluent verbal output can be related to articulation or syntactic difficulties. For example, difficulty in performing oral movements for the articulation of speech sounds and/or sequencing these into words results in reduced and nonfluent verbal output. This has also been termed oral apraxia (or apraxia of speech) and has been associated with damage to the left frontal lobe (for review see De Renzi & Faglioni, 1999) and particularly the insula (Dronkers, 1996). Nonfluent verbal output can also result from the omission of grammatical words (e.g., conjunctions) from an otherwise normal sentence (for review see Miceli, 1999). Alternatively, as will be discussed below, reduced and nonfluent speech may arise because of initiation and/or elaboration difficulties. In a clinico-anatomical study of a large number of aphasic patients, low speech fluency was associated with damage to the left inferior frontal region and underlying subcortical structures (Kreisler et al., 2000). Also related to fluency and the left frontal lobe is the extreme case of mutism, or absence of speech. Mutism can result from damage confined to the superior medial (parasagittal) frontal region or brief mutism that rapidly recovers may present following small supplementary motor area lesions (Alexander, Benson, & Stuss, 1989). Reduced verbal output is a central feature in the nonfluent forms of clinically defined aphasias (Goodglass & Kaplan, 1983) and it may present in the context of degenerative or acquired conditions.

1.2.1 Nonfluent Progressive Aphasia

It is only towards the end of the 20th Century that the neurodegenerative condition of *nonfluent progressive aphasia* was recognised as a distinct clinical disorder. Primary progressive aphasia was initially defined as a slowly progressive aphasia without generalised dementia (e.g., Mesulam, 1982; Mesulam & Weintraub, 1992; Weintraub, Rubin, & Mesulam, 1990). More specifically, diagnostic criteria proposed that a progressive language deterioration with preservation of nonverbal abilities and activities of daily living should occur for at least 2 years in order to warrant a diagnosis of primary progressive aphasia (Mesulam et al., 1992). Based on early descriptions of the language disorder in primary progressive aphasia, Hodges and Patterson (1996) explicitly outlined two distinct forms: semantic dementia and nonfluent progressive aphasia. The cognitive profile of nonfluent progressive aphasia was characterised by impaired speech fluency, phonological errors in spontaneous speech and/or naming, deficits in the production and comprehension of syntax, relatively preserved single word comprehension, intact visual perceptual and non-verbal intellectual functions, and relatively preserved episodic and autobiographical memory. More specifically, speech was characterised not only as nonfluent, but also containing distortions with prominent articulatory difficulties. In addition, phonemic word fluency was suggested to be more impaired than semantic word fluency. Although the presenting form of this nonfluent progressive language disorder has been argued to be heterogeneous (Croot, Patterson, & Hodges, 1998; Tyrrell, Warrington, Frackowiak, & Rossor, 1990), the nonfluent verbal output remains a core and distinguishing feature.

Within the cluster of neurodegenerative conditions, nonfluent progressive aphasia has been recognised as one of the clinical entities of frontotemporal degeneration, which is distinct from Alzheimer's Disease (e.g., Neary et al., 1998; Neary, 1999). The focus of atrophy is in the left peri-sylvian region (Cappa, Perani, Messa, Miozzo, & Fazio, 1996; Hodges, 2001) with recent PET studies showing hypometabolism in the left anterior insula and frontal opercular region (Nestor et al., 2003; Gorno-Tempini et al., 2004). The underlying pathology is less clear, however, as some patients presenting with this nonfluent language disorder have confirmed Alzheimer's pathology (e.g., Croot, Hodges, Xuereb, & Patterson, 2000; Greene, Patterson, Xuereb, & Hodges, 1996).

1.2.2 Broca's Aphasia

Historically, disruption to speech and verbal output has been linked to the left frontal lobe and what is referred to as Broca's area (Broca, 1861; Hughlings Jackson, 1879, reprinted in Taylor et al., 1932; Head, 1926). Although reference to this can be found prior to Broca, it was his precise demonstration of damage to the posterior left frontal lobe with a disturbance to language output that established a specific relationship. Broca's area includes the pars opercularis and pars triangularis, also referred to as Brodmann Areas 44/45 or the posterior portion of the left inferior frontal gyrus (LIFG). *Broca's aphasia* is firmly established as a clinical syndrome, although there has been a long debate surrounding the exact clinical features and underlying anatomy (for discussion see Cappa et al., 1999; Taubner, Raymer, & Heilman, 1999). Broca's aphasia is characterised by sparse and nonfluent verbal output that is effortful, hesitant, somewhat dysprosodic and agrammatic. In addition, it presents in the context of impairments in repetition, reading and naming (e.g., Alexander et al., 1989; Goodglass et al., 1983; Stuss et al., 1986). Although comprehension is thought to be relatively better, evidence suggests syntax comprehension is impaired (e.g., Caramazza, Capitani, Rey, & Berndt, 2001). According to early conceptualisations of the language system, Broca's aphasia was viewed as arising because of damage to the motor output area (Lichtheim, 1885).

1.2.3 Transcortical Motor Aphasia

In 1885, Lichtheim described *transcortical motor aphasia* as a language output disorder characterised by extremely reduced verbal output in the context of well-preserved nominative and speech production skills. According to Lichtheim's (1885) conceptualisation, transcortical motor aphasia was due to a disconnection of conceptual processes from the output motor areas. In 1948, Goldstein identified a defect in the impulse to speak as one of the two main types of transcortical motor aphasia. The first type was investigated by Luria (1966; 1970) and will be discussed in detail below (1.3.1). The second type involved partial damage to the motor speech area resulting in defects to the motor act of speaking.

Since Goldstein's pioneering work in 1948, several studies of transcortical motor aphasia have been reported (e.g., Alexander & Schmidt, 1980; Alexander, Naeser, & Palumbo, 1990; Ardila & Lopez, 1984; Benson & Ardila, 1996; Berthier, 1999; Freedman, Alexander, & Naeser, 1984; Goodglass et al., 1983; Luria, 1970; Cappa et al., 1999). These studies identified different sub-clinical types of transcortical motor aphasia. In the majority of studies, at least two broad types of transcortical motor aphasia have been identified: pure and mixed. Pure transcortical motor aphasia has been described as being characterised by sparse speech output with near normal repetition, comprehension, grammar and articulation. Pure transcortical motor aphasia has also been termed dynamic aphasia subtype (Ardila et al., 1984), 2nd profile (Alexander et al., 1990), and Type I (Benson et al., 1996). Mixed transcortical motor aphasia has been described as being characterised by articulatory and prosodic impairments and has also been termed supplementary motor area subtype (Ardila et al., 1984), 1st profile (Alexander et al., 1990), and Type II (Benson et al., 1996). A few studies have proposed that more than two types of transcortical motor aphasia exist. For example, Freedman et al. (1984) suggested the existence of four subtypes: classical transcortical motor aphasia and three near-variants. Classical transcortical motor aphasia is characterised by reduced propositional speech without any other linguistic impairments (i.e., articulation, naming, comprehension, and repetition are normal). However, it should be noted that 5/7 patients that Freedman identified with classical transcortical motor aphasia were also anomic. Near-variant syndromes of transcortical motor aphasia are characterised by impairments of articulation, stuttering or comprehension in the context of reduced verbal output and intact repetition.

These accounts of transcortical motor aphasia have primarily focussed on describing clinical symptoms. Since Lichtheim's seminal work in 1885, there has been a surprising paucity of theoretical accounts for transcortical motor aphasia. Indeed, no theoretical explanation has been offered regarding the cognitive mechanism underpinning the core impairment of transcortical motor aphasia, namely the marked reduction in verbal output. Luria (1966; 1970; 1973) was the first to provide a theoretical account and designated the term dynamic aphasia that will be adopted henceforth.

1.3 DYNAMIC APHASIA

1.3.1 Luria's Account of Frontal Dynamic Aphasia

Luria investigated the underlying mechanism of the first type of transcortical motor aphasia described by Goldstein (1948) and initially referred to it as a gross disturbance to the "dynamics of verbal thinking" (1966, p. 358-360). Luria subsequently coined the term *frontal dynamic aphasia* (Luria & Tsvetkova, 1968; Luria, 1970; 1973). The core feature of *frontal dynamic aphasia* is a disturbance in propositional language such that spontaneous propositional speech is severely reduced, with a key being an inability to "use speech for generalising or for the expression of thoughts and desires" (Luria, 1970, p. 199). These patients were completely incapable of spontaneous expression and storytelling, particularly if long narratives were required. For example, Luria reported that when patients with dynamic aphasia were engaged in a storytelling task they complained of an "...emptiness in the head...." as if their thoughts "...stand still and don't move.." (1970, p. 200). In contrast, their ability to answer direct questions was satisfactory. Thus, a sentence may be produced but difficulty remains in the formation of thoughts in connected novel speech. Luria referred to the loss of the ability to use words in a dynamic or predicative manner, as opposed to using words in a designative or nominative manner. For instance, Luria described that patients could name an object standing before him relatively easily, but that expressing verbally any kind of desire or thought about it was not possible. Luria showed that patients with dynamic aphasia did not have any naming, reading and repetition impairments. Luria thought the associated structures to be the lower part of the left frontal lobe just anterior to Broca's area, with the premotor cortex remaining intact.

Luria's (1966; 1970; 1973) account of dynamic aphasia focussed on an inability to form a *linear scheme of a sentence*. This was explained as a breakdown in the transitional stage of inner speech, which translates the general plan into a linear scheme of a sentence. According to Luria, propositional speech is initiated by a plan.

This account of dynamic aphasia assumed that the original plan or intention was present. However, a subsequent breakdown in internal speech resulted in a failure to form the linear scheme and, thus, reduced propositional speech.

1.3.2 Dynamic Aphasia after Luria: Patients and Accounts

Since Luria, approximately 9 patients presenting with dynamic aphasia have been described in the literature. A detailed investigation was conducted by Costello and Warrington (1989) of a patient (ROH) who presented with dynamic aphasia following a left posterior frontal lesion. ROH presented with intact naming, comprehension, repetition and reading skills, but an almost complete lack of spontaneous speech. For example, when asked to describe his last holiday he produced only "*I'm....*" in 30 seconds. One of the prominent features was his poor performance on phrase and sentence generation tasks. In these tasks, ROH was given a word (e.g., *run*) and asked to generate a sentence incorporating it or a phrase (e.g., *The children were...*) and asked to generate a phrase to complete it. In a further sentence generation task ROH was given a complete sentence and asked to generate a second related sentence. He either failed to produce a response or his response latencies were extremely slow. However, the few responses that he did produce were normal in form and content. In particular, no morphological or syntactic errors were present. No formal investigation of syntactic processing skills was reported; however, his performance was noted to be impaired on a sentence construction task involving rearranging individual words to form a meaningful and grammatical sentence. His impaired performance led the authors to hypothesise the underlying deficit to be a selective impairment in verbal planning in the context of his average performance on the Picture Arrangement subtest of the WAIS. This deficit was thought to be prior to the implementation of narrative expressive speech.

A recently reported patient (ADY) was stated to resemble ROH (Warren, Warren, Fox, & Warrington, 2003). ADY presented with dynamic aphasia in the context of frontal lobe degeneration. MRI showed ADY had bi-frontal atrophy that was more marked on the left than right and included the inferior frontal gyri and frontal opercula. ADY's speech was described as grossly impoverished although it was grammatical and without errors. Reading and repetition skills were normal whilst naming and sentence comprehension skills were mildly impaired. ADY had some difficulty on word and sentence generation tests. Specifically, ADY was poor at generating a single word to complete low probability sentences (e.g., *There was nothing wrong with the…*). In addition, ADY was poor when generating a sentence from a single word (e.g., *garage*) or elaborating a given sentence (e.g., *The children listened to the story* ADY elaborated to *The children were listening intently to the exciting story*). By contrast, music generation skills were intact. Warren and colleagues (2003) attributed ADY's verbal generation deficit to defective generation of new pre-verbal messages, a process thought to be pre-linguistic and reflecting a similar impairment as that of dynamic aphasic ROH (Costello & Warrington, 1989).

Dynamic aphasia was the presenting problem in 3 patients with progressive supranuclear palsy (PSP; Esmonde, Giles, Xuereb, & Hodges, 1996). Frontal lobe atrophy was noted in 2 of these patients. These PSP patients had severely reduced propositional speech in the context of preserved naming and comprehension skills. Repetition was said to be intact, although it was not formally tested. In narrative and picture description tasks these 3 patients presented with reduced verbal output that was characterised by morphological and syntactic deficits. Phrase generation tasks were given to 2 of these patients and their performance was very poor. For example, when given a phrase (e.g., *The girls had tried hard but…*) one patient produced no response for a number of phrases whilst the other gave a high number of bizarre responses (e.g., *freedom*). All 3 patients performed poorly on standard verbal fluency tests, with phonemic fluency more impaired than semantic fluency. Esmonde and colleagues concluded that the PSP patients' language disorder most closely resembled Luria's designation of dynamic aphasia.

Dynamic aphasia was documented in KC who presented with a progressive language disorder in association with frontal lobe degeneration (Snowden, Griffiths, & Neary, 1996). KC's propositional language was profoundly reduced in both general conversation and storytelling tasks, despite well preserved naming, single word comprehension, and repetition. Similar to the 3 PSP patients described by Esmonde et al., KC's severely reduced verbal output was also characterised by some mild syntactic difficulties. But KC, unlike other dynamic aphasic patients, was unimpaired in phrase and sentence generation tasks. Similar to ROH, however, KC was impaired on a sentence construction task although only in the manual modality as she could verbalise the correct sentence. A SPECT scan indicated that KC had a reduction in the uptake of tracer in the frontal regions. KC's dynamic aphasia was accounted for by a failure in the temporal integration of propositional language. Snowden et al. (1996) viewed this failure as having many similarities to Luria's transitional stage of transcoding a plan or intention into the linear scheme of the sentence.

Following bilateral striatocapsular infarctions, CO presented with dynamic aphasia (Gold et al., 1997). CO's verbal output was described as being limited to single words or short phrases, but with normal articulation and no phonological or semantic errors. This was particularly when asked open-ended questions, in contrast to producing several short phrases when asked to describe pictorial scenes. Naming, repetition and comprehension were normal. CO's ability to generate words on phonemic and semantic fluency tasks was impaired, as was his ability to generate designs. Dynamic aphasia was only observed after the second infarct, which involved the right hemisphere, and was also associated with impaired design fluency performance. Thus, it was tentatively suggested that dynamic aphasia may not be restricted to the verbal domain or to language, and may be related to associated executive dysfunction. In addition, CO performed poorly on a semantic sorting task but only when items were closely related and no retrieval cue was provided. CO's dynamic aphasia was attributed to a specific impairment in the development of a "strategy to search the lexical/semantic network and difficulty in endogenous concept formation" (Gold et al., 1997; p. 390).

A treatment study was based on the dynamic aphasia of MP (Raymer, Rowland, Haley, & Crosson, 2002). Following an infarction to the left frontal subcortical region and part of the anterior insula, MP's verbal output was impoverished in conversation, picture description and when retelling familiar stories (e.g., Noah's Ark). The authors noted that MP would often initiate an utterance but then stop to think of a word or phrase, and then he would either restart an utterance or reiterate an already completed sentence. In addition to reduced verbal output, semantic word fluency performance was impaired. By contrast, MP's repetition, reading and comprehension abilities were relatively well-preserved. MP's sentence generation abilities were reduced in response to single words that activated a number of competing response options. This pattern is in keeping with the performance of the dynamic aphasic patient ANG (see below). Treatment of reduced verbal initiation involved a technique that paired nonsymbolic limb movements with cued sentence production. This technique has predominantly been used to facilitate single word production. After treatment, MP's ability to generate semantically and grammatically correct sentences in response to trained and untrained words improved, more so for the trained words. Raymer et al. hypothesised that initiating movement sequences may activate the intact right prefrontal cortex. This activation may subsequently engage the left prefrontal cortex, which is involved in language initiation. Facilitation of verbal initiation was thought to involve complex movements, not simple repetitive movements, as only the former has been associated with activation of the prefrontal cortex (Pickard & Strick, 1996). The extent to which impaired verbal generative ability is specific to the verbal domain is of interest, particularly given this treatment involving the use of a nonverbal strategy. In the context of dynamic aphasia, apart from preserved music generation skills in ADY (Warren et al., 2003), the relationship between verbal and nonverbal generation has not been directly investigated.

1.3.3 A New Account of Dynamic Aphasia: The Case of ANG

In a previous study, my colleagues and I reported an experimental investigation of the dynamic aphasia of ANG who had a malignant left frontal meningioma particularly impinging on Brodmann's Area (BA) 45 (Robinson, Blair, & Cipolotti, 1998). ANG's propositional language output was extremely reduced. She rarely initiated conversation and her responses to questions were sparse consisting of either a single word or sentence. For example, when asked about what had happened in former Yugoslavia, she only produced, after a long pause *"..civil war.."*. Similarly, when invited to describe the contents of "Awakening" by Oliver Sacks, one of her favourite books, she replied, after a long pause, *"...it's about a sleeping sickness epidemic...it's a wonderful book.."*. She also had pronounced difficulties defining words that were well within her vocabulary. For example on the vocabulary subtest of the WAIS-R she could not define words such as *repair* for which she replied *"..difficult to express"* and *fabric* for which she replied *"..it's a..."*. However, when she did produce sentences in response to simple questions or in the word definition task her speech was fluent, well articulated, and with normal prosody and syntax. No morphological, phonological and/or semantic errors were noted. In contrast to her markedly reduced speech output, her repetition performance was flawless for three-syllable low frequency words and sentences. Nominal and single word comprehension abilities were intact.

ANG's performance was severely impaired on word, phrase and sentence generation tasks. However, she was able to simply describe pictorial scenes or complex actions on the Reporter's Test (De Renzi & Ferrari, 1978b; e.g., "you have selected 4 squares and 4 circles, you have then tapped the circles harder than the squares..."). In addition, ANG was able to pass a sentence construction task that was failed by ROH (Costello et al., 1989) suggesting that her verbal planning skills were intact, unlike ROH. A series of experimental investigations found that ANG's severe generative impairment was only present for tasks involving stimuli that activated many competing response options. Thus, ANG was unable to generate a sentence from a common word that has multiple referents (e.g., *table* – I eat on the dining table; We inherited an antique table; I have a wooden bedside table). By contrast, she had no difficulty generating a sentence from a proper noun that has singular or few referents and, hence, a dominant or 'prepotent' response (e.g., *Gandhi* – Gandhi is an Indian pacifist). A second task demonstrated that ANG was also impaired in generating a phrase to complete a phrase with low response predictability (e.g., *The man walked into the house…*) compared to high response predictability (e.g., *The man walked into the cinema…*) as the former should activate more response options than the latter with no clear prepotent response identified. In a third experimental test, ANG was found to be impaired for word pairs with low inter-word associations (e.g., *cat-neck*) whereas she was unimpaired in generating a sentence from word pairs with high inter-word associations (e.g., *giraffe-neck*). Although both *giraffe-neck* and *cat-neck* will activate response options associated with their individual words, only for *giraffe-neck* will both individual words strongly activate the same dominant response option *"..giraffes have long necks.."*. Thus, word pairs with high inter-word associations strongly activate a 'prepotent' response in addition to weakly activating other response options. In contrast, word pairs with low inter-word associations activate many competing response options to a comparable degree. ANG's performance on both phrase and sentence generation tasks was determined by manipulating the number of potential response options associated with the stimulus. This contrast between her impaired performance when many response options were activated and her relatively preserved performance on tasks where the number of response options was constrained, was also present in her performance on word fluency tasks. ANG had profound difficulty in generating words from phonemic and open semantic categories but she had reasonable skill in generating words from restricted semantic categories (e.g. books of the Bible). This pattern is opposite to that observed in Alzheimer's disease and semantic dementia (Hodges, Salmon, & Butters, 1992; Hodges, Graham, & Patterson, 1995; Hodges & Patterson, 1995).

ANG's dynamic aphasia was accounted for by an impairment in the ability to select a verbal response option whenever a stimulus activated many competing responses. This account focused on the basic idea that activated verbal response options compete with each other through mutual inhibition. The greater the number of competing verbal response options activated by a stimulus, the greater the amount of inhibition each response receives from its competitors and the lower the probability of one response option becoming dominant. In this account, a control system is necessary to resolve the conflict by allowing one verbal response option to become dominant. For phrase and sentence generation, when stimuli activate only a single response option, it will be dominant and receive minimal inhibition from competitors, thus, additional activation for conflict resolution is negated. In contrast, when stimuli activate many response options, there is no automatic activation of one response and, in this case, the control system must preferentially activate one of the competing response options. We suggested that this system was damaged in ANG, directly leading to a failure on phrase and sentence generation tasks involving stimuli that activate many potential response options.

1.4 AIMS OF THIS THESIS

This phenomenon first observed in ANG's propositional language prompted the investigations that will be detailed in this thesis. Thus, the aim is to explore the contribution of the frontal lobes to propositional language and the voluntary generation of novel verbal and non-verbal responses. In particular, what are the cognitive mechanisms involved in generating propositional language? Are these cognitive mechanisms specific to language or do they encompass the generation of both verbal and non-verbal responses? What are the neuroanatomical substrates that support these cognitive mechanisms? What is the role of the frontal lobes in the voluntary generation of verbal and non-verbal responses? In order to address these questions the thesis is organised as follows. Chapter 2 and 3 are investigations of two single cases that present with a severe impairment in propositional language, namely dynamic aphasia. These two cases (and ANG) suggest the existence of two functionally distinct cognitive mechanisms responsible for the generation of propositional language that are underpinned by different neuroanatomical substrates. Chapter 4 investigates the neuroanatomical substrates of the cognitive mechanisms involved in propositional language generation and voluntary generation of verbal and non-verbal responses on fluency tasks. This is conducted in a group study that enrolled 39 patients with focal frontal lesions and 15 patients with posterior lesions. The convergence of the findings from the dynamic aphasic cases, the group study and the neuroimaging literature are discussed in this Chapter 4. General conclusions are drawn in Chapter 5.

CHAPTER TWO: DYNAMIC APHASIC PATIENT CH

2.1 INTRODUCTION

The dynamic aphasia of ANG (Robinson et al., 1998) was accounted for by an impairment in the ability to select a verbal response option whenever a stimulus activated many competing responses. However, the study of ANG did not address whether this applied to single word generation, as well as phrase and sentence generation, as no formal investigation of single word generation was undertaken. Moreover, the question of whether this deficit was specific to the language domain remains open as her performance on non-verbal generation tasks was not documented. Another consideration is that there are now several alternative accounts that attempt to explain dynamic aphasia (detailed in Chapter 1 - 1.3.2). Most of these accounts interpret dynamic aphasia broadly within the domain of language; however, some accounts extend beyond this domain. This chapter will attempt to address the two unanswered questions raised by ANG, and in the process will consider all of the accounts of dynamic aphasia, including that proposed by myself and colleagues to account for the pattern of performance in ANG.

First, the clinical syndrome of dynamic aphasia needs to be clarified. From Luria's clinical descriptions, it is clear that some cases with dynamic aphasia presented with additional articulatory, linguistic, or frontal impairments. For example, Luria (1970) provided qualitative descriptions of 12 patients with decreased propositional speech (see Table 1). Case 7 was described to have effortful articulation and errors when repeating more than one word (p. 203), whereas Case 8 produced disconnected grammatically disordered word sequences when telling a story (p. 207). From his descriptions, it is clear that heterogeneity exists and that dynamic aphasia in a pure form was present in only a few of Luria's series. Indeed, most patients presented with impairments in speech production, repetition, naming, or comprehension ability. In all cases, however, the central feature was a disturbance to propositional speech that was *disproportionate* to any other language impairment.

From the clinical descriptions in the literature, it appears that dynamic aphasia can present in either a *pure* or *mixed* form. Luria (1966; 1970) hinted that the more pure form of dynamic aphasia might not involve the posterior parts of the left frontal lobe and that if the premotor system was involved anteriorly, dynamic aphasia may be accompanied by additional language impairments (e.g., a disturbance to the motor aspects of speech). In both the pure and mixed form, the hallmark of dynamic aphasia is severely reduced propositional speech. However, the pure variant consists of this hallmark in the absence of any other language impairment (e.g., grammatical, articulatory, or lexical). *Pure* dynamic aphasic patients have intact naming, repetition, and comprehension skills (for examples see Costello et al., 1989; Gold et al., 1997; Robinson et al., 1998; Table 1). Examples of the *mixed* variant of dynamic aphasia are Cases 7 and 8 described by Luria (1970) who presented with additional grammatical and articulatory difficulties (for other examples see Esmonde et al., 1996; Snowden et al., 1996; Warren et al., 2003; Table 1). Crucially, the core impairment of both the pure and mixed form of dynamic aphasia remains the same; namely, severely reduced propositional language skills in the context of relatively well preserved nominal, repetition, and word comprehension skills.

Another clinical consideration is that dynamic aphasic patients have been documented in the context of both neurodegenerative conditions and focal lesions. All of the neurodegenerative cases presented with the *mixed* form of dynamic aphasia. The 3 patients described by Esmonde et al. (1996) had the neurodegenerative condition of progressive supranuclear palsy (PSP). These PSP patients initially presented with mixed dynamic aphasia (see Table 1) as their reduced verbal output was agrammatical and mild difficulty was evident in syntactic comprehension. Two patients presented with mixed dynamic aphasia in the context of frontal lobe degeneration and a progressive language disorder (KC - Snowden et al., 1996; ADY - Warren et al., 2003; see Table 1). KC's dynamic aphasia was mixed as her verbal output was not only sparse but agrammatical. By contrast, ADY's verbal output was reduced although, unlike the other neurodegenerative cases, no syntactic difficulties or errors were noted; however, mild nominal and comprehension difficulties were evident.

A few cases of dynamic aphasia in focal lesions have been put on record. Most of the patients with focal lesions present with a *pure* form of dynamic aphasia, although not all. For example, ANG presented with a pure form of dynamic aphasia as no other language impairments were present. This was in the context of a meningioma that impinged on the left posterior frontal region (BA 45) (Robinson et al., 1998). Similarly, pure dynamic aphasia was documented in ROH following a posterior left frontal lesion (Costello et al., 1989; see Table 1) and CO following bilateral striatocapsular infarctions (Gold et al., 1997; see Table 1). By contrast, MP was noted to have mild nominal dysphasia and thus presented with mixed dynamic aphasia following a left frontal/subcortical infarction involving the anterior insula.

Table 1. *Summary of Language Functions in Dynamic Aphasia Cases*

	Luria[1] (*n* = 12)	ANG[2]	ROH[3]	PSP[4] (*n* = 3)	KC[5]	CO[6]	MP[7]	ADY[8]
Propositional Speech	x	x	x	x	x	x	x	x
Speech Production								
Articulation	x (4)	√	√	x mild (1)	√	√	√	√
Grammatical (Sentences)	x (6)	√	√	x mild (1)	x mild	√	√	√
Repetition								
Words	√ (2)	√	√	nt	√	√	√	nt
Sentences	x (2)	√	√	nt	√	√	√	√
Oral Naming (Pictures)	√ (4) x (7*)	√	√	√	√	√	x mild	x mild
Comprehension								
Words	√ (3)	√	√	x (1)	√	√	√	x mild
Sentences	√ (5) x (2)	nt	√	x mild (2)	x mild	√	√	x mild
Reading	√ (4) x (1)	√	√	nt	nt	nt	√	√

√ = intact; x = impaired; nt = not tested; ( ) = number of patients with this function reported; * = naming difficulties in propositional speech. 1. Luria, 1970. 2. Robinson et al., 1998. 3. Costello & Warrington, 1989. 4. Esmonde et al., 1996. 5. Snowden et al., 1996. 6. Gold et al., 1997. 7. Raymer et al., 2002. 8. Warren et al., 2003.

This chapter will consider the five accounts put forward to account for dynamic aphasia that were outlined in the previous chapter (1.3.2). Three positions attempt to account for dynamic aphasia within the domain of language. (1) Luria (1970; 1973) first proposed that the critical deficit is in the transitional stage of forming a linear scheme of a sentence. More specifically, Luria argued that there is a breakdown in the translation of internal speech into a plan that subsequently initiates propositional speech. (2) Costello and Warrington (1989) suggested that dynamic aphasia is due to a selective impairment in verbal planning, a deficit recently defined as a defective message generation (Warren et al., 2003). This was thought to be prior to the implementation of narrative expressive speech. (3) Robinson et al. (1998) hypothesised that dynamic aphasia is underpinned by an inability to select between competing verbal responses. This is when many competing verbal response options are activated by a stimulus with no prepotent or dominant response available. Two positions attempt to account for dynamic aphasia in terms of a deficit extending beyond the domain of language. (4) Gold et al. (1997) suggested that dynamic aphasia is attributable to an impairment in forming an efficient strategy to search the lexical/semantic network. This impairment was speculated to be associated with executive dysfunction. (5) Raymer et al. (2002) hinted that the deficit underpinning dynamic aphasia may not be selective for verbal generation but may involve, more generally, the ability to generate verbal and nonverbal responses.

This chapter details the case of CH who presented with a *mixed* form of dynamic aphasia. This was in association with frontotemporal degeneration and nonfluent progressive aphasia. CH had a marked reduction in propositional speech in the context of relatively intact naming, reading, and single word repetition and comprehension skills. In addition to a slight dysarthria, there were additional articulatory and grammatical difficulties in spoken language. The aim was to investigate the underlying mechanism responsible for the core impairment in dynamic aphasia; namely, reduced propositional language. A second aim was to investigate the extent to which this verbal generation impairment was specific to the verbal domain.

2.2 CASE REPORT[4]

CH is a 60 year-old, right-handed, retired electronics lecturer who subsequently worked as a quality control manager for an electronics company. In September 1998, following a 4-year history of progressive nonfluent speech difficulties, CH was referred to the Department of Neuropsychology at the National Hospital for Neurology and Neurosurgery. Neurological examination was normal apart from the cognitive impairments described below.

[4] The data presented in this chapter have been published: Robinson, G., Shallice, T., & Cipolotti, L. (2005). A failure of high level verbal response selection in progressive dynamic aphasia. *Cognitive Neuropsychology, 22(6)*, 661-694.

A MRI brain scan in December 1998 revealed focal atrophy in the left frontal lobe, especially involving the superior and inferior frontal gyri (see Figure 1). The insula is involved in the left with some atrophy of the inferior part of the left superior temporal gyrus. The areas involved with maximal atrophy include BA 44 and 22. Closer examination of the MRI scan was undertaken in order to ascertain which areas were unequivocally involved. Thus, left and right frontal and temporal areas were investigated. In the left frontal lobe, BA 44 was moderately atrophic and BA 43, 45, and 46 were mildly atrophic. BA 47 was normal bilaterally. In the right frontal lobe, BA 43, 44, 45, and 46 were normal. In the temporal lobe, BA 22 was moderately atrophic on the left and only mildly atrophic on the right. BA 21 and 38 were only mildly atrophic on the left and normal on the right. BA 37 was normal bilaterally. In addition, BA 41 and 42 (primary auditory cortex) were only indicative of probable atrophy on the left and were normal on the right. A clinical diagnosis of frontotemporal dementia was made.

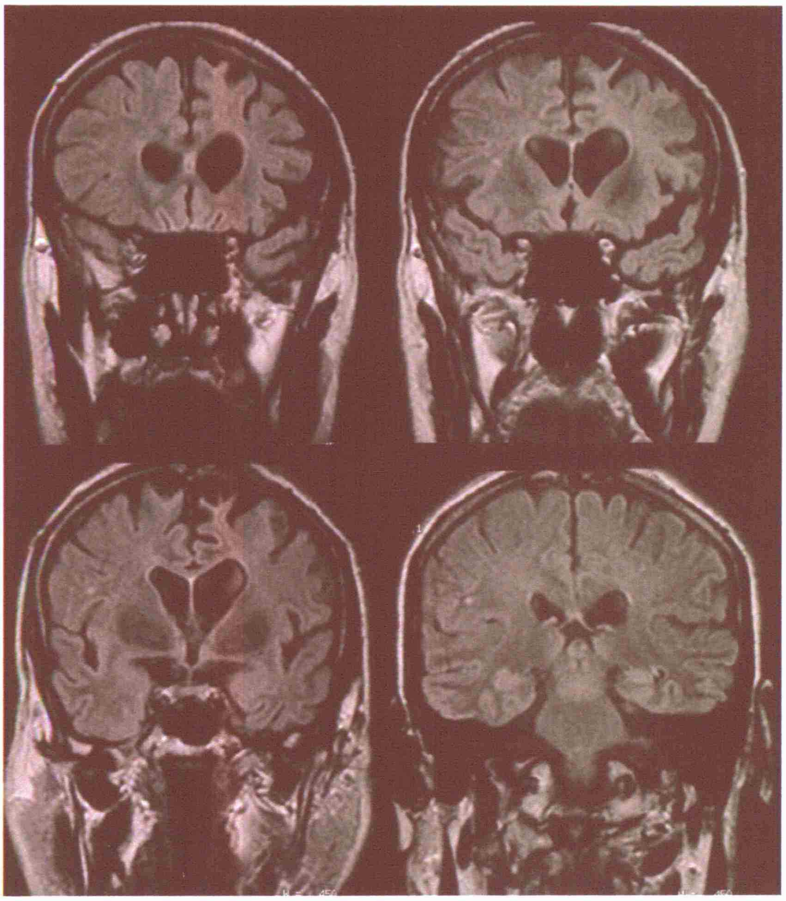

Figure 1. Coronal T_1 weighted MRI of Dynamic Aphasic CH

Initial assessment of cognitive functioning was undertaken in October 1998. He was assessed on two further occasions in June 1999 and August 2000. Only the first two assessments will be reported as these were carried out at the same time as the experimental investigations. Importantly, CH's condition was relatively stable between these two assessments as no significant decline was observed in the cognitive baseline.

2.2.1 Cognitive Function Baseline

CH was assessed on a shortened form of the Wechsler Adult Intelligence Scale - Revised (WAIS-R; Wechsler, 1981; see Table 2). On both assessments, he obtained low average Verbal IQ's. On the first assessment he obtained a superior Performance IQ and on the second assessment he obtained a high average Performance IQ. On an un-timed test of non-verbal general intelligence, the Advanced Progressive Matrices Set 1 (Raven, 1976a), he performed in the high average range on the first assessment and the average range on the second assessment. As his pre-morbid level of optimal functioning was estimated to be superior on the basis of occupational and educational background, these results indicate a moderate degree of intellectual decline, particularly in the verbal domain. Verbal and visual memory functions were normal on both assessments. His performance was in the good average range or above on recognition memory tests (Warrington, 1984; 1996). Visual perceptual and visuo-spatial skills remained normal as assessed by two sub-tests from the Visual Object and Space Perception Battery (Warrington & James, 1991). Oral calculation skills were mildly impaired as he performed in the low average range on the Oral Graded-Difficulty Calculation Test (Jackson & Warrington, 1986). Psychomotor speed was somewhat slowed on the Symbol Digit Modalities Test (Smith, 1982). On the first assessment, a severe orofacial apraxia was evident. Similarly, on the first assessment a mild limb dyspraxia was observed, as his copy of meaningless gestures with both hands was slightly weak.

2.2.2 Frontal Executive Function

CH's performance on a series of tests considered to be sensitive to frontal lobe damage was only impaired on verbal fluency tasks and the Brixton Spatial Anticipation Test (Burgess et al., 1996a; see Table 2). On verbal fluency tasks his performance was severely impaired for phonemic tasks. Verbal fluency for semantic categories was considerably better, although impaired. In contrast, his performance was normal on a modified version of the Wisconsin Card Sorting Test (Nelson, 1976) and the Trail Making Test (Army Individual Test Battery, 1944), although mildly slowed on the second assessment. The Hayling Sentence Completion Test (Hayling; Burgess et al., 1996b) was only administered in the first assessment. His performance was impaired on Section 1 (response initiation) as he was unable to complete 5/15 sentences and responded with "*yeah*" to a further sentence. However, on Section 2 (response suppression) he was able to complete all sentences with unrelated responses and performed in the average range for both time and errors.

Table 2. *Cognitive Baseline and Frontal Executive Function Scores for CH*

	October 1998	June 1999
	Cognitive Baseline Scores	
Verbal IQ	81	82
Digit Span*	4	6
Vocabulary*	6	4
Arithmetic*	8	8
Similarities*	9	9
Performance IQ	120	111
Picture Completion*	13	12
Picture Arrangement*	10	12
Block Design*	14	12
Advanced Progressive Matrices	8/12 (75-90th %ile)	6/12 (50-75th %ile)
Recognition Memory Tests		
Words	44/50 (50-75th %ile)	47/50 (75-90th %ile)
Faces	48/50 (> 95th %ile)	44/50 (50-75th %ile)
Topographical	-	23/30 (50th %ile)
Object Decision	17/20	19/20
Cube Analysis	10/10	10/10
Oral calculation	8/24 (25th %ile)	-
Symbol Digit Modalities Test	35 (M = 41.5 ± 8.6)	25 (M = 41.5 ± 8.6)
Limb Praxis	left = 7/10, right = 8/10	

Frontal Executive Function Scores		
Word Fluency		
Phonemic F	2	7
A	1	1
S	5	7
FAS Total (M = 42, SD = 12.1)#	8 (<1st %ile)	15 (<1st %ile)
Semantic		
Animals (M = 18.2, SD = 4.2)#	11 (< 10th %ile)	9 (< 5th %ile)
Food	12	10
Tools	11	-
Politicians	-	8
Farm Animals	-	5
Countries	-	6
Brixton Spatial Anticipation Test	Impaired (SS = 1)**	-
Wisconsin Card Sorting Test	6/6 categories	6/6 categories
Trail Making Test A	56" (25-50th%ile)	52" (25-50th%ile)
B	130" (25-50th%ile)	152" (10-25th%ile)
Hayling Sentence Completion Test	Low Average (SS = 4)**	-
Section 1 (sensible completion)	Impaired (SS = 1)**	-
Section 2 (unrelated completion)	Average (SS = 6)**	-
Section 2 (errors)	Average (SS = 6)**	-

Spreen and Strauss, 1998; SS = scaled score; * = age scaled score; ** = SS is from 1-10 with 6 being average.

2.2.3 Language Function Baseline

The language baseline was completed between October and November 1998. A second assessment of a select number of language functions was completed at the same time as the second cognitive assessment (June 1999).

2.2.3.1 Speech Production

Spontaneous speech was extremely sparse, effortful, somewhat dysprosodic, and slightly dysarthric. Initiation of conversation was rare, and he was only able to produce phrases of no more than four to five words, often responding to questions with a single word. No phonological, semantic, or word order errors were made. Although the content was appropriate, there was some evidence for initiation of articulation difficulties that resulted in false starts (e.g., wiping → wip-wiping). His descriptions of complex scenes (Beach, Cookie Theft) were reduced, nonfluent, and agrammatical in that there were relatively few function words (e.g., "boy jump, make a sand castle, tip-pee over boat..."). The sparseness of speech precluded formal analysis of one speech sample elicited from a story (e.g., Quantitative Production Analysis [QPA]; Berndt, Wayland, Rochon, Saffran, & Schwartz, 2000). However, CH's responses from three other tasks that elicited speech from pictorial stimuli were analysed. The three tasks were: (1) Descriptions of Complex Scenes (Beach, Cookie Theft); (2) Descriptions of simple scenes from the Psycholinguistic Assessments of Language Processing in Aphasia (PALPA; Kay, Lesser, & Coltheart, 1992; see 2.3.2.3 below); and (3) Story Generation from Pictorial Scenes (see below 2.3.2.5). The three tasks provided a speech sample of 151 words (of these 69 nouns, 35 verbs) that formed the basis for calculating some QPA measures. A broad comparison was possible between CH's speech production and the descriptive statistics reported in the QPA training manual for a sample of nonfluent aphasic patients and normal control subjects by Berndt et al. (2000). The most striking measure was CH's markedly reduced speech rate of 11 words/minute, calculated from Task 1 (nonfluent aphasic patients = 39.0, normal control subjects = 160.8). The overall proportion of verbs [verbs/(verbs + nouns)] CH produced was 0.34 (nonfluent aphasic patients = 0.37, SD = 0.10, normal controls = 0.48, SD = 0.06). Of note, the proportion of verbs CH produced on Task 1 and 3 involving more complex scenes was just within the range of normal controls (Task 1 = 0.44, Task 3 = 0.43). By contrast, CH produced an extremely low proportion of closed class words [(narrative words – open class words)/narrative words] (CH = 0.24, nonfluent aphasic patients = 0.41, SD = 0.11, normal control subjects = 0.54, SD = 0.04).

In contrast to his severely reduced spontaneous speech, the Reporter Test was performed virtually at ceiling (De Renzi et al., 1978b; see Table 3a). This test requires the production of a sentence to describe a sequence of actions executed by the examiner. It taps the ability to observe a series of actions, comprehend the actions, formulate a narrative that describes the actions, and produce a narrative of speech that explains the action sequence accurately so that it can be executed by a third party. CH could explain the sequence of actions executed by the examiner, although his descriptions were agrammatic in that some function words were omitted (e.g., to the action: "Touch the green circle, then take the green square" CH said "*...touch green circle, take that one, green square...*"). Only two errors were recorded: a response that included gestures of the action and an incomplete description of the entire action sequence (i.e., to the action: "Put the red circle on the green triangle" CH said "*...circle on top...*"). His agrammatism suggests that he had difficulties in the formulation of a sentence structure. However, his preserved ability to describe the executed actions clearly indicated that he did not have a problem in verbal planning in the sense of Costello and Warrington (1989) on this particular task.

2.2.3.2 Repetition

CH's repetition skills were predominantly intact (see Table 3a). Repetition of consonant-vowel pairs (e.g., ba) was largely intact, although repetition of sequences of consonant-vowel pairs was poor (e.g., ba-ta-ka). Repetition of single digits was flawless. Single letter repetition was almost flawless except for the addition of "e" to three letters (i.e., s, n, and f → *esse, enne, and effe*). Word repetition skills were slightly weak (93% correct; 167/180). A very slight dysarthria was present. In addition, words repeated with some articulatory distortion but *without* phonemic errors were scored correct if the target was clearly identifiable (21/167 correct words). Word length and frequency effects were absent. The errors were mainly phoneme and morpheme omissions (e.g., wilderness → *wildness,* wonderful → *wonder*) and false starts (e.g., gigantic → *gi-gi-gi-gigantic*). Nonword repetition was weak (80%). The distribution of errors was similar to word repetition (e.g., false starts, inima → *in-inima*; phoneme omissions, crealth → *creal*) except for two real-word substitutions (i.e., ampty → *empty*, plonth → *plonk*). Repetition of cliche and non-cliche 3- to 7-word sentences was impaired (36.7% correct). Similar to spontaneous speech, the errors CH made in sentence repetition mainly consisted of omission of functors (73.7% errors; e.g., "Give him a hand" → "*Give him hand*"). However, there were a few errors involving the repetition of functors (21.1%; e.g., "He shut the door" → "*He shut the the door*") and there was only one instance of a content word omission.

It seems unlikely that CH's orofacial dyspraxia is a confound for his verbal generation impairment. A double dissociation has been documented where patients have been described with a relative preservation of repetition and/or speech production despite a severe orofacial apraxia (De Renzi, Piezcuro, & Vignolo, 1966; Tyrrell, Kartsounis, Frackowiak, Findley, & Rossor, 1991). Conversely, patients with impaired sentence generation but no orofacial apraxia are also on record (e.g., Gold et al., 1997).

Table 3a. *Spoken Language Scores for CH*

Task			October/November 1998	June 1999
		Production		
Reporter Test			-	13/15
		Repetition		
Phonemes		Single	5/6	-
		Sequence	3/10	-
Single digits			9/9	-
Letter names			21/24	-
Words	High frequency	1-syllable	30/30	-
		2-syllable	27/30	-
		3-syllable	28/30	-
	Low frequency	1-syllable	30/30	-
		2-syllable	28/30	-
		3-syllable	24/30	-
Nonwords		1-syllable	7/10	-
		2-syllable	10/10	-
		3-syllable	7/10	-
Sentences		Cliché	4/15	-
		Non-cliché	7/15	-
		Word Retrieval		
Graded Naming Test			24/30	26/30
Nouns			71/75	-
Verbs			58/75	-
		Word Comprehension		
Synonym Test			46/50 (75-90th %ile)	44/50 (50-75th %ile)
BPVS			145/150	-
Phoneme Discrimination			72/72	-
		Sentence Comprehension		
TROG			73/80	67/80
Token Test			11/15	-

TROG = Test for the Reception of Grammar; BPVS = British Picture Vocabulary Scale.

2.2.3.3 Word Retrieval

Picture naming skills were well preserved. CH's responses on the picture naming tasks were scored correct if they were clearly identifiable with all phonemes and contained no more than one phonological error. Using this slightly lenient criteria, on the Graded Naming Test (McKenna & Warrington, 1980) he performed in the high average range on the first assessment and in the superior range on the second assessment (see Table 3a). Across the two assessments there were 3 semantic errors (e.g., cowl → *shroud*), 2 phonological errors (e.g., yashmak → *ashmak,* tutu→ *petu*), 4 no responses and one instance of a phonological fragment (corkscrew → *c*). CH was given an oral naming task using a set of verbs and nouns matched for frequency (Kucera & Francis, 1982). In response to each picture, CH was asked to name the action or object depicted. He performed this task well, with oral naming of objects being significantly better than oral naming of actions ($\chi^2_{(1)} = 7.99$, $p < 0.005$, with Yates correction applied; see Table 3a).

2.2.3.4 Word Comprehension

Word comprehension skills were well preserved. His performance on the Synonym Test (Warrington, McKenna, & Orpwood, 1998) was in the high average range on the first assessment and upper end of the average range on the second assessment (see Table 3a). Similarly, his performance on the British Picture Vocabulary Scale (Dunn, Dunn, Whetton, & Pintilie, 1982) was almost at ceiling.

Word-sound processing skills were investigated using a phoneme discrimination task. CH was asked to judge whether two similar sounds (e.g., choke-joke, heef-haff) were the same or different. His performance on this task was flawless (see Table 3a). This indicates that his speech perception skills were intact and not contributing to repetition or production difficulties. In sum, his ability to understand word meanings and sounds was well preserved as his performance on word and word-sound comprehension tasks was intact.

2.2.3.5 Sentence Comprehension

Sentence comprehension skills were mildly impaired (see Table 3a). His performance on the Test for the Reception of Grammar (Bishop, 1983) was weak on the first assessment and mildly impaired on the second assessment. His errors were restricted to the syntactically complex sentences and not those indicative of semantic or vocabulary problems as detailed in the manual. On a shortened version of the Token Test (De Renzi & Faglioni, 1978a), his performance was weak.

2.2.3.6 Reading

CH's reading ability was weaker than expected. Reading aloud Arabic numerals and letter names was almost flawless (see Table 3b). On the National Adult Reading Test (NART; Nelson & Willison, 1991) he performed within the average range on the first assessment and the low average range on the second assessment. The effect of frequency, regularity, imageability, and lexicality on his ability to read aloud was further investigated using stimuli from the PALPA (Kay et al., 1992) and a revised version of Patterson and Hodges (1992; stimuli provided by Patterson). Word frequency was found to have a significant effect on CH's reading ability ($\chi^2_{(1)} = 11.12$, $p < 0.005$, with Yates correction applied). However, there was no effect of regularity or imageability (see Table 3b). Further, nonword reading was relatively good. Speed of reading a passage was significantly slower than controls. Numerous omission errors were noted, with omission of *"the"* representing the greatest proportion of these errors.

Table 3b. *Written Language Scores for CH*

Task	October/November 1998	June 1999
	Reading	
Arabic numerals	9/9	-
Letter names	38/40	-
NART	20/50 (25-50th %ile)	13/50 (10-25th %ile)
Words		
Regular	30/30	41/50 (HF); 33/48 (LF)
Exception	29/30	43/48 (HF); 27/46 (LF)
High Imageability	35/40	-
Low Imageability	35/40	-
Nonwords	20/24	-
Passage	108 seconds (M = 30, SD = 8)	129 seconds (M = 30, SD = 8)
	Spelling	
GDST (written)	20/30	19/30
Words		
Regular	50/50	28/28
Exception	39/50	25/32

NART = National Adult Reading Test; HF = high frequency; LF = low frequency;

GDST = Graded-Difficulty Spelling Test.

2.2.3.7 Spelling

Spelling skills were slightly weak as assessed by writing-to-dictation tasks. On a graded-difficulty spelling test (Baxter & Warrington, 1994) CH performed at an average level (stimuli partly from the PALPA, Kay et al., 1992; see Table 3b). Upon further investigation, a regularity effect was found for either Assessment (1: $\chi^2_{(1)}$ = 10.21, $p < 0.005$; and 2: $\chi^2_{(1)} = 5.1$, $p < 0.025$, with Yates correction applied).

2.2.4 Summary and Diagnosis

The cognitive baseline and frontal executive assessment showed that CH presented with a severe degree of verbal intellectual decline on the WAIS-R and a severe orofacial apraxia. In addition, mild dysexecutive impairment and a mild limb apraxia were evident. In contrast, his non-verbal intellectual functions were in keeping with his pre-morbid optimal level of function. Similarly, memory and visual perceptual functions remained intact across assessments.

The language baseline revealed that the most remarkable feature of CH's nonfluent dysphasia was a severe reduction of propositional speech in the context of relatively well preserved nominal, comprehension, repetition, and reading skills. By comparison, written language was less affected.

CH could be classed as fulfilling previously proposed criteria for nonfluent progressive aphasia (e.g., Chawluk et al., 1986; Hodges & Patterson, 1996; Mesulam, 1982; Mesulam et al., 1992; Snowden et al., 1996). Within the domain of nonfluent progressive aphasia, CH's dysphasic impairment is best classified as a dynamic aphasia (Luria, 1966; 1970; 1973; Luria et al., 1968). His severe propositional language impairment is with a relative preservation of repetition and naming. This would make it unlikely that his language impairment can be clinically classed as Broca's aphasia.

CH presented with a mixed form of dynamic aphasia in that the core feature of reduced propositional language skills was present in association with additional articulatory and grammatical difficulties. In the following series of experimental investigations, the nature and basis of CH's propositional language generation impairment was explored.

2.3 PHRASE AND SENTENCE GENERATION INVESTIGATION

The first series of tests were designed to investigate the extent of CH's dynamic aphasia. The tasks are based on those used by Robinson et al. (1998).

2.3.1 Method and Procedure

The experimental investigations were undertaken and completed in a 6-month period between the first two cognitive assessments. CH's condition was relatively stable during the time of the experimental investigations as no significant decline was observed in the cognitive baseline. For all tests, the examiner recorded the number correct and response time (RT) with the use of a stopwatch. For all sentence generation tests, RT was defined as the time from the end of stimulus presentation to the time CH started to generate a response. For test 2.3.2.6, RT was defined as the time taken from stimulus presentation to the time of task completion. Mean RT was calculated for correct responses only.

A summary of scores obtained by CH is presented in Table 4. For comparison purposes the scores previously reported for the pure dynamic aphasic patient ANG (Robinson et al., 1998) are included in Table 4. ANG's RTs are not reported, as all correct responses were produced in less than 2 seconds for Tests 2.3.2.1 -2.3.2.5.

2.3.2 Tests and Results

2.3.2.1 Generation of a phrase to complete a sentence

CH was orally presented with phrases and required to complete each with a second phrase to form a meaningful sentence (e.g., The children were...). His performance was poor and very slow. He was unable to produce any response for four phrases and only produced responses for the remaining phrases after a long pause (e.g., The children were... *playing together* after 8 seconds).

2.3.2.2 Generation of a sentence from a single common word

CH was orally presented with single common words and asked to produce a whole sentence incorporating the target word. His performance was poor and slow. CH was only able to generate sentences containing at least three words for only 55% of the target stimuli (e.g., drove→ *I drove a car.*). Three of the responses generated were grammatically incorrect (e.g., old→ *He's old man.*); however, for the purpose of this task these were counted as correct. Errors consisted of five no responses and four repetitions of the target word.

2.3.2.3 Generation of a sentence to describe a pictorial scene

CH was presented with simple pictorial scenes selected from the PALPA (Kay et al., 1992) and asked to produce a sentence to describe it. His performance was flawless, although responses were produced after a long pause. He was able to generate meaningful sentences for all of the pictures (e.g., *A girl* [is] *washing the horse),* although most contained at least one grammatical error.

2.3.2.4 Generation of a sentence from a pictorial scene: "what might happen next?"

CH was presented with simple pictorial scenes from the PALPA that were not used in the previous task. He was asked to generate a sentence describing what might happen next. His performance was extremely impaired and slow. It was noticeable that although CH was almost completely unable to generate sentences concerning "what might happen next," he was able to describe the contents of presented scenes (as in 2.3.2.3).

Table 4. *Phrase and Sentence Generation Scores for CH and ANG: Number Correct and Mean RT*

	CH		ANG
	No. Correct	Mean RT	No. Correct
Generation of a phrase to complete a sentence	6/10	6.0 (2.5)	3/20
Generation of a sentence from a single common word	11/20	11.1 (4.7)	2/15
Generation of a sentence given a pictorial scene	20/20	12.9 (8.4)	34/34
Generation of sentences from a given pictorial scene: "what might happen next?"	3/20	13.3 (3.8)	3/20
Story generation from a pictorial context	0/10	-	0/5
Sentence construction task	9/10	16.4 (11.4)	14/15

RT = response time in seconds with standard deviation in parentheses.

2.3.2.5 Story generation from a pictorial context

CH was presented with five simple picture stimuli, such as a man sawing a log. The stimuli were presented on two separate occasions. He was asked to produce a short story that would include the content of the picture. His performance was severely impaired. He was only able to describe the pictures (e.g., *Sawing it...yeah.... log... trestle).*

2.3.2.6 Sentence construction task

The sentence construction task has been considered a test of verbal thought or planning (Costello & Warrington, 1989). In this task, single words are printed on separate pieces of paper and presented in a grammatically incorrect order. Each group of words has to be arranged to construct a meaningful sentence. Their dynamic aphasic patient (ROH) failed this task as he was only able to correctly arrange 5/27 sentences. However, the dynamic aphasic patient ANG showed no difficulty with the task, nor did ADY (Warren et al., 2003). The dynamic aphasic patient KC also performed normally in the oral modality and failed only when asked to manually move the cards (Snowden et al., 1996). In order to compare CH's performance with that of other dynamic aphasics, we gave him 10 sentences to rearrange (3-7 words in length). He performed almost flawlessly (see Table 4). There was no significant difference from five age-, education-, gender-, and occupation-matched controls (M = 9.8/10, range 9-10). The only error CH made involved the 5-word sentence "The suitcase was too heavy" → "*The was too suitcase heavy*". Similar to ANG, ADY, and to an extent KC, CH passed this task, which represents a difference from ROH. For the previous dynamic aphasic patients no information regarding the time taken to complete this task is available. We timed CH's responses and found he was slower than controls. However, it should be noted that his performance was generally slow on all tasks involving language (see for example his RTs when asked to generate a sentence to describe pictorial scenes as in Test 2.3.2.3). Thus, the significance of his slow performance on this task is unclear. Moreover, it is unclear whether a sentence construction task should really be regarded as a more general problem solving task rather than an online language planning task.

2.3.3 Summary

The phrase and sentence generation investigation clearly demonstrates that CH had a severe generation impairment only in conditions where a response to words, phrases, and pictorial stimuli required him to generate sentences that were not constrained by the stimulus. In contrast, CH had no difficulty generating sentences when these were constrained by the stimulus; that is, when describing pictorial scenes or action sequences (i.e., Reporter Test). CH was also unimpaired in the sentence construction task.

CH's performance on phrase and sentence generation tasks is directly comparable to that of ANG, who had a severe verbal generation impairment in response to words, phrases and sentences. However, like CH, she was able to generate sentences without difficulty to describe pictorial scenes and action sequences. ANG's verbal generation deficit was accounted for in that she was unable to select a verbal response in situations where the stimulus activated many competing response options (i.e., the stimulus is unconstrained). In a situation where a stimulus activated a single prepotent response option, or when one verbal response option among competitors is considerably more activated (i.e., the stimulus is constrained), ANG showed no impairment.

2.4 THE EFFECT OF COMPETING RESPONSE OPTIONS ON PHRASE AND SENTENCE GENERATION

In this section, the hypothesis that impaired phrase and sentence generation is underpinned by an inability to select a verbal response when the stimulus activates many response options was investigated in CH.

2.4.1 Method and Procedure

The tasks and stimuli are based on Robinson et al. (1998). The same method and procedure was adopted as described in the previous section (2.3.1). A summary of scores is given in Table 5. For comparison purposes the scores previously reported for the pure dynamic aphasic patient ANG and 5 matched controls (Robinson et al., 1998) are included in Table 5. CH's response times were compared to controls using the modified t-test, which was specifically developed to compare an individual's score with a small control sample (see Crawford & Garthwaite, 2002).

2.4.2 Tests and Results

2.4.2.1 Generation of a sentence from a single Proper Noun and Common Word

CH was randomly presented with single proper nouns (e.g., Bosnia, Sean Connery) and single common words (e.g., glass, red) and asked to produce a whole sentence incorporating the target. A highly significant difference was found between

CH's good ability to generate meaningful sentences for proper nouns (e.g., Tony Blair → *Tony Blair is the prime minister)* and his very impaired performance for common words ($\chi^2_{(1)}$ = 8.10, $p < 0.005$, Yates correction applied). Of the sentences CH generated, 17 contained at least one grammatical error or were only partial sentences (e.g., door → *Opened the front door*). Responses were produced after a long pause and were significantly slower than controls for both proper nouns ($t_{(4)} = 5.24$, $p < 0.05$) and common words ($t_{(4)} = 5.10$, $p < 0.01$). Errors were all no responses, except on one occasion in which only a single word was generated (red → *dread).*

Table 5. *The Effect of Competing Response Options on Phrase and Sentence Generation: Number Correct and Mean RT*

	CH		ANG		Controls	
	No. Correct	Mean RT	No. Correct	Mean RT	No. Correct	Mean RT
	Sentence Generation from a Single Word					
Proper Noun	22/30	13.1 (5.9)*	26/28	3.1 (1.6)	28/28	2.2 (1.9)
Common Word	10/30***	11.8 (8.2)**	11/28***	7.8 (2.2)	28/28	2.3 (1.7)
	Sentence Generation from a Phrase					
High predictability	19/22	6.1 (3.9)*	9/12	4.3 (3.2)	12/12	1.9 (1.6)
Low predictability	11/22*	8.3 (3.7)	3/12*	5.7 (4.7)	12/12	2.2 (3.0)

RT = response time in seconds with standard deviation in parentheses; * = p<0.05; ** = p<0.01; *** = p<0.001.

2.4.2.2 Generation of a phrase to complete a sentence with High and Low Response Predictability

CH was presented with 22 sentences that had few verbal response options for their completion (e.g., The man walked into the cinema…) and 22 sentences that had many (e.g., The man walked into the house...). He was required to complete each phrase with a second phrase (i.e., more than one word) to form a meaningful sentence. CH produced appropriate responses for almost all the high response predictability

(HRP) phrases, such as "She opened her purse... *bought an item.*" In contrast, his performance was significantly impaired for low response predictability (LRP) phrases (e.g., "She took the bag and... *no response*"; $\chi^2_{(1)} = 5.13$, $p < 0.025$, Yates correction applied). Of the phrases completed with a phrase, 15 of the HRP and 10 of the LRP sentences contained at least one grammatical error (e.g., "She walked into the bar... *[to] buy a drink*"). Responses were generated after a considerable pause and were significantly slower than controls for HRP phrases ($t_{(1)} = 2.40$, $p < 0.05$) and approached significance for LRP phrases ($t_{(1)} = 1.86$, $p < 0.10$). Errors consisted of no response for 1 HRP and 8 LRP phrases and a single word response for 2 HRP and 3 LRP phrases.

2.4.3 Summary

CH's ability to generate a sentence from a proper noun, which should activate a single prepotent response, was superior to his ability to generate a sentence from a common word, which should activate many verbal response options. In addition, his ability to generate a phrase to complete a phrase high in response predictability, which should strongly activate a single prepotent response, was superior to his ability to generate a phrase to complete a phrase low in response predictability, which should activate many verbal response options. Thus, his ability to generate a verbal response was significantly better when stimuli activate a prepotent response.

This performance of CH replicates the findings of ANG, the pure dynamic aphasic patient. This suggests that CH's verbal generation impairment was underpinned by an inability to select a verbal response where a stimulus activates many competing alternative response options with no prepotent response available.

2.5 THE EFFECT OF COMPETING RESPONSE OPTIONS ON SINGLE WORD GENERATION

As the tests in section 2.4 required the generation of a phrase or sentence, it is uncertain whether the same process operates at the level of single words. This test was designed to investigate whether CH's ability to generate a single word is affected by the number of possible response options activated by a stimulus. Thus, a sentence completion task was devised that systematically varied the number of alternative completion words (i.e., level of constraint) and the probability for a dominant response. This task was based on the Hayling Sentence Completion Test (Burgess et al., 1996b).

2.5.1 Hypotheses

It was noted in the Cognitive Baseline that CH's performance on the Hayling was unusual as he was more impaired at generating a word to complete a sentence on the initiation part (Section 1) than the suppression part (Section 2). The reverse performance is usually observed in that Section 2 is typically performed more poorly than Section 1. Upon closer scrutiny of the sentences in Section 1, it was noted that the sentences vary in level of constraint. Each sentence has a probability for a dominant response based on the Bloom and Fischler (1980) completion norms ranging from 0.99-0.68. Interestingly, three of the five sentences for which CH did not produce a response were in the lowest ranked probabilities for having a dominant response (i.e., 0.68, 0.70, 0.71). Thus, in part A, the effect of level of constraint on CH's ability to generate a single word to meaningfully complete a sentence was investigated further (2.5.4.1). The task demands of Section 2 of the Hayling are that a sentence must be completed with an unrelated response (one that is not guided by the sentence frame). This is in contrast to Section 1 that requires the generation of a meaningful completion word (guided by the sentence frame). In part B, CH was asked to complete each sentence with a single word that was unrelated to the meaning of a sentence (2.5.4.2). The process of generating a single word to complete a sentence remains constant; however, the response generated is no longer connected to, or constrained by, the stimulus. This allows for several hypotheses regarding CH's performance:

1. If CH has a generalised verbal generation impairment, manipulating the task demands will be irrelevant, as he is still required to generate a single word to complete all sentences. Hence, the pattern of performance for part A and B will be the same.

2. If CH's verbal generation impairment is underpinned by an inability to select a verbal response when many competing response options are activated by a stimulus without a clear prepotent response, then his performance will be affected by the level of constraint only in the meaningful completion task in which the response is connected to the stimulus (A). Furthermore, as the level of constraint and probability for a dominant response becomes lower, and the number of activated completion words increases, his performance on part A will deteriorate. By contrast, on the unrelated completion task (B) CH's performance will not be affected by level of

constraint, as responses are no longer connected to, or constrained by, the sentence frame. In this case there are two possibilities:

a) CH's performance on part B will be reduced for all levels of constraint as each sentence has multiple competing response options; or

b) CH's performance on part B will be relatively good for all levels of constraint if another intact cognitive process is used. Why is this proposed? Given CH's ability to complete many sentences from the Hayling, particularly on Section 2, and relatively well-preserved cognitive functioning, it seems plausible that another cognitive process could overcome his verbal generation impairment, such as the formation and use of a strategy.

2.5.2 Materials

A set of sentences with the final word omitted was selected from the Bloom and Fischler norms (1980). The stimuli were selected so that the number of alternative completion words varied such that the probability of a dominant response varied accordingly. The stimuli were grouped to form four different levels of constraint: very high constraint, medium-high constraint, low constraint, and very low constraint (stimuli provided by C. Frith & D. Nathaniel-James). For example, the sentence "Water and sunshine help plants..." is high in constraint with only 1 listed completion word (i.e., grow) that has a probability of 0.99 for being the dominant response produced. By comparison, the sentence "There was nothing wrong with the..." is very low in constraint and has 16 listed alternative completion words, each with a probability no larger than 0.14 for being the dominant response produced. Formation of the four levels of constraint was achieved by calculating the mean of the highest probability response for each sentence in each level. This resulted in four levels, each containing 32 sentences: Very High Constraint (VHC) = 0.93; Medium-High Constraint (MHC) = 0.73; Low Constraint (LC) = 0.53; Very Low Constraint (VLC)= 0.20. The stimuli were used in both part A and B.

2.5.3 Method and Procedure

CH was given the stem of a sentence and asked to generate an appropriate single word to complete it in two experimental conditions. In part A, the *Meaningful Completion condition* (2.5.4.1), he was asked to generate a single word connected to the sentence. In part B, the *Unrelated Completion condition* (2.5.4.2), he was asked to generate a single word unrelated to the sentence, such that the completed sentence did not make sense (e.g., London is a very busy... *elephant*). The Meaningful Completion condition was based on Section 1 of the Hayling whereas the Unrelated Completion condition was based on Section 2. The sentences were presented in a pseudo-random order. The Meaningful Completion condition was given on three separate occasions over a 6-month period. The Unrelated Completion condition was given on one occasion after the third administration of the Meaningful Completion condition. The number correct and mean RTs are reported in Table 6.

2.5.4 Results

2.5.4.1 Part A: Meaningful Sentence Completion

CH's performance was almost at ceiling when generating single words to complete the VHC sentences that have a high probability for a dominant response. In contrast, his ability to generate single words to complete the VLC sentences that have a very low probability for a dominant response was severely impaired. As this test was administered on three occasions, CH's performance on each sentence across trials was analysed. Each sentence was given a score between 0 and 3 that represented the frequency with which CH generated a correct response over the three trials (see Appendix 1). The basis for comparison between levels of constraint was the frequency with which CH scored 3, indicating a correct response on all three trials. CH's ability to generate a correct response was not independent of the level of constraint ($\chi^2_{(3)}$ = 18.85, $p < 0.005$). Upon closer scrutiny, CH's performance for the two most constrained levels (VHC and MHC) just fell short of significance ($\chi^2_{(1)}$ = 3.78, n.s., p (0.05) = 3.84, with Yates correction applied). However, CH performed significantly better for VHC than LC sentences ($\chi^2_{(1)}$ = 8.38, $p < 0.005$, with Yates correction applied), and by implication VLC sentences. Similarly, MHC sentences were performed better than VLC sentences ($\chi^2_{(1)}$ = 5.15, $p < 0.025$, with Yates correction applied). The difference between the lowest two levels of constraint (LC and VLC) did not reach significance. Errors consisted of no responses, responses that were meaningless, responses that were repetitions of words contained in the sentence frame, or responses with more than one word. Analysis of variance was used to examine the effect of mean RTs, with no significant differences found between the four levels of constraint for the three times it was administered, $F_{(3,8)}$ = 1.53, n.s. However, CH's response times were considerably slower than normal controls on the original Hayling Section 1 (M = 0.67 seconds/sentence; CH see Table 6).

2.5.4.2 Part B: Unrelated Sentence Completion

CH's performance was virtually at ceiling for all four levels of constraint in this condition. Remarkably, his performance was equally good for the VHC as well as the VLC sentences ($\chi^2_{(3)}$ = 0.23, n.s). In other words, his ability to generate an unrelated single word to complete "Water and sunshine help plants..." was as good as his ability to generate an unrelated single word to complete "There was nothing wrong with the..." There was no significant difference between mean RTs for levels of constraint ($F_{(3)}$ = 1.08, n.s). CH's response times were comparable to normal controls on the original Hayling Section 2 (M = 3.4 seconds/sentence; CH see Table 6).

Table 6. *The Effect of Competing Response Options on Single Word Generation: Number Correct and Mean RT*

		A. Meaningful Sentence Completion		B. Unrelated Sentence Completion	
Level of Constraint	Trial	No. Correct	Mean RT	No. Correct	Mean RT
Very High Constraint	T1	29/32	1.8 (1.2)	-	-
(Probability = 0.93) [a]	T2	29/32	1.85 (1.6)	-	-
	T3	30/32	1.97 (2.1)	31/32	3.26 (2.7)
Medium-High Constraint	T1	23/32	3.05 (2.8)	-	-
(Probability = 0.73) [a]	T2	25/32	2.50 (2.6)	-	-
	T3	28/32	4.08 (4.3)	31/32	4.39 (3.7)
Low Constraint (Probability = 0.53) [a]	T1	21/32	3.42 (2.5)	-	-
	T2	21/32	3.41 (3.9)	-	-
	T3	25/32	4.13 (3.7)	31/32	4.13 (3.4)
Very Low Constraint (Probability = 0.20) [a]	T1	17/32	2.70 (2.9)	-	-
	T2	16/32	2.80 (1.8)	-	-
	T3	18/32	7.59 (7.7)	30/32	3.17 (3.6)

RT = response time in seconds with standard deviation in parentheses; T1 = trial 1; T2 = trial 2; T3 = trial 3; [a] the probability of the dominant response being generated.

2.5.5 Summary

CH's ability to generate a single word to complete sentences meaningfully (2.5.4.1) was influenced by the level of constraint and probability for a dominant response. His ability to generate a single word to complete a sentence was best when the level of constraint and probability for a dominant response was high. In contrast, it was poorest when the level of constraint was low with no dominant response option. Remarkably, CH's ability to complete sentences with single words in the unrelated completion condition (2.5.4.2) was almost at ceiling and clearly not affected by the level of constraint of a sentence. The fact that CH's pattern of performance ranged from impaired in the meaningful condition to unimpaired in the unrelated condition clearly indicates that his word generation difficulties are not underpinned by a more generalised verbal generation impairment. That level of constraint only affected performance in the meaningful completion task provides evidence that CH's word generation impairment is underpinned by an inability to select a verbal response when many competing response options are activated by a stimulus. CH's virtually intact performance on all four levels of constraint in the unrelated completion condition leads to the conclusion that in certain conditions CH is remarkably able to overcome his verbal generation impairment.

Of particular interest was his intact performance in generating a single word unrelated to the sentence frame. This task has the greatest number of potential responses. We suggest that CH was able to form and use a semantic strategy allowing him to generate unrelated words. Burgess and Shallice (1996b) described two of the most common strategies used by controls on Section 2 of the Hayling that required generation of unrelated words. One strategy consisted of choosing objects from the examiner's office and the other consisted of generating exemplars from a semantic category. These are precisely the strategies that CH used. First, he described objects in the examination room (e.g., computer). Second, he generated items from different semantic categories (i.e., kitchen items, railway objects, colours, electronic items and machinery, household items, tools, musical instruments, furniture, money, body parts, and car parts). These two strategies, resulting in generating approximately 10 items from 12 categories, is consistent with his poor performance on semantic fluency tasks (e.g., animals < 10^{th} percentile, see Table 2). This observation does not support Gold et al.'s (1997) hypothesis that dynamic aphasia may be due to defective semantic strategy formation and/or use.

2.6 SEMANTIC STRATEGY FORMATION: SEMANTIC CATEGORISATION

2.6.1 Materials

A set of 80 words printed on individual cards was selected for this task (based on Gold et al., 1997). The stimuli formed 16 categories, with each containing five highly associated items (e.g., fruit = orange, pineapple, grapefruit, cherries, apple). Pairs of categories were created, with the degree of association being manipulated such that category pairs were *close* or *distant*. Close was defined as being closely related across the two categories. Distant was defined as being distantly related across the two categories. The close category pairs were field animals-African animals, office items-bedroom items, outdoor clothing-beach clothing, and sharks-fish. The distant category pairs were animals-clothing, food-sport equipment, flowers-vehicles, and sea animals-furniture.

A set of 80 coloured pictures depicted on individual cards was selected for this task (based on Gold et al., 1997). The stimuli formed 16 categories, with each containing five highly associated items. Pairs of categories were created with the degree of association being manipulated as outlined above. The four close category pairs were field animals-African animals, office items-bedroom items, kitchen appliances-household appliances, and fruit-vegetables. The four distant category pairs were clothing-animals, food-sport equipment, wheels-furniture, and office items-fish.

2.6.2 Method

CH was given a stack of 10 cards containing a pair of categories and asked to sort the stimuli into two piles under two conditions: cued and un-cued. In the cued condition, the names of the two categories were stated prior to sorting. In the un-cued condition, the category names were not given at any stage. The number of items correctly sorted and the mean RT taken to complete the sorting were recorded. Five age- and education-matched controls completed these tasks.

2.6.3 Results

CH's performance on this task was virtually at ceiling for sorting closely and distantly related categories in both the cued and un-cued conditions (see Table 7). Further, there was no difference in his good performance for word or picture stimuli. For the critical un-cued condition when sorting close categories, CH made 3 errors for word stimuli and 2 errors for picture stimuli, which was almost identical to controls. Although the number of total errors CH made on this task was less than the average number of errors made by controls, the time taken for CH to complete each sort was consistently longer[5].

Table 7. *Semantic Categorisation Task: Number Correct (Max = 40) and Mean RT*

		Cued		*Un-cued*	
		CH	Controls	CH	Controls
		Words			
Close	No. Correct	40	39.5	37	36.3
	Mean RT	18.8	11.3 (6.2)	34.8	15.6 (6.5)
Distant	No. Correct	40	40	40	40
	Mean RT	20.0	8.8 (4.2)	19.3	8.2 (1.6)
		Pictures			
Close	No. Correct	39	38.5	38	37.3
	Mean RT	28.3	11.8 (4.5)	47.0	20.9 (5.3)
Distant	No. Correct	40	40	40	39.5
	Mean RT	25.5	10.3 (2.0)	28.3	14.8 (4.7)

RT = response time in seconds; SD = standard deviation for controls in parentheses.

2.6.4 Summary

CH has a severe single word generation impairment only when many competing response options are activated by a stimulus. However, his ability to generate an unrelated single word is normal. We attribute this to his intact ability to form and use a semantic strategy when a response is unrelated to the stimulus.

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[5] The picture version of this task was administered to the group of Frontal and Posterior patients, and Controls, reported in Chapter 4. Frontal patients were slower to complete each condition compared to Controls. For errors, the only significant finding was that Frontals were poorer than Controls for the cued condition when sorting distantly related categories, which is not the critical condition according to Gold et al. In fact, this finding was most likely due to a ceiling effect in both Controls (M = 40, SD = 0) and Frontals (M = 39.61, SD = 0.9). This task is concluded to be insensitive to frontal and posterior lesions.

2.7 RANDOM NUMBER GENERATION

The aim of the next two investigations was to address CH's ability to generate other non-linguistic responses. In this series, we investigate CH's ability to generate items from the category of numbers, which are known to dissociate from other lexical categories (e.g., Dehaene & Cohen, 1997). In our task we use random number generation that involved only a restricted number set between 1-9 (e.g., 1-4). In this sense CH was asked to generate numbers from a restricted response set.

For the random number generation tasks we used 10 age-, gender- and education-matched controls. Of these 10 male controls, 5 were occupation-matched (i.e., engineers; E controls) and 5 were not (NE controls). The E controls were all employed as consultant engineers with the same company. The mean age of the E controls was 56.4 years (range 54-60) and the mean level of intellectual functioning was 123.4 (range 122-127) as estimated by their performance on the NART. The NE controls were recruited on the basis that all five had professional jobs, but were not engineers. The mean age of the NE controls was 53.6 years (range 50-61) and the mean estimated level of intellectual functioning was 119.6 (range 113-123). CH's performance was compared to controls using the modified t-test, df = 4 (Crawford et al., 2002).

2.7.1 Materials and Method

CH was asked to generate numbers in a random order for 100 trials in synchrony with a pacing tone that occurred once every three seconds (partly based on Jahanshahi et al., 1998b). The concept of randomness was explained with the use of the hat analogy as follows: 'Imagine the numbers 1-9 were written on separate pieces of paper and placed in a hat. You take one out of the hat, call out the number, and then return it to the hat before choosing again. The series of numbers you call out would in this way be random'. The size of the response set was varied so that the task was performed under three conditions: a) number set 1-9, b) number set 1-4, and c) number set 1-2. Responses were recorded and errors were numbers outside of the identified response set. The percentage of responses that were repeats of the previous number (e.g., 1-1), ascending series (e.g., 1-2 would be counted as 1, and 1-2-3 would be counted as 2), or descending series (e.g., 2-1) was calculated. Repetition and seriation have been identified as important factors in human random number generation (Ginsburg & Karpiuk, 1994). A summary of percentages is presented in Table 8.

2.7.2 Results

In the first condition (a), CH was asked to randomly generate numbers between 1 and 9. The percentage of CH's responses that were repeats and descending series was comparable to all controls. By contrast, the percentage of ascending series given by CH was significantly greater than that of both E and NE controls.

Table 8. *Random Number Generation Tests: Percentage of Total Responses and Modified t-test Comparison between CH and Controls*

	CH	Engineer Controls		Non-Engineer Controls		Chance
	% Responses	% Responses	*t* *(df = 4)*	% Responses	*t* *(df = 4)*	% Responses
a. Number Set 1-9						
Repeats						
T1	0	3.8 (5.4)	-0.60	3.6 (2.5)	-1.30	11.1
T2	5		-0.20		0.50	
Ascending Series						
T1	24	7.0 (3.5)	4.38**	14.4 (3.5)	2.49*	9.8
T2	24		4.38**		2.49*	
Descending Series						
T1	12	13.2 (5.4)	-0.20	11 (5.4)	0.20	9.8
T2	15		-0.30		0.70	
b. Number Set 1-4						
Repeats	30	16 (7.3)	1.76	10.4 (6.5)	2.74*	25
Ascending Series	21	18.8 (2.7)	0.75	17.8 (5.8)	0.50	18.7
Descending Series	25	23.6 (6.2)	0.21	24.4 (4.3)	0.13	18.7
c. Number Set 1-2						
Repeats	48	43.6 (4.8)	0.83	32.8 (24.2)	0.57	48
Ascending Series	28	28 (2.4)	0.00	23.6 (4.5)	0.89	25
Descending Series	23	27.2 (2.2)	-1.77	24.2 (2.2)	-0.27	25

Standard deviations for controls in parentheses; T1 = trial 1; T2 = trial 2; * $p < 0.05$; ** $p < 0.01$

In the second condition (b), CH was asked to randomly generate numbers between 1 and 4. CH's performance was indistinguishable when compared to E controls in that the percentage of responses that were repeats, ascending series, and descending series was comparable. In comparison to NE controls, the percentage of CH's responses that were ascending and descending series was comparable, although CH did produce significantly more repeats. However, this higher percentage of repeats that CH produced (30% comparing with NE controls 10.4%) is actually the more correct pattern, as the chance level for repeating a digit when one is drawing a digit randomly from a small set is 25%.

In the third condition (c), CH was asked to randomly generate the numbers 1 and 2. The percentage of CH's responses that were repeats, ascending series, and descending series was not significantly different from that of E and NE controls.

2.7.3 Summary

Overall, CH's ability to generate random numbers is comparable to controls on all measures. In this task CH is behaving in a different fashion from the other generation tasks where he is unable to produce a verbal response. In this respect, he is able to generate answers, as with the unrelated completion part of the Hayling task (and 2.5.4.2). Again, the type of response that is required is dependent on the specific cognitive requirements induced by the task instruction; responses are not produced by the language mechanism in normal generation mode. There was, however, one condition involving the largest number set 1-9 where CH, although still able to generate a response, produced a number of responses that were part of an ascending series. This type of response has been documented in the context of TMS studies involving the left dorsolateral prefrontal cortex (Jahanshahi et al., 1998b) and therefore raises the possibility of their occurring as an associated deficit. In the next experimental section, we address the extent to which CH's verbal generation impairment was domain specific.

2.8 NON-VERBAL GENERATION

This section was designed to investigate whether CH's propositional language impairment was limited to verbal output or was part of a more generalised novel response generation impairment. Non-verbal generation tasks included design fluency, gesture fluency, and motor movement generation. For the following tests, we used the same controls as those described in the previous investigation (2.7). The E controls completed all non-verbal fluency tests, whereas the NE controls completed all non-verbal fluency tests except for two design fluency tests where standardised data was available (2.8.1.1 and 2.8.1.2). CH's performance was compared to controls using the modified t-test, df = 4 (Crawford et al., 2002).

2.8.1 Design Fluency

The design fluency tasks are partly based on Jones-Gotman and Milner (1977) and Regard, Strauss, and Knapp (1982). For all design fluency tasks, CH was provided with a pencil and as many A4 sheets of blank paper as was required, except for the Five-Point Test (2.8.1.5) where sheets with arrays of five dots were provided. The total number of responses generated and errors were recorded for all tasks. Errors included perseverative responses (i.e., a repeat of one previously given) and inappropriate responses (i.e., if it clearly broke the rules given). A summary of scores is given in Table 9.

2.8.1.1 Free Condition

In this task, based on Jones-Gotman and Milner (1977), CH was asked to draw as many designs as possible in 4 minutes. The standard instructions were given. The total number of drawings generated by CH was comparable to both E controls and an age-matched control group reported by Jones-Gotman (1996; cited in Spreen & Strauss, 1998). CH generated no errors. Occasional errors consisting of recognisable drawings (e.g., letter of the alphabet) were produced by E controls.

2.8.1.2 Fixed Condition

In this task, based on Jones-Gotman and Milner (1977), CH was asked to draw as many designs with four straight lines as possible in 4 minutes. The standard instructions were given. The number of designs CH generated was comparable to both E controls and an age-matched control group reported by Jones-Gotman (1996; cited in Spreen et al., 1998). Although the E control mean was slightly higher than both CH and normal controls, there was great variability in their performance (range = 15-38). CH made only one perseverative error. Occasional errors consisting of partial perseverations or recognisable drawings were produced by E controls.

2.8.1.3 Geometric Shape Fluency

CH was asked to draw as many different geometric shapes as possible in 4 minutes. He performed this task well and generated no errors. CH's performance was not significantly different from E or NE controls.

2.8.1.4 Object Fluency

CH was asked to draw as many recognisable objects as possible in 4 minutes. He was instructed that each drawing must be nameable. CH's performance was not significantly different than controls, although it was somewhat lower. No errors were made.

Table 9. *Design and Gesture Fluency: Total Number Generated and Modified t-test Comparison between CH and Controls*

		CH	Engineer Controls		Non-Engineer Controls	
		Total No. Generated	Total No. Generated	*t* (*df* = 4)	Total No. Generated	*t* (*df* = 4)
Design Fluency						
Free Condition		11	13.8 (3.9)	-0.16	11.8 (4.4)	-0.17
Fixed Condition		17	28 (9.6)	-0.11	12.6 (4.3)	0.97
Geometric Shapes		14	17.8 (4.7)	-0.74	16.6 (3.8)	-0.63
Objects		12	18.6 (5.6)	-0.52	14.6 (11.6)	-0.20
5-point test		20	39.5 (7.19)	-2.43*	18.8 (9.4)	0.12
Gesture Fluency						
Meaningless movements						
	T1	26	22.2 (5.3)	0.65	22.0 (5.8)	0.63
	T2	26				
Meaningful movements						
i. Use of objects	T1	12	18.6 (2.9)	-1.92	16.0 (4.9)	-0.65
	T2	13				
ii. Use of tools	T1	8	11.4 (1.8)	-1.47.	11.2 (1.6)	-1.26
	T2	10				

Standard deviations for controls in parentheses; T1 = trial 1; T2 = trial 2; * $p<0.05$.

2.8.1.5 Five-Point Test

In this task, based on Regard et al. (1982), CH was presented with the standard record sheet containing an array of five dots and asked to connect the dots in as many different ways as possible. The instructions and 3-minute time limit was based on the version used by Lee, Strauss, Loring, McCloskey, and Haworth (1997). It was noticeable that E controls tended to use a strategy on this task that allowed a much higher number of designs to be produced. Upon closer scrutiny, it seems the E controls produced the same number of unique designs, although, many designs were repeated but from a rotated angle (i.e., at 90°, 180° and 270°). The scoring criteria allow these responses, however, this approach was clearly not adopted by CH and NE controls. CH's performance is indistinguishable from the NE controls and just significantly below the E controls. CH made no errors, whereas one E control made 2 perseverative errors.

2.8.1.6 Design Fluency Comment

CH's performance on the design fluency tests was entirely normal when compared to the NE controls. When compared to the E controls, CH's performance was only slightly weaker on 1 of the 5 tests. Overall, the results of the design fluency tasks indicate that CH does not present with a clear impairment in the ability to produce meaningful and meaningless designs in a structured or less structured format.

2.8.2 Gesture Fluency

These tests are based on Jason (1985). CH was asked to generate as many movements as possible with the upper limbs in 2 minutes. A video camera recorded responses to aid scoring. The total number of responses generated, perseverative responses, and inappropriate responses were recorded. CH completed these tasks twice on different days, with the average score used for comparison with the controls, who only completed these tasks once. A summary of scores is given in Table 9.

2.8.2.1 Meaningless Movements

CH was asked to make as many different meaningless positions with the fingers of his hands as possible. Although CH generated slightly more responses than controls, this was not significant. CH made 6 perseverative errors over the two trials, NE controls made an average of 4.6 perseverative errors (range = 2-9) and E controls made no errors.

2.8.2.2 Meaningful Movements

In this task, CH was asked to demonstrate as many different things he could do with his hands in two conditions: i) use of objects, and ii) use of tools. For each condition, one example was demonstrated (i.e., i. opening a jar, ii. using a saw). CH generated slightly fewer responses than controls in both conditions, although this did not reach significance. CH made no errors in either condition. By contrast, in the first condition two controls made no more than 2 errors and in the second condition two controls made 1 error each.

2.8.2.3 Gesture Fluency Comment

CH's ability to generate meaningless and meaningful gestures with the hands was comparable to controls. It may be noteworthy that CH's performance was above the mean of controls for meaningless gestures and slightly below controls for meaningful gestures. A PET study by Decety et al. (1997) found that observation of meaningless actions was mainly associated with a right occipitoparietal pathway while observation of meaningful actions strongly engaged left frontotemporal regions. CH's strong performance for meaningless gestures and relatively weaker performance for meaningful gestures would fit with this data and may be due to his left frontotemporal degenerative process. In terms of errors, both CH and NE controls made slightly more perseverative errors than E controls only when generating meaningless movements. Overall, these results suggest that CH does not present with a gesture fluency impairment.

2.8.3 Motor Movement Generation

In this task, based on Deiber et al. (1991), CH was asked to select motor movements using a joystick that could be moved in four directions: up (U), down (D), left (L) and right (R). CH held the joystick positioned on a table with his right hand. In time with a tone every 3 seconds, CH was asked to select a motor movement which did not correspond to a sequence or pattern. This task was carried out under two conditions that varied the number of possible movement options he could select: a) two movement options, which comprised either U and D, or L and R; and b) four movement options, which comprised U, D, L and R. Each condition lasted 4 minutes. To familiarise the patient with the task a baseline condition was administered first, in which CH was asked to move the joystick in only one direction (U) in time with the tone. The baseline condition lasted for 2 minutes. The examiner observed all responses and recorded the position selected. The percentage of total responses that were repeats (e.g., U-U) and opposites (e.g., U-D or L-R) was calculated. This enabled an analysis of fixed or random response patterns, and allowed comparison between CH and controls. A summary of percentages is given in Table 10.

2.8.3.1 Two-Movement Options

In the two-movement condition, CH was requested to select between one of the two options and move the joystick accordingly in a manner that did not represent a pattern. CH completed both variations of this task separately (U and D, L and R). The percentage of CH's responses that were repeats and opposite movements for both tasks was comparable to all controls.

Table 10. *Motor Movement Generation: Percentage of Total Responses and Modified t-test Comparison between CH and Controls*

		CH	Engineer Controls		Non-Engineer Controls		Chance
		% Responses	% Responses	*t* *(df = 4)*	% Responses	*t* *(df = 4)*	% Responses
			Two Options				
U-D	Repeats	52	50.5 (5.5)	0.25	44.6 (16.1)	0.42	50
	Opposites	48	49.5 (5.5)	-0.25	55.4 (16.1)	-0.42	50
L-R	Repeats	42.9	53.3 (7.1)	-1.34	45.2 (16.2)	-0.13	50
	Opposites	57.1	46.6 (7.3)	1.31	54.8 (16.2)	0.13	50
			Four Options				
U/D/L/R	Repeats	38.8	26.2 (5.8)	1.98	20.1 (15.2)	1.12	25
	Opposites	23.8	27.0 (8.6)	-0.34	31.5 (9.5)	-0.74	25
	Other	37.4	46.8 (10.0)	-0.86	48.4 (11.8)	-0.85	50

Standard deviations for controls in parentheses; none of the t-tests reached significance level of $p<0.05$.

2.8.3.2 Four-Movement Options

In the four-movement condition, CH was asked to select between one of the four options and move the joystick accordingly in a manner that did not represent a pattern. There was no difference in the percentage of responses that were repeats and opposite movements between CH and all controls.

2.8.3.3 Motor Movement Generation Comment

CH's performance on the motor movement generation task that required the selection of movements from a response set that had either two or four options was comparable to controls. The percentage of sequences (repeats or opposite movements) was not different to that generated by controls, suggesting that CH does not have an impairment in the ability to generate and select motor movements.

2.8.4 Non-Verbal Generation Summary

CH's performance on design fluency, gesture fluency, and motor movement generation tasks was comparable to both engineer and non-engineers controls on 14 out of 15 measures. Overall, these results suggest that CH does not have a non-verbal generation impairment and that his impaired ability to generate verbal responses is domain specific.

2.9 DISCUSSION

Primary progressive aphasias have been divided into fluent and nonfluent subtypes (Grossman, 2002; Hodges et al., 1996). CH's clinical presentation is consistent with nonfluent progressive aphasia. Within this clinical category, CH presented with a language disorder that is best described as dynamic aphasia (Luria, 1966; 1970; 1973; Luria et al., 1968). In addition, CH presented with a mild peripheral speech disorder as his severely reduced spoken language contained some articulatory errors and was somewhat halting. CH rarely initiated conversation or connected speech. The largest sample of connected speech was elicited when he was describing complex scenes. However, his speech was reduced and asyntactic predominantly due to the omission of function words (e.g., *The girl [is] washing the horse*). He responded to most questions with single word answers, although occasionally phrases of no more than five words long were produced. CH's severely reduced spoken language was not underpinned by a primary deficit in naming, reading, repetition, or comprehension, as these were predominantly preserved. Moreover, other cognitive skills were intact and remained stable over the time of this investigation (e.g., non-verbal intellectual, visual perceptual and episodic memory functions). Thus, CH presented with the mixed form of dynamic aphasia. That is, the core feature of reduced propositional language was present in association with additional articulatory and grammatical difficulties.

On standard verbal generation tests, CH was severely impaired. In particular, CH's performance on word fluency tasks was impaired, more so for phonemic than semantic tasks. In the cognitive baseline, his performance on the Hayling Sentence Completion Test was impaired only on the verbal initiation section.

CH's severely reduced phrase and sentence generation skills were demonstrated in Section 2.3 to be comparable to the pure dynamic aphasic patient ANG (Robinson et al., 1998) and other dynamic aphasic patients (e.g., Costello et al., 1989; Esmonde et al., 1996; Gold et al., 1997; Warren et al., 2003). Similar to ANG, CH had profound difficulty in the generation of phrases and sentences when more than a simple description was required from stimuli that included single words, phrases, and pictorial scenes. Section 2.4 demonstrated that like ANG, CH's ability to generate sentences and phrases was best from stimuli that strongly activated a dominant response (proper nouns, phrases with high response predictability). By contrast, CH's ability to generate phrases and sentences was impaired when many competing response options were activated by stimuli (common words, phrases with low response predictability). This replicated the findings of the pure dynamic aphasic ANG.

This finding was extended to the single word level for the first time in the single word generation investigation (Section 2.5). CH's ability to complete sentences with a single word was significantly better when there was a high probability for a dominant response. CH's performance was virtually at ceiling when completing a sentence that had a highly associated dominant single word response (e.g., Water and sunshine help plants...). By contrast, his ability to complete sentences with a single word was impaired when many alternative completion words were activated. That is, in a situation where each activated completion word had a low probability for being the dominant response (e.g., There was nothing wrong with the...). Interestingly, CH performed at ceiling when he was required to complete sentences with a single word unrelated to the frame (e.g., London is a very busy... *elephant*). In this condition, there was no stimulus-response connection and the response was not constrained by the sentence. We speculated that CH's good performance in this condition was attributable to a strategy used, in that he systematically generated a single word to complete each sentence by either choosing objects from the examiner's office (e.g., computer) or generating exemplars from semantic categories (e.g., machinery, colours, musical instruments). These results suggested that CH had an intact ability to generate and apply a semantic strategy. The formal investigation in Section 2.6 confirmed that CH's ability to form and use a semantic strategy was entirely normal.

As discussed earlier, CH did not have a deficit in randomly generating numbers from a restricted set (Section 2.7). Further, the non-verbal generation investigation (Section 2.8) showed CH's non-verbal novel response generation skills were normal. CH's ability to generate designs and gestures, and to generate and select motor movements was comparable to two groups of carefully matched controls on almost all 15 measures. Indeed, he was normal ($p > 0.05$) or better than normal on 14 out of 15 measures. Thus, CH does not have an impairment in the ability to voluntarily generate novel non-verbal responses. CH is the first dynamic aphasic patient in whom the characteristic propositional language impairment is clearly demonstrated to be specific to the language production domain. It is important to note that language impairments are not always the first cognitive domain to be involved in dementia. For example, De Renzi (1986) reported one case of slowly progressive pure apraxia and two cases of slowly progressive visual agnosia without generalised dementia. Therefore, CH's intact performance on non-verbal generation tasks cannot be explained by a greater sensitivity of verbal than non-verbal responding to the initial stages of a degenerative disorder.

Following Luria's (Luria et al., 1968; Luria, 1970) terminology CH's impairment has been termed dynamic aphasia. This has been described in the context of a progressive nonfluent language impairment and raises the possibility that dynamic aphasia can be a distinct clinical manifestation within the nonfluent progressive aphasias (for examples of clinical variations within progressive aphasias see Croot et al., 2000).

2.9.1 Explanations of Dynamic Aphasia

Can the main accounts of dynamic aphasia explain the pattern of language impairment observed in CH? The accounts interpreting the deficit as extending beyond the domain of language will be discussed first. Dynamic aphasia has been explained as a failure in the strategy used to search lexical/semantic networks (Gold et al., 1997). The patient Gold and colleagues described was impaired on a semantic categorisation task. In addition, the patients' dynamic aphasia was associated with impaired design fluency. CH's performance was entirely normal on a semantic categorisation task. Also, his semantic fluency was superior to his phonemic fluency and he did not have a design fluency impairment. Indeed, CH was unimpaired on a large series of non-verbal generation tasks (gesture fluency, random number generation, motor movement selection). These findings suggest that CH had an intact ability to use a semantic strategy to search the lexicon. Thus, CH's dynamic aphasia is not underpinned by a semantic strategy deficit and his verbal generation deficit does not extend beyond the verbal domain.

Can dynamic aphasia be due to a deficit in appropriate strategy use? A deficit in appropriate strategy use has been suggested to account for reduced verbal initiation on the Hayling test by patients with frontal lobe lesions (Burgess et al., 1996b), and for reduced word fluency performance in an autistic population (Turner, 1999). If a deficit in appropriate strategy use underpins reduced propositional language, we would expect a more generalised deficit on generation tasks. For example, Turner (1999) argued that design fluency tasks place even greater demands upon generative skills than word fluency tasks. This is because stored knowledge is of little use in design fluency tasks as all responses must be original. However, CH was able to generate novel non-verbal designs on five different design fluency tasks. This would argue against a general deficit in appropriate strategy use. Moreover, this intact performance rules out a deficit in producing novel responses. Within verbal based tasks, we only need to examine CH's intact performance in the unrelated sentence completion task (2.5.4.2). CH was able to generate unrelated single words in a systematic manner that strongly suggested that he was able to form an appropriate strategy and produce novel responses. Thus, it seems that a deficit in appropriate strategy use, or indeed in producing novel responses, cannot explain CH's dynamic aphasia.

To consider the accounts of dynamic aphasia that interpret the disorder within the domain of language. Luria's (1970; 1973) account proposed the critical deficit to be an inability to form a linear scheme of a sentence; namely, the transitional stage of internal speech breaks down (see for empirical support Esmonde et al., 1996; Snowden et al., 1996). The account described by Luria is vague at several key points. First, Luria did not define either the process of translating internal speech into a plan or internal speech. Second, the plan that arises from this translation process is what, in Luria's formulation, should initiate verbal expression of thought. A breakdown in this translation process would presumably result in a more generalised propositional language impairment. One could speculate that this would affect every attempt to generate verbal output when formation of a sentence scheme is required. However, this cannot explain why CH was able to generate a verbal response when a dominant response was activated by a stimulus.

A second account is that dynamic aphasia arises from a selective impairment in verbal planning (Costello et al., 1989)[6]. Costello and Warrington specified that it is "the initial thought or plan that is impoverished not the ability to implement it" (p. 111). A diagnostic indicator of a verbal planning impairment for these authors was a deficit on a sentence construction task. However, CH, in a similar fashion to the pure dynamic aphasic patient ANG (Robinson et al., 1998) and the mixed dynamic aphasic ADY (Warren et al., 2003), was able to order constituent words to form a sentence. The extent to which this task relates to the online production of language is unclear. Further, CH's good performance on the Reporter Test (Language Baseline) indicates that he does not have a general deficit in the initial planning of language.

2.9.2 Robinson et al.'s (1998) Account of Dynamic Aphasia

My colleagues and I (Robinson et al., 1998) previously proposed that dynamic aphasia could be explained in terms of a deficit in the ability to select between competing verbal response options. Our account focused on the basic idea that activated verbal response options compete with each other through mutual inhibition. The greater the number of competing verbal response options activated by a stimulus, the greater the amount of inhibition each response receives from its competitors and the lower the probability of one response option becoming dominant.

Within a model of the language system, the level of the units at which response competition may be occurring needs to be considered. CH demonstrated that impairment in the ability to select between verbal response options applies not only to the sentences and phrases studied in ANG but also to single word generation. Thus, the degree of stimulus-response association determined CH's ability to generate a single word to complete a sentence (2.5.4.1). CH did not have verbal generation impairment when a dominant or prepotent response was strongly associated with a stimulus (highly constrained sentences). However, as the constraint became weaker moving from medium to low to very low constraint sentences, CH's ability to generate a word from a sentence frame became increasingly impaired. These data indicate that with increasing strength of stimulus-response association he was more able to overcome competition between alternative responses.

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[6] Warrington and colleagues recently referred to this deficit as defective message generation based on the performance of the dynamic aphasic ADY (Warren et al., 2003).

This investigation suggests that CH's impairment was within the language domain. CH did not present with a generation impairment in any other non-verbal domain encompassing the generation of designs, gestures, and motor movements. Therefore, an account of CH's impairment needs to be given within the context of a model of speech production. In most speech production models, the stage of processing on which we have been focusing is not well addressed. An exception is Levelt's (1989; 1999) model for producing spoken language, which is also one of the most detailed (see Figure 2). It contains a number of processing components that are involved in speech generation. According to this model, once the *surface structure* of the utterance – namely, a linear, relational pattern of lexical items ('lemmas') - is achieved, the phonological/phonetic system will then translate it into overt speech. The mechanisms involved in the production of the *surface structure* are the mechanisms that have been focused on in this study. In particular, Levelt specifies that two processing components play a key role in the realization of the *surface structure*. The first processing component is termed *conceptual preparation.* In the *conceptual preparation* component, the speaker generates a message. Messages are conceptual structures. According to Levelt, conceptual structures consist of lexical concepts, namely concepts for which there are words in the language. Levelt acknowledged that not all concepts are lexical, but in his model a message must eschew those that are not expressible in words. In Levelt's model, the message is then realized by the *grammatical encoding* processing component. Specifically it is assumed that the lexical concepts of the message activate the corresponding syntactic words (lemmas) in the mental lexicon. The speaker uses this lexical-syntactic information to build up the appropriate syntactic pattern (the *surface structure).*

In terms of the Levelt model, CH would have impairments arising both at the level of *grammatical encoding* as well as at the level of *conceptual preparation.* His agrammatism would be due to difficulties in realizing the message by *grammatical encoding*. His severe propositional language impairment would be due to an impairment in *conceptual preparation*, in other words he has difficulties at the stage of lexical concept generation. Our account of CH's dynamic aphasia attempts to specify some of the complex mechanisms involved in the generation of lexical concepts. We suggest that when many competing verbal response options are activated by a stimulus,

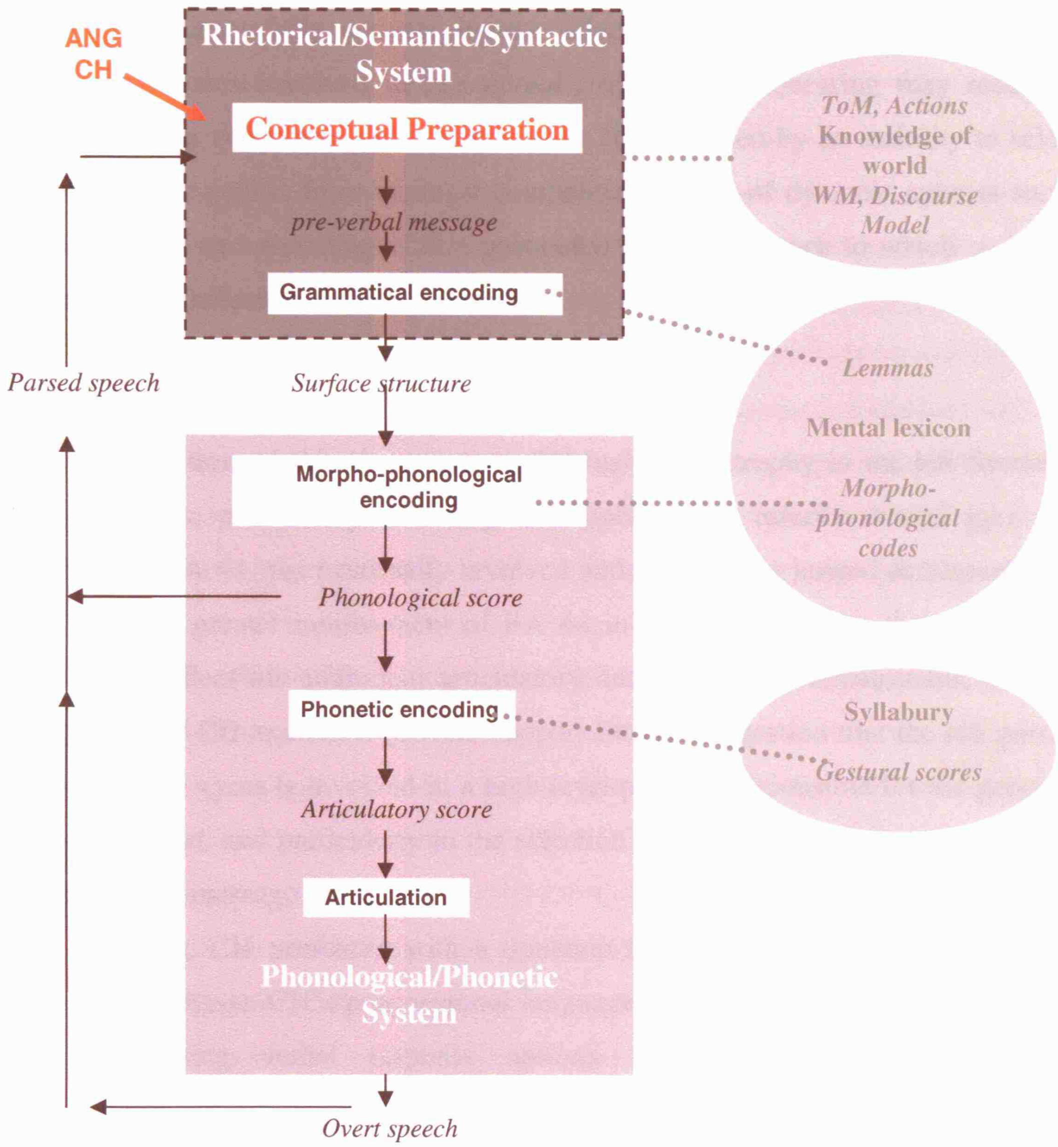

Figure 2. Levelt's Model for Producing Spoken Language (1999)

additional stress is placed on the *conceptual preparation* processes. When these processes are damaged, difficulties will arise when one verbal response must become preferentially activated over the other competing responses in order to satisfy task requirements. This in turn will not allow the speaker to achieve a satisfactory message that is able to drive *grammatical encoding* and lemma selection. By contrast, when there is a single dominant verbal response option, as for example in naming or describing scenes and actions, less stress is placed on the damaged *conceptual* *preparation* processes. These are then able to successfully generate lexical concepts that in turn successfully activate lemma selection. Thus, damage to some of the complex processes involved in *conceptual preparation* processing may result in a highly selective verbal generation impairment characterised by an inability to select a verbal response option from amongst competitors. Cases of dynamic aphasia such as CH add to our understanding of this postulated processing stage to which so far very little empirical evidence directly relates.

2.9.3 Conclusion

At the time of this investigation, CH had focal atrophy in the left frontal and temporal lobes, particularly involving the superior and inferior frontal gyri. More specifically, BA 44 was maximally involved and BA 45 was judged as somewhat less impaired. The greater involvement of BA 44 in CH, compared to that of BA 45 in ANG, may reflect his additional articulatory and syntactical impairments. Thus, the lesion cases of CH and ANG provide support for the suggestion that the left posterior inferior frontal gyrus is involved in a high level process responsible for the generation of verbal output, and particularly in the selection between competing verbal responses at Levelt's pre-message level.

In sum, CH presented with a dynamic aphasia in the context of nonfluent progressive aphasia. CH's propositional language impairment was only present when many competing verbal response options were activated. This impairment encompassed the generation of phrases, sentences, and single words. Further, it was clearly demonstrated that his propositional language impairment was specific to the production of language. CH provides evidence for the suggestion that the left inferior frontal plays a crucial role as a language control system responsible for the generation of verbal output.

CHAPTER THREE: DYNAMIC APHASIC PATIENT KAS

3.1 INTRODUCTION

The dynamic aphasia of ANG and CH was accounted for by a failure in one cognitive mechanism; namely, the selection between competing verbal response options. Is dynamic aphasia always underpinned by this failure or can the generation of propositional language fail because of damage to a different cognitive mechanism? Upon review of the *pure* and *mixed* dynamic aphasic patients, the literature suggests that when their performance on specific propositional language generation tasks is closely examined there may be a further subdivision. The majority of dynamic aphasic patients have been shown to have difficulty on experimental tasks requiring them to generate a word or sentence level response; including phrases (e.g., generate a meaningful sentence that incorporates the word *cup*). However, a few dynamic aphasic patients appear to be unimpaired on such tasks.

First, patients with dynamic aphasia who are impaired on word and sentence level generation tests will be discussed. Typically, these patients failed to generate a single response on word, phrase, and sentence generation tests (e.g., Costello et al., 1989; Warren et al., 2003). As detailed in Chapter 2 the word and sentence level generation impairment of the dynamic aphasic patients ANG and CH was present only when a stimulus activated many response options. Their impairment was absent for tests involving stimuli that activate few or a single dominant response option. In these tests, almost all the errors ANG and CH made consisted of no responses. For example, when generating a sentence from a common noun 84% of ANG's and 96% of CH's errors were no responses.

A somewhat similar dissociation in the ability to generate sentence level responses was observed in the dynamic aphasic MP (Raymer et al., 2002). This patient was able to generate a sentence from a single word with one primary meaning. By contrast, MP was impaired when generating a sentence from words that activate more than one meaning (e.g., fork).

Nonverbal generation skills have been investigated very rarely in this type of dynamic aphasia. Music generation skills were reported to be normal in ADY (Warren et al., 2003). As detailed in the previous chapter, the nonverbal generation skills of CH were demonstrated to be intact on a large series of nonverbal generation tests including design fluency, gesture fluency, and motor movement generation. This suggests that in this type of dynamic aphasia the sentence level generation impairment is specific to the language production domain.

The selective verbal impairment of this type of patient with dynamic aphasia who fail word and sentence level generation tests appears to be underpinned by a unilateral posterior left frontal lesion. Thus, Luria (1973) implicated the left inferior frontal region anterior to Broca's area. ROH had an astrocytoma in the left posterior frontal gyrus (Costello et al., 1989). MP had a left frontal subcortical infarct that included part of the anterior insula (Raymer et al., 2002). ANG and CH both showed involvement of the LIFG. ANG had a meningioma that specifically impinged on BA 45 and BA 44 to a lesser extent. CH had focal atrophy in the left frontal lobe, with maximal involvement of BA 44, and BA 45 to a lesser extent.

Second, patients with a preserved performance on word and sentence level generation tests, despite presenting with dynamic aphasia, will be discussed. Only three patients have been reported who were unimpaired in generating a single response on word and sentence level generation tasks. The dynamic aphasic patient KC (Snowden et al., 1996) flawlessly generated sentences from single words, phrases, sentence contexts, and pictorial contexts. In addition, KC had no difficulty in completing sentences with a single word. Similarly, two dynamic aphasic patients (Patient 2 and 3) with progressive supranuclear palsy (PSP) were able to generate a single response for all items on a sentence completion task, although some responses were scored as errors as they were not a single word or consisted of perseverations (Esmonde et al., 1996). For example, patient 3 generated short phrases instead of a single word for 30% of the sentence frames. Patient 2 generated a perseverative word from the sentence stem, or the previous response, for 30% of the frames.

Interestingly, all three patients with this second type of dynamic aphasia had bilateral frontal lobe involvement. In particular, SPECT showed KC had reduced uptake of tracer in the frontal region (Snowden et al., 1996). Frontal lobe atrophy was reported in two of three dynamic aphasic patients with PSP (Esmonde et al., 1996). Neuropathological and radiological investigations of PSP have shown neuronal changes and loss bilaterally in the frontal lobes, basal ganglia, and brain stem (Brenneis et al., 2004; Jellinger, Bancher, Hauw, & Verny, 1995).

In sum, patients with the *1^st^ subtype* of dynamic aphasia have word and sentence level generation impairments that result in an inability to produce a single response on word, phrase and sentence generation tests. This impairment appears to be specific to the domain of language and is associated with left posterior frontal lobe lesions. Although much less investigated, it appears there is a 2^{nd} *subtype* of dynamic aphasia characterised by an unimpaired performance on word and sentence level generation tests and more generalised bilateral frontal (and possibly subcortical) involvement.

In this chapter, I report a patient KAS who presented with a pure dynamic aphasia in the context of PSP, a neurodegenerative disease associated with generalised atrophy, including frontal and subcortical structures bilaterally. Despite her dynamic aphasia, KAS was unimpaired on word and sentence level generation tests. The aim is to attempt to further characterise this so far poorly described 2^{nd} *subtype* of dynamic aphasia.

3.2 CASE REPORT[7]

KAS was a 51 year-old, right-handed, retired American actress with a High School education. In June 1998, following a three-year history of worsening gait and increasing falls, KAS was referred to the Department of Neuropsychology at the National Hospital for Neurology and Neurosurgery. Neurological examination revealed an almost complete supra-nuclear vertical gaze palsy and slow horizontal gaze with very slow saccades and smooth motor pursuit movements. Initiation of speech was noted to be slow, but then it was produced in complete sentences rapidly. KAS also presented with dysarthria, a dystonic face, postural instability, and some Parkinsonism in the limbs with increased tone and mild bradykinesia. These were in addition to the cognitive impairments described below.

Clinically, there was no indication that KAS was apathetic or amotivated. For example, although KAS required physical assistance when carrying out motor tasks due to her unsteady gait, there were numerous instances witnessed by nursing and occupational therapy (OT) staff that basic care needs were initiated. In particular, she asked for assistance to void or mobilise, she put on make-up independently, she identified the clothes she wanted to wear, and she initiated feeding when meals were placed before her. In addition, drawing, writing letters to friends and reading the paper

[7] The data presented in this chapter have been submitted for publication: Robinson, G., Shallice, T., & Cipolotti, L. Dynamic Aphasia in Progressive Supranuclear Palsy: A deficit in generating a fluent sequence of novel thought.

(or flicking through the pictures) were all referred to as daily activities that she engaged in. The OT conducted an art session as drawing was KAS's favourite hobby and documented that she incorporated the type of clothing worn by the OT into her drawing of women's fashion without any prompting. The OT did note, however, that KAS tended to perseverate when using a colour or when drawing certain lines (e.g., the eyes in a woman's profile). These examples demonstrate that KAS does not lack initiative with regard to basic activities and that she was not generally apathetic and amotivated. There was evidence, however, that KAS was slow to respond, carry out tasks, and answer questions and that her speech was produced slowly.

A MRI brain scan in 1998 showed a severe degree of atrophy in the midbrain with the classic *Mickey Mouse* appearance noted (see Fig. 3). Signal change was found in other brain stem structures (pons and medulla), thalamus, and basal ganglia (caudate nucleus and putamen). In addition, white matter change was evident in the frontal lobes bilaterally. A clinical diagnosis of progressive supranuclear palsy (PSP) was given.

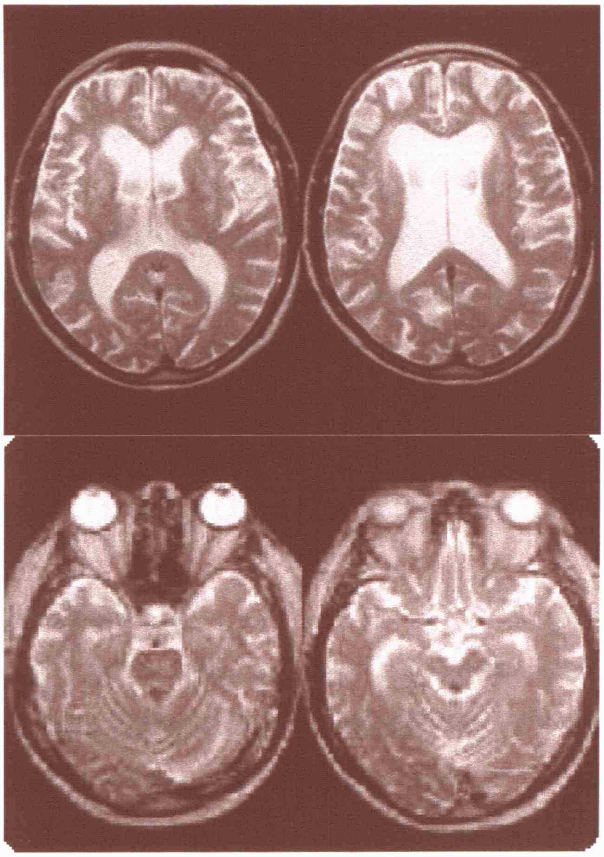

Figure 3. Horizontal T_1 weighted MRI of Dynamic Aphasic KAS

3.2.1 Patient Controls

For the two Discourse Level Generation experimental tasks below, three patients (two female and 1 male) without aphasia were recruited as controls; 1 patient with probable PSP (74 years, retired actress, 7 year history of PSP symptoms), 1 patient with a vascular left frontal (LF) lesion (40 years, teacher, LF bleed involving the inferior and middle frontal gyri); and 1 patient with a traumatic brain injury (TBI) (42 years, engineer, bifrontal and right temporal damage, severe frontal executive dysfunction) (see Appendix 2). The PSP patient was chosen to control for KAS's neurological condition. The LF patient was chosen to control for the effect of the left frontal lesion. The TBI patient was chosen to control for the effect of severe frontal executive dysfunction. For ease of comparison, their cognitive and language baseline scores are reported in Tables 11 and 13 alongside KAS's scores.

3.2.2 Cognitive Function Baseline

KAS was assessed on a shortened form of the WAIS-R (Wechsler, 1981; see Table 11). She obtained a borderline defective Verbal IQ and a defective Performance IQ. Her performance on an un-timed test of non-verbal general intelligence, the Coloured Progressive Matrices (Raven, 1976b), placed her at a low average level. Of note, however, the time taken to obtain this low average score was abnormally long, even when compared to a much older control sample (see Table 11). Pre-morbid level of optimal function, based on her reading performance on the NART (Nelson et al., 1991), and occupational and educational background, was estimated to be in the good average range. Thus, these results indicate a moderate to severe degree of intellectual decline. Verbal and visual memory functions were severely impaired as ascertained by her performance on easy recognition memory tests (Clegg & Warrington, 1994). Visual perceptual and spatial skills were normal as assessed by two sub-tests from the Visual Object and Space Perception Battery (Warrington et al., 1991).

3.2.3 Frontal Executive Function

Her performance on a series of tests considered sensitive to frontal lobe damage was impaired (see Table 11). She achieved one of the two solutions on the Weigl sorting test (Weigl, 1941). On an easy version of the Stroop Test, she was unable to perform on the ink conflict condition (Stroop, 1935). Her performance was impaired on the Hayling Sentence Completion Test (Burgess et al., 1996b).

Interestingly, this impaired performance was almost entirely due to prolonged response times. On the harder response suppression part, most of her responses were unconnected and she made only 4 connected errors.

Table 11. Cognitive Baseline and Frontal Executive Function Scores for KAS and the Patient Controls (PSP, LF, TBI)

			Patient Controls	
	KAS	PSP	LF	TBI
Cognitive Baseline Scores				
Verbal IQ	76	100	-	80
Performance IQ	67	90	-	68
Raven's Progressive Matrices	CPM = 24/36	-	APM = 12/12	APM = 3/12
(Coloured or Advanced)	(10-25th%ile)	-	(>90th%ile)	(5-10th%ile)
Time to Complete	16 minutes [a]	-	-	-
RMT: Words	18/25	48/50	46/50	12/25
	(<5th %ile)	(75-90th%ile)	(25-50th%ile)	(<5th %ile)
Faces	16/25	33/50 [#]	47/50	17/25
	(<5th %ile)	(<5th%ile)	(75-90th%ile)	(<5th %ile)
Visual Perception	IL = 18/20	OD = 18/20	OD = 18/20	IL = 19/20
Space Perception	PD = 18/20	-	-	-
Frontal Executive Function Scores				
Weigl Sorting Test	Fail	-	-	Fail
Modified Card Sorting Test	-	6/6	-	1/6
Trail Making Test Part A	-	-	>90th %ile	<10th%ile
Part B	-	-	25-50th %ile	<10th%ile
Proverb Interpretations	-	Mildly concrete	Mildly concrete	Fail
Cognitive Estimates Test	-	-	Pass	Fail
Stroop Test	Fail	Fail	Pass	Fail
Hayling Sentence Completion Test: 1 - sensible RT	SS = 2*	-	SS = 6*	SS = 4*
2 - unrelated RT	SS = 1*	-	SS = 6*	SS = 6*
2 - unrelated errors	SS = 4*	-	SS = 7*	SS = 1*
Word Fluency: S in 1 minute	4	10	14	7

PSP = progressive supranuclear palsy; LF = left frontal; TBI = executive dysfunction; CPM = Coloured Progressive Matrices; APM = Advanced Progressive Matrices; [a] - Clegg and Warrington, 1994, Normative data for 64-81 years, M = 6 minutes, S.D. = 2.5; [#] - Also administered the Topographical Recognition Memory Test and scored 19/30 (25th%ile); IL = Incomplete Letters; OD = Object Decision; PD = Position Discrimination * = SS is from 1-10 with 6 being average.

3.2.3.1 Verbal and Non-Verbal Fluency

3.2.3.1.1 Word fluency.

KAS was asked to generate as many words as possible on a series of phonemic (FAS) and semantic category tasks (see Table 12). There were two time conditions: 1 minute; and Unlimited. In the Unlimited condition, KAS was allowed to generate as many words as possible until she did not generate any item for 30 seconds. At this point, an additional 1 minute was allowed. The total numbers of correct responses generated and perseverative errors were recorded.

The total number of words generated on the standard 1 minute phonemic task was severely impaired (>2.5 SD below the mean; see Table 12). Interestingly, her performance was not improved when given unlimited time. Similarly, the total number of words generated on semantic category tasks was poor, although in the Unlimited time condition her performance improved particularly for one category (food). All errors were perseverations and in fact, 38% of the total words generated were perseverations. By contrast, the previous dynamic aphasic patients ANG and CH produced no perseverative responses on numerous verbal fluency tasks (i.e., 0% of the total words generated). The only error KAS made that was not strictly a perseveration was producing *alone* on the 'S' phonemic task, which was a correct response for the preceding phonemic task ('A').

3.2.3.1.2 Design fluency.

KAS was asked to generate as many drawings as possible under three different conditions: (a) free; (b) fixed; and (c) nonliving objects. The free and fixed conditions were based on Jones-Gotman and Milner (1977) with the standard instructions given. For the nonliving objects condition, KAS was asked to draw as many recognisable (i.e., nameable) nonliving objects as possible. KAS was given 4 minutes for each condition. The total number of responses generated and errors (perseverative and inappropriate responses) were recorded.

KAS produced only 1 abstract design in the free condition although she produced 11 errors. Of these, 5 were perseverative responses and 6 were nameable (i.e., inappropriate responses; see Table 12). No acceptable designs were produced in the fixed condition except for 1 inappropriate response (an abstract design) which was subsequently repeated. The total number generated for the free and fixed conditions is markedly below the controls reported by Jones-Gotman and Milner (1977; see Table 12). For the nonliving objects condition, KAS produced only 3 drawings, and 7 errors

(4 perseverative responses and 3 animals). The total number generated is clearly below the number produced for object fluency by controls used for CH (2.8.1.4; see Table 12). Overall, perseverations accounted for 42% of the total number of designs generated. Of note, the number of novel drawings produced by the previous dynamic aphasic CH was within the normal range and he produced only 1 perseverative error on the same three design fluency tasks (i.e., 2.5% of the total number of designs generated).

Table 12. *Word and Design Fluency Scores for KAS: Total Number Generated and Errors*

		Total Number of Correct Responses		Errors: Perseverative Responses		Errors: Inappropriate Responses	
Word Fluency							
		1 min.	Unlimited	1 min.	Unlimited	1 min.	Unlimited
Phonemic	F	5	6	3	10	0	0
	A	3	5	2	3	0	0
	S	4	4	2	0	0	1
	FAS Total [a]	12	15	7	13	0	1
Semantic	Animals [b]	6	10	3	1	0	0
	Food	9	21	1	12	0	0
	Objects	7	5	10	4	0	0
Design Fluency							
Free [c]		1		5		6	
Fixed [d]		0		1		1	
Nonliving Objects [e]		3		4		3	

Note: Spreen & Strauss, 1998, Normative data for [a] FAS, M = 44.7, SD = 11.2 and [b] Animals, M = 21.9, SD = 5.4; Jones-Gotman and Milner, 1977, Normative data for Design Fluency [c] Free Condition, M = 16.2 and [d] Fixed Condition, M = 19.7; [e] CH controls for Object Fluency, M = 16.6.

3.2.4 Language Function Baseline

3.2.4.1 Speech production

Initiation of conversation was exceedingly rare. Indeed, KAS presented with a degree of mutism. During unstructured interview very long pauses of several minutes occurred. Thus, spontaneous speech was extremely sparse, effortful, and mildly dysarthric and dysprosodic. The content was appropriate and syntax was normal, with some echolalia evident. No phonological, semantic, or word order errors were made. Descriptions of complex scenes (Cookie Theft, Beach) were initiated after a long pause (e.g., 45 seconds [s]) and over a long period of time (e.g., 150s). The quantity produced was extremely reduced and somewhat perseverative, although normal in syntax. For example, KAS produced the following description of the Cookie Theft Scene: *Well she looks like she is baking, no, she is washing dishes .... (34s) and there is water flowing ..... (65s) the boy is stealing cookies out of the cookie jar .... because mummy is wiping dishes ... water is spilt on the floor, water is spilt on the floor .... (102s) the girl is asking for cookies .... (125s).* Similarly, when asked to produce a story narrative from a simple pictorial scene of an ice skater, after a long pause she produced very little over a long time. After 45s, KAS only generated one sentence - *He's dreaming when he is a man ... what kind of house he'll have* - and after a further 45s, she generated a second sentence that was perseverative - *He's a boy skating and he's dreaming of a house he'll have and he's dreaming.*

3.2.4.2 Repetition

Word repetition skills were only slightly weak (94% correct; see Table 13). Word length and frequency effects were absent. The errors were mainly phonological (e.g., newt → *mute,* notify → *modify*). Repetition of cliche and non-cliche 3- to 7-word sentences was almost at ceiling. The only error was an omission (i.e., "As blind as a bat" → "*As blind as bat*").

3.2.4.3 Word retrieval

Picture naming skills were relatively preserved (see Table 13). KAS was given three oral naming tasks: Oldfield Picture Naming Test (Oldfield & Wingfield, 1965); a set of verbs and nouns matched for frequency (Kucera et al., 1982); and a category naming test based on high frequency items (for details see Cipolotti, 2000). She was able to name all of the common items on the Oldfield Picture Naming Test. Oral naming of actions and objects was satisfactory, with no significant difference between verbs and nouns found ($\chi^2(1) = 1.72$, n.s). Her performance was almost at ceiling on the category naming test.

Table 13. *Spoken and Written Language Scores for KAS and Patient Controls (PSP, LF, TBI): Number Correct*

	KAS	Patient Controls PSP	LF	TBI
Repetition				
Words High frequency (1,2,3-syllable)	88/90	-	-	-
Low frequency (1,2,3-syllable)	81/90	-	-	-
Sentences	29/30	-	10/10	10/10
Word Retrieval				
Graded Naming Test	-	21/30 (50-75th %ile)	27/30 (>95th %ile)	20/30 (50th%ile)
Oldfield Picture Naming Test	25/30	-	-	-
Nouns	33/40	-	-	-
Verbs	28/40	-	-	-
Category Naming Test				
Colours	8/10	-	-	-
Body Parts	10/10	-	-	-
Animals	8/10	-	-	-
Objects	9/10	-	-	-
Word Comprehension				
Synonym Test	37/50 (10-25th%ile)	-	47/50 (75-90th%ile)	48/50 (75-90th%ile)
British Picture Vocabulary Scale	145/150	-	-	
Sentence Comprehension				
Token Test	14/14	-	-	-
Test for the Reception of Grammar	75/80	-	-	-
Sentence construction task	8/10	-	-	-
Reading and Spelling				
National Adult Reading Test	25/50	40/50	40/50	35/50
Graded Word Reading Test	85/100	-	-	-
Oral Graded-Difficulty Spelling Test	12/30 (10-25th %ile)	-	-	-

PSP = progressive supranuclear palsy; LF = left frontal; TBI = executive dysfunction.

3.2.4.4 Word comprehension

Word comprehension skills were preserved. Her performance was within the normal range on the Synonym Test (Warrington et al., 1998) and almost at ceiling on the British Picture Vocabulary Scale (Dunn et al., 1982; see Table 13).

3.2.4.5 Sentence comprehension

Sentence comprehension skills were preserved (see Table 13). Her performance was flawless on a shortened version of the Token Test (De Renzi et al., 1978a) and only slightly weak on the Test for the Reception of Grammar (Bishop, 1983).

3.2.4.5.1 Sentence construction test.

KAS was given a sentence construction task that was failed by the dynamic aphasic ROH (Costello et al., 1989). KAS was given 10 sentences to rearrange (3-7 words in length). The time taken from stimulus presentation to task completion was recorded. She performed this task well (see Table 13) although slowly (M = 35.9s, SD = 21.0s). This performance is similar to several other dynamic aphasics including CH, ANG (Robinson et al., 1998) and ADY (Warren et al., 2003). Of note, KAS was given an oral version of this task due to her eye movement difficulty and her performance was similarly almost flawless and faster (9/10, M = 1.6s, SD = 1.5s)

3.2.4.6 Reading and Spelling

KAS's single word reading and spelling ability was intact (see Table 13). Her performance was in the average range on both the NART (Nelson et al., 1991) and the Schonell Graded Reading Test (Schonell, 1942). She performed within the lower limit of the normal range on an Oral Graded-Difficulty Spelling Test (Baxter et al., 1994).

3.2.5 Summary and Diagnosis

In summary, KAS presented with a severe impairment in her intellectual, memory and executive functions. In contrast, visual perceptual functions were intact. KAS's ability to generate both single words and drawings on fluency tasks was severely impaired and perseverative responses were a common feature on both tests. Her poor performance on verbal fluency tasks was due to the sparseness of items generated and not to slow production. She failed to produce significantly more words when allowed to continue generating items without a time restriction.

The most remarkable feature of KAS's nonfluent dysphasia consisted of a severe reduction of propositional speech in the context of well-preserved repetition, nominal, comprehension, and reading skills. KAS's dysphasic impairment falls within the classification of pure dynamic aphasia (Luria, 1966; 1970; 1973; Luria et al., 1968).

KAS presented with a prominent and severe reduction in verbal output. The following tests were designed to investigate whether KAS's dynamic aphasia encompassed the generation of both word and sentence level responses and multiple connected sentences (i.e., discourse). Further, the nature of KAS's discourse level generation was investigated in terms of whether it was equally severe under different conditions (e.g. with and without external support).

3.3 WORD AND SENTENCE GENERATION INVESTIGATION

In this section, the nature and extent of KAS's word and sentence level generation impairment was explored using the same tests previously administered to ANG and CH. These tests require the generation of a single response (i.e., a word, a phrase or a sentence) to different types of input (e.g., words, phrases, sentences, single pictures, pictorial scenes). These tasks contrast with both fluency tasks that require the generation of multiple single responses (e.g., word and design fluency) and discourse level tasks that require the generation of multiple connected sentences. In order to ensure that comparison between KAS and previous dynamic aphasic patients was appropriate, KAS's speech production was analysed and compared with ANG and CH.

3.3.1 Speech Production Analysis and Comparison with ANG and CH

The speech elicited from two complex scene descriptions (total number of words = 94) was analysed since the sparseness of speech precluded formal analysis from only one speech sample elicited from a story (e.g., QPA; Berndt et al., 2000). KAS's speech rate was severely reduced (23.0 words per minute [wpm]; Table 14). Moreover, KAS's speech rate was lower than ANG (see Table 14). The speech rate of all three dynamic aphasic patients was much lower than nonfluent aphasic patients and profoundly below normal control subjects reported by Berndt et al.[8]. The overall proportion of verbs KAS produced was comparable to previous dynamic aphasic patients (see Table 14). The proportion of verbs produced by the three dynamic

[8] Descriptive statistics for a group of non-fluent aphasics and a group of normal healthy controls are reported in the QPA training manual (Berndt et al., 2000). The statistics are based on speech samples that were elicited from different material (i.e., not from Complex Scene descriptions). The speech rate reported for the non-fluent aphasic patients was 39.01 wpm (SD = 19.63) and for the normal controls speech rate was 160.82 wpm (37.00).

aphasic patients was between the proportion for normal controls and nonfluent aphasic patients[9]. The overall proportion of closed class words KAS produced was comparable to both ANG (see Table 14) and normal controls[10], but higher than CH (see Table 14) and nonfluent aphasic patients[10]. Overall, this analysis indicated that KAS indeed was worse than ANG and comparable to both ANG and CH in terms of the production of verbs and nouns.

Table 14. *Speech Production Analysis Scores for KAS, ANG and CH*

Complex Scenes (Cookie Theft, Beach)	**KAS**	**ANG**	**CH**
Speech Rate (words per minute)	23.0	29.2	12.0
Proportion of Verbs	0.42	0.39	0.44
Proportion of closed class words	0.56	0.51	0.22

3.3.2 Word and Sentence Generation Tests

For comparison purposes the performance of ANG, CH and controls on word and sentence level generation tasks are included. For all tests, the examiner recorded the number correct and response time with the use of a stopwatch. For all tasks, response time (RT) was defined as the time from the end of stimulus presentation to the time the patient started to generate a response. A summary of scores is presented in Table 15.

3.3.2.1 Generation of a single word to complete a sentence

A set of 30 sentences with the final word omitted was selected from Bloom and Fischler (Bloom & Fischler, 1980). The number of alternative completion words for each sentence varied such that the level of constraint and probability of a dominant response varied accordingly as was described for CH in Chapter 2 (2.5.2). Similarly, the stimuli were grouped to form four different levels of constraint, with the following mean highest probability response: (a) Very High Constraint = 0.93; (b) Medium-High

[9] The overall proportion of verbs produced by the non-fluent aphasic patients was 0.37 (SD = 0.10) and by the normal controls was 0.48 (SD = 0.06) (Berndt et al., 2000).
[10] The overall proportion of closed class words produced by the non-fluent aphasic patients was 0.41 (SD = 0.11) and by the normal controls was 0.54 (SD = 0.04) (Berndt et al., 2000).

Constraint = 0.74; (c) Low Constraint = 0.55; (d) Very Low Constraint = 0.38. Each level contained 8 sentences except for the very low constraint level that had 6 sentences. The sentence frames were orally presented to KAS who was then asked to generate an appropriate single word to complete it meaningfully. She was able to generate an appropriate word for almost all sentences after only a slight delay. The only error was a semantically related response for a very high constraint sentence (i.e., The boat passed easily under the ...canal).

3.3.2.2 Generation of a phrase to complete a sentence

KAS was orally presented with phrases and required to complete each with a second phrase to form a meaningful sentence. There were three conditions: (a) baseline phrases (e.g., "The children were..."); (b) high predictability phrases that had few verbal response options for their completion (e.g., The man walked into the cinema...); and (c) low predictability phrases that had many verbal response options for their completion (e.g., The man walked into the house...). She was required to complete each phrase with a second phrase (i.e., more than one word) to form a meaningful sentence. KAS's performance in all three conditions was flawless although slow.

3.3.2.3 Generation of a sentence from a single word

KAS was orally presented with a single word and asked to produce a whole sentence incorporating the target word. There were two conditions: (a) proper nouns (e.g., Sean Connery), which elicit a dominant or few verbal response options; and (b) common nouns (e.g., glass), which elicit many verbal response options. KAS performed this task almost at ceiling, although somewhat slowly.

3.3.2.4 Generation of a sentence from word pairs

KAS was orally presented with a word pair and instructed to produce a complete sentence that incorporated both target words. There were two conditions: (a) highly associated word pairs (e.g., "butter-bread"); and (b) lowly associated word pairs (e.g., "butter-finger"). Her performance in both conditions was flawless although slow.

3.3.2.5 Generation of a sentence from a sentence

KAS was orally presented with 5 complete sentences and asked to generate a second sentence around the theme of the first. She had no difficulty with this task and generated a correct response for all sentences although she performed this task slowly (e.g., The children went down to the beach...*They built sandcastles in the sand).*

Table 15. *Word and Sentence Generation Scores for KAS (data also reported for ANG, CH and Controls): Total Number Correct and Mean RT*

	Number Correct (RT, SD)			
	KAS	ANG	CH	Controls
	Generation of a Single Word to Complete a Sentence			
Total	**29/30**	66/91	282/384	nt
	(3.3, 3.1)	*	(3.3, 3.1)	nt
Very High Constraint	**7/8**	nt	88/96	nt
Medium-High Constraint	**8/8**	nt	76/96	nt
Low Constraint	**8/8**	nt	67/96	nt
Very Low Constraint	**6/6**	nt	51/96	nt
	Generation of a Phrase to Complete a Phrase			
Baseline	**10/10**	3/20	6/10	nt
	(5.5, 2.1)		(6.0, 2.5)	nt
High predictability	**10/10**	9/12	19/22	12/12
	(4.6, 2.5)	(4.3, 3.2)	(6.1, 3.9)	(1.9, 1.6)
Low predictability	**10/10**	3/12	11/22	12/12
	(7.2, 4.9)	(5.7, 4.7)	(8.3, 3.7)	(2.2, 3.0)
	Generation of a Sentence from a Single Word			
Proper Nouns	**15/15**	26/28	22/30	28/28
	(7.1, 4.0)	(3.1, 1.6)	(13.1,5.9)	(2.2, 1.9)
Common Nouns	**14/15**	11/28	10/30	28/28
	(7.0, 5.7)	(7.8, 2.2)	(11.8,8.2)	(2.3, 1.7)
	Generation of a Sentence from Word Pairs			
High association	**15/15**	22/30	nt	30/30
	(7.9, 4.6)	(4.4, 3.3)	nt	(2.6, 3.2)
Low association	**15/15**	4/30	nt	30/30
	(11.0, 4.5)	(4.6, (1.9)	nt	(2.8,4.6)
	Generation of a Sentence from a Sentence			
Total	**5/5 (11.0, 5.2)**	3/20	nt	nt
	Generation of a Sentence given a Pictorial Scene			
Baseline description	**15/15**	34/34	20/20	nt
	(10.9, 7.1)	nt	(12.9, 8.4)	nt
What might happen next?	**15/15**	3/20	3/20	nt
	(14.2,11.0)	nt	(13.3, 3.8)	nt
	Generation of a Sentence from a Single Picture			
Total	**9/10 (11.2, 5.9)**	0/6	nt	nt

RT = response time in seconds; nt = not tested; * All correct responses were given in < 2 seconds.

3.3.2.6 Generation of a sentence given a pictorial scene

KAS was presented with simple pictorial scenes selected from the PALPA (Kay et al., 1992) and asked to produce a sentence to describe it under two conditions: (a) baseline description; and (b) generate a description of "what might happen next?". Her performance was flawless, although responses were produced after a long pause.

3.3.2.7 Generation of a sentence from a single picture

KAS was presented with pictures of common objects (e.g. man, dog) and asked to produce a whole sentence incorporating the target item. She was able to generate a sentence for almost all pictures although after a long pause.

3.3.3 Summary

The speech production analysis showed that KAS's propositional speech impairment was as severe as ANG and CH. The word and sentence level generation investigation demonstrated that KAS was able to generate a single response (i.e., a word, a phrase and a sentence) when given a stimulus. Her preserved performance on these tests was not affected by stimulus type. KAS performed virtually at ceiling both for stimuli that activate a dominant response (e.g., proper nouns, phrases high in response predictability, word pairs high in association) as well as for stimuli that activate many response options (e.g., common words, phrases low in response predictability, word pairs low in association). Although KAS was able to generate a single response on word and sentence level generation tests, her response times were long.

3.4 DISCOURSE GENERATION INVESTIGATION

This investigation was designed to further explore KAS's propositional speech impairment. The contrast between KAS's severely reduced propositional speech and her unimpaired ability to generate a single response on word and sentence level generation tasks was puzzling. Thus, two discourse tasks were devised in order to collect and analyse samples of KAS's ability to generate multiple connected sentences in an attempt to understand the deficits underlying her impairments.

3.4.1 Controls

For the two discourse tasks the 3 patient controls described previously (PSP, LF, TBI; see Appendix 1) and 3 female healthy controls (C1 = 56 years, C2 = 50 years, C3 = 40 years; all occupations within the artistic domain) were used.

3.4.2 Statistical Analyses

The performance of KAS and the performance of the patient controls were each compared to normal healthy controls using the modified t-test, df = 2 (Crawford et al., 2002).

3.4.3 Topic-Based Discourse

In this task KAS, patient controls, and healthy controls were asked to talk about 3 different topics. A previous sample of speech from 1 topic for the dynamic aphasic patient ANG was included in the novelty analysis presented below.

3.4.3.1 Materials and Procedure

KAS was asked to talk about 3 topics: films, actresses and stage shows. There were two conditions: a) KAS was asked to talk about one of her favourite examples of a topic (e.g., Tell me about one of your favourite films); and b) KAS was asked by the examiner to talk about a given example of the topic (e.g., Tell me about the film Titanic). Topic-familiarity was ensured prior to the experiment by probing prior knowledge of the topic. If an example was unknown or only relatively familiar, a suitable alternative was given. KAS, patient controls and healthy controls were given 2 minutes in which to talk about each topic. Therefore, the total time was 6 minutes.

3.4.3.2 Scoring Procedure

The method of scoring included some of the QPA measures (Berndt et al., 2000) and some new measures that were termed novelty measures. The QPA measures used were: speech rate (words per minute); number of sentences (i.e., a group of words containing a subject-verb combination); and total words uttered[11]. The novelty measures used were: novel sentences, novel words and perseverative words. A novel sentence was a group of words containing a subject-verb combination <u>and</u> expressing a new conceptual idea not previously given. The number of novel sentences was expressed as a percentage of the total number of sentences (i.e., novel/total). A word was considered novel if it was not present in the immediately preceding sentence

[11] This is equivalent to the Berndt et al. (2000) *complete words uttered* measure except that non-linguistic fillers (e.g., *um*) or false starts were not excluded at this stage.

produced either by KAS or by myself, and if it was not a neologism, a non-linguistic filler (e.g., *um*) or a false start. The number of novel words was expressed as a percentage of the total words uttered (i.e., novel/total). A word was considered perseverative if it was a repetition of a word produced in the same or immediately preceding sentence. The number of perseverative words was expressed as a percentage of the total words uttered (i.e., perseverative/total).

These scoring procedures were applied only to the condition in which KAS was asked to talk about one of her favourite examples of the topic. Unfortunately, in the condition in which KAS was asked by the examiner to talk about a given example of the topic, her performance was extremely impaired. Her propositional speech was virtually abolished. Indeed she was only able to produce 1 sentence for the stage show Miss Saigon (e.g., Tell me about the stage show Miss Saigon. *Miss Saigon was... {60s}...Miss Saigon was ... {90s} a poor unfortunate... poor unfortunate...poor unfortunate lady {120s})*. The paucity of her production precluded any formal analysis for this condition. A summary of scores is presented in Table 16.

3.4.3.3 Results

On the QPA measures, the performance of the 3 patient controls did not statistically differ from that of the healthy controls. The only exceptions were the reduced speech rate and total words uttered by the PSP patient. Similarly, the 3 patient controls' performance was indistinguishable from the healthy controls on all three novelty measures.

In contrast, KAS performed significantly worse than both patient and healthy controls on all three QPA measures; speech rate, number of sentences and total words uttered. Therefore, overall KAS produced far fewer words and sentences. In addition, KAS performed significantly worse than healthy controls on all three novelty measures. The overall percentage of novel sentences and novel words was significantly reduced. In contrast, the overall percentage of perseverative words was significantly higher than patient and healthy controls.

KAS's impairment is not a general characteristic of dynamic aphasia. Interestingly, the performance of the dynamic aphasic patient ANG on all three novelty measures was virtually indistinguishable from that of both the patient and healthy controls. Overall, KAS's ability to produce multiple connected sentences was sparse, lacking novel sentences and words, and perseverative.

Table 16. *Topic-Based Discourse (6 minutes): KAS and Controls Scores*

	KAS	Controls				ANG[a]
		PSP (1)	LF (1)	TBI (1)	Healthy (3)	
QPA Measures						
Speech Rate (words per minute)	**25.2***	60.5*	139.7	85.7	183.6 (34.9)	-
Number of Sentences	**20***	55	117	65	140 (27.9)	-
Total Words Uttered	**151***	363*	838	514	1101 (209)	-
Novelty Measures						
% Novel Sentences	**75%***	98%	96%	98%	97% (2.1%)	96%
% Novel Words	**68%***	97%	98%*	95%*	97% (0.1%)	100%*
% Perseverative Words	**29%***	0%	0.9%	0.4%	0.8% (0.6%)	0%

Standard Deviation for healthy controls in parentheses; PSP = progressive supranuclear palsy; LF = left frontal; TBI = executive dysfunction; QPA = Quantitative Production Analysis; - = not calculated; * $p < 0.05$, Modified t-test (df = 2) comparisons between each patient (KAS, PSP, LF, TBI) and Healthy Controls. [a] Robinson et al., 1998 – analysis based on a sample of 157 words.

3.4.4 Discourse With and Without External Support

The previous task provides further evidence that KAS presented with a severe reduction in propositional speech. She was impaired on a task requiring the production of multiple connected sentences. Despite this severe impairment, and in contrast to previous dynamic aphasic patients, she was able to generate a single response on word and sentence level generation tasks. It is hypothesised that one of the main differences between discourse level propositional speech and word and sentence level propositional speech is that the latter contain a stimulus that could be viewed as providing *external support*. It may be that this *external support* facilitates propositional speech generation. In order to investigate the role of *external support* in KAS's ability to produce multiple connected sentences (i.e., discourse), two interviews were developed: 1) with *external support* (i.e., with substantial verbal prompting); and 2) with *no external support* (i.e., little or minimal verbal prompting).

3.4.4.1 Materials and Procedure

KAS was interviewed at bedside, an environment that had numerous familiar items surrounding her. KAS was familiar with the examiner given several testing sessions had been conducted prior to the interview. She was interviewed under two conditions: a) *external support*; and b) *no external support.* In the interview with *external support,* she was asked a series of questions that focused on either autobiographical or recent episodic material. In this condition she was provided with substantial external verbal support in order to help KAS initiate and elaborate on her answers (e.g., GR: What did you do this morning? *KAS: I had breakfast.... I had a shower*; GR: Do you have a nurse that helps you? *KAS: I have a carer*). Indeed, 90% of the examiner's comments were questions designed to elicit responses and only 10% were comments that required no response (e.g., GR: That's nice). In the interview with *no external support,* she was similarly asked questions focussed on recent episodic material. However, in this condition the examiner provided minimal verbal support. KAS was asked as many questions as in the previous condition, however, only half of these were designed to elicit responses. This meant that half of the examiner's responses were single comments that required no response. Thus, in this condition questions were less frequent with the examiner more often simply repeating KAS's responses (e.g., GR: Do you like drawing? *KAS: Yes there is a ski suit.* GR: A ski suit?). The duration of both interviews was 8 minutes. Each interview was recorded on tape for transcription and scoring purposes.

3.4.4.2 Scoring Procedure

For each condition, the same QPA and novelty measures as for the previous test (4.3) were calculated. In the novelty measures, a fourth parameter was added: echolalic words. A word was considered echolalic if it was a repetition of a word produced by the examiner in the immediately preceding sentence. The number of echolalic words was expressed as a percentage of the total words uttered (i.e., echolalic/total). Patient and healthy controls produced a much larger sample of speech than KAS. Therefore, a sample of 150 words was chose from which the number of sentences and novel sentences were calculated. The totals reported are prorated from this sample, the minimum amount recommended by Berndt et al. (2000) for the QPA method. A summary of scores is presented in Table 17.

3.4.4.3 Results

The performance of the 3 patient controls did not statistically differ from that of the healthy controls in the interview with *external support* on all QPA measures. In the interview with *no external support,* the LF and TBI patient controls' performance was again indistinguishable from that of the healthy controls. However, the PSP patient controls performance was significantly worse in the interview with *no external support* on all QPA measures. The performance of all patient controls was indistinguishable from healthy controls on all four novelty measures.

KAS performed worse than both patient and healthy controls on all three QPA measures (speech rate, number of sentences and total words uttered) in both the condition with and without external support. Indeed performance was significantly worse for all three QPA measures in comparison to healthy controls. Therefore, similar to the results of the topic-based discourse task, overall KAS produced far fewer sentences and words. In addition, she also performed significantly worse on all four novelty measures. The overall percentage of novel sentences and novel words was significantly reduced. In contrast, the overall percentage of perseverative words and echolalic words was significantly higher than both healthy controls and patient control. Thus, KAS's discourse level generation was extremely sparse, characterised by a paucity of novel sentences and words, and it was marred by perseverations and echolalia.

A comparison of QPA and novelty measures was also made across the two conditions (*external* and *no external support*) between KAS, patient controls, and healthy controls. For all three QPA measures (speech rate, number of sentences, total words uttered), there was no difference in the healthy controls on the two conditions. Qualitatively, the healthy controls were slightly better in the condition with *no external support.* Thus, speech rate was slightly faster with a tendency to produce more sentences and words in the condition with *no external support.* The performance of the 3 patient controls on the three QPA measures did not statistically differ from the healthy controls in the two conditions, except for the PSP patient's performance in the condition with *no external support.* Although the PSP patient performed significantly worse than healthy controls, the PSP patient's speech rate, number of sentences produced and total words uttered in the two conditions are almost identical. KAS performed worse than healthy controls on all three QPA measures in both conditions. Qualitatively it was noticeable that her performance on all three measures was markedly better in the condition with *external support*. Indeed, for example, she produced almost twice as many words per minute in the interview with *external support* than in the interview with *no external support*.

Table 17. *Discourse With and Without External Support (8 minutes): KAS and Controls Scores*

External Support = ES+ No External Support = ES–		KAS	Controls			
			PSP (1)	LF (1)	TBI (1)	Healthy (3)
QPA Measures						
Speech Rate	ES+	**21.4***	48.9	166.7	74.9	145.0 (36)
	ES–	**12.8***	48.5*	184.5	96.8	168.9 (27)
Number of Sentences	ES+	**23***	63	178	88	128 (27)
	ES–	**16***	59*	181	99	165 (20)
Total Words Uttered	ES+	**171***	391	1334	599	1160 (287)
	ES–	**102***	388*	1430	774	1356 (208)
Novelty Measures						
% Novel Sentences	ES+	**74%***	100%	100%	100%	97% (0.9)
	ES–	**75%***	100%	100%	95%	96%(2.9)
% Novel Words	ES+	**68%***	97%	99%	95%	97% (0.9)
	ES–	**73%***	99%	100%	96%	98% (0.8)
% Perseverative Words	ES+	**20%***	0.7%	0.2%	0.8%	1.1% (0.8)
	ES–	**24%***	0%	0%	0.8%	0.9% (0.6)
% Echolalic Words	ES+	**12%***	0.5%	0.5%	0.8%	1.0 % (0.3)
	ES–	**3%***	0%	0%	0%	0.5% (0.3)

Standard Deviation for healthy controls in parentheses; PSP = progressive supranuclear palsy; LF = left frontal; TBI = executive dysfunction; QPA = Quantitative Production Analysis; * $p < 0.05$, Modified t-test (df = 2) comparisons between each patient (KAS, PSP, LF, TBI) and Healthy Controls.

Secondly, to address the comparison between the two conditions on the four novelty measures; novel sentences, novel words, perseverative words and echolalic words. On all four novelty measures, there was virtually no difference between the two conditions for healthy controls. Similarly, the performance of the 3 patient controls on the four novelty measures did not reach statistical significance in comparison to the healthy controls for the two conditions. KAS performed worse than healthy controls on all four novelty measures in both conditions. Qualitatively, however, there was a noticeable difference in her performance on the two conditions for one novelty measure; namely echolalic words. The percentage of echolalic words KAS produced was four times higher in the condition with *external support.* In the interview with *no external support,* she rarely produced echolalic responses. Further, unlike the QPA measures, KAS received no advantage from external support on the novelty measures, apart from producing more words that were echolalic.

3.4.5 Summary

The results of the discourse level generation tests demonstrated that KAS's ability to produce multiple connected sentences was severely impaired. Her propositional speech was sparse and characterised by a paucity of novel sentences and words and a tendency for responses to become *stuck* (i.e., persist in activity for a long time once initiated). Notably, this lack of novelty was not present in the propositional speech of the dynamic aphasic ANG. The findings of the discourse task with and without external support suggest that *external support* in the form of verbal prompts may generally assist discourse level generation by aiding the elicitation of propositional speech. This is in line with the suggestion that external support drives narrative production as it functions as a processing prosthesis (Linebarger, Schwartz, Romania, Kohn, & Stephens, 2000; Linebarger, McCall, & Berndt, 2004a; 2004b). However, *external support* did not assist KAS's discourse production to become rich in novel concepts and words or less perseverative and echolalic.

3.5. DISCUSSION

KAS presented with severely reduced propositional language in the context of the neurodegenerative condition PSP. Propositional speech was almost abolished. Initiation of conversation was rare and only after very long pauses and it was characterised by perseverations and echolalia. KAS's severely reduced spoken language was not underpinned by a primary deficit in naming, comprehension or transcoding as these functions were intact. This pattern is consistent with dynamic aphasia (Luria et al., 1968; Luria, 1970; 1973) or broadly transcortical motor aphasia (e.g., Alexander et al., 1990; Benson et al., 1996; Berthier, 1999; Cappa et al., 1999; Freedman et al., 1984). More specifically, this pattern of presentation is one of *pure dynamic aphasia* as no other language impairments were evident.

The severity of KAS's dynamic aphasia was demonstrated to be comparable with that of the dynamic aphasic patients ANG and CH. Quantitative production analysis (QPA) found that when describing complex scenes her speech rate (i.e., words/minute) was severely reduced, and even lower than ANG's. On standard word fluency tasks, like other dynamic aphasic patients including ANG, her performance was extremely impaired. Of note, KAS not only produced few items, but unlike ANG and CH, she produced a high number of perseverations (38%). KAS's generation impairment was not confined to language output. Her nonverbal fluency (i.e., design fluency) performance was severely impaired. Similar to her word fluency performance, KAS produced a high number of perseverative responses (42%). KAS also produced a number of errors (i.e., nameable drawings), similar to the right frontal patients of Jones-Gotman and Milner (1977). Nonverbal generation skills have been investigated rarely in dynamic aphasia and the findings are mixed. For example, CH was intact on a series of nonverbal generation tasks, as was ADY for music generation skills (Warren et al., 2003). By contrast, CO's nonverbal generation skills were impaired as measured by design fluency ability (Gold et al., 1997).

Remarkably, despite KAS's severe dynamic aphasia and severe verbal and nonverbal fluency impairment, her performance on word and sentence level generation tests was intact although response times were prolonged. KAS was able to generate almost flawlessly a single word, phrase or sentence when presented with a verbal or pictorial stimulus. For example, KAS had no difficulty generating a phrase to complete the phrase; *The children were...* . This good performance is dissimilar to that of the majority of the previously reported dynamic aphasic patients (CH; ANG; ROH - Costello et al., 1989; ADY - Warren et al., 2003). Interestingly, KAS's ability to generate a word and sentence level response was not affected by stimulus type. She was able to generate a single response regardless of whether stimuli activated a dominant response (e.g., *London*) or many response options (e.g., *table*), unlike ANG and CH. Thus, in contrast to ANG and CH, KAS's propositional language impairment was not underpinned by an inability to select a single response where a stimulus activates many competing alternative response options.

In contrast to well preserved word and sentence level generation, KAS was impaired in generating *multiple* connected sentences as demonstrated by the two discourse level generation tasks: Topic-based Discourse, Discourse with and without External Support. The discourse samples were analysed using both QPA (Berndt et al., 2000) and novelty measures. The QPA measures showed that KAS performed worse than the 3 patient controls and healthy controls both in terms of speech rate and word and sentence production. The novelty measures showed that KAS performed significantly worse than the 3 patient controls and healthy controls both in terms of percentage of novel sentences and words, which were lower, and percentage of perseverative and echolalic words, which were higher. Notably, this pattern of performance was present both with and without external support. External support only marginally improved speech rate and production of words but not novelty of content. The pattern of reduced novel sentences and words and higher perseverative and echolalic words observed for KAS is not a typical feature of dynamic aphasia. The performance of ANG was indistinguishable from both patient and healthy controls on novelty measures.

In the literature, a pattern of performance similar to KAS can be found in the dynamic aphasic KC (Snowden et al., 1996) and Patient 2 and 3 (Esmonde et al., 1996). Although these patients' word and sentence level generation skills were somewhat less investigated, they were able to flawlessly generate sentences from verbal and pictorial contexts (KC), as well as complete sentences with single words (KC and Patient 2 and 3). Also similar to KAS was the high number of perseverative type responses Esmonde et al. noted in one of the three PSP patients (Patient 2), which has not been documented in previous dynamic aphasic patients. KAS's dynamic aphasia was present in the context of generalised cerebral atrophy that included the frontal lobes bilaterally and subcortical structures (e.g., basal ganglia). Similarly, KC and the 2 PSP patients were reported to have bilateral frontal damage. In contrast, dynamic aphasic patients such as ANG and CH who fail word and sentence level generation tasks typically have unilateral left posterior frontal lesions.

These results suggest that there may be two different subtypes of dynamic aphasia. The *1st subtype* is exemplified by patients such as ANG and CH who fail word and sentence level generation tests and have an impairment specific to the language domain. These patients have LIFG lesions. A 2^{nd} *subtype* is exemplified by patients like KAS who pass word and sentence level generation tasks but fail discourse level generation tests. The deficit of this second type extends beyond the language domain to encompass novel verbal and nonverbal response generation. These patients have bilateral frontal (and possibly subcortical) involvement.

It is slightly counterintuitive that bilateral cortical (and possibly subcortical) damage, such as that of KAS, results in a less severe word and sentence level generation deficit than unilateral damage on the left, such as that of ANG and CH. One can speculate that the bilateral cortical and subcortical damage spared the LIFG, consequently sparing the function that is responsible for selecting a single response when many competing verbal response options are activated. Alternatively, the bilateral cortical and subcortical damage may result in substantial lowering of the number of word and sentence level responses generated. As there would be a low number of single response options activated, little or no competition between the responses would arise, and thus, the function of the LIFG (i.e., selection between competing verbal response options) would be unnecessary.

3.5.1 Interpretations of dynamic aphasia

Given KAS's extensive bilateral damage and dysexecutive syndrome, the executive accounts of dynamic aphasia will be addressed first followed by a new speculation.

3.5.1.1 Executive Functioning Accounts

It is well documented that patients with dysexecutive impairment may present with apathy and amotivation; namely, a deficit of initiation and drive (Stuss et al., 1986; van Reekum et al., 2005). One would expect that such a deficit might impact also on the ability to generate verbal and non-verbal responses on fluency and experimental tasks. For example, KAS's globally impaired performance on word and design fluency tests could be viewed as a facet of apathy. However, there are two problems with this explanation. First, KAS does not present with a generalised apathy according to clinical activity reports. Second, a generalised apathy cannot account for her preserved performance on word and sentence level generation tasks. This preserved ability also cannot easily be accounted for by Gold et al.'s (1997) proposal.

These authors suggested that dynamic aphasia is due to a failure to develop a semantic or lexical search strategy, a process thought to be a component of executive functioning. Clearly KAS was able to develop a semantic strategy when performing the word and sentence generation tests.

Raymer and colleagues (2002) suggested that sentence generation involves executive skills responsible for generating verbal and nonverbal responses. Therefore, according to this account an executive impairment that impairs generation of novel responses more generally should result in a sentence generation deficit. However, there are at least two patients with severe frontal executive impairments who performed well on word and sentence level generation tests (JT reported in Robinson et al., 1998) and discourse level generation tasks (TBI control reported in this chapter). Moreover, CH did not fail executive tests despite dynamic aphasia. Finally, a novel response generation impairment cannot account for KAS's spared performance on single word and sentence level generation tasks.

3.5.2 Interpretation of Dynamic Aphasic KAS

Levelt's (1989; 1999) theoretical model for producing spoken language has been previously used to account for the performance of the dynamic aphasic patients ANG, CH and ADY (Warren et al., 2003) on word and sentence level generation tasks. In this model the *conceptual preparation* processes are responsible for the generation of new conceptual structures or messages that are subsequently realised as overt speech. There is as yet little empirical evidence that relates to the mechanisms underlying *conceptual preparation* and also little theoretical specification of these. The investigation of dynamic aphasic patients allows further specification of such mechanisms. For example, the pattern of performance documented in patients ANG and CH allowed specification of one set of cognitive mechanisms involved in the *conceptual preparation* stage; that is, damage at this stage may result in a highly selective generation impairment characterised by an inability to select a single response option from amongst competitors.

By contrast, KAS's preserved performance on word and sentence level generation tests, albeit with prolonged response times, implies that her ability to select a single response option from amongst competitors is intact. Analysis of KAS's performance on the two discourse level generation tasks would suggest that her impairment lies in the production of *multiple* connected sentences rather than a single word or sentence. Thus, her deficit lies in the set of mechanisms involved in *discourse generation*. Levelt (1999) hypothesised that conceptual generation for speech involves discourse focus that was defined as the "...focus [of] attention on something specific to be expressed (the 'current focus') ..." (p. 90). This model offers no further theorisation of the mechanism involved in discourse generation that can encompass KAS's language and non-language impairments. Several key properties of discourse structure have been highlighted by two computational linguistic theories (Grosz & Sidner, 1986; McKeown, 1992). Although there are some theoretical differences, these authors draw attention to the importance of *focusing* and *attention*; whereby focusing is defined as a process of directing attention to a particular set of concepts or topic in conversation.

With regard to KAS, it is hypothesised that her dynamic aphasia is due to an impairment in a set of mechanisms required for generating *multiple* connected sentences, that is termed an impairment in generating a *fluent sequence of novel thought*. It seems that KAS is unable to generate potential topics of discourse (i.e., multiple messages) that can become the basis for focusing attention on one topic (i.e., the current focus). In a conversation, each participant needs to be capable of preparing multiple messages that are intended to be communicated and relevant to the topic. Each one of these possibilities can become the current focus, or be retained for a future focus, depending on the communications of the other participant or the purpose of the communication. In addition to a deficit in *generating* multiple potential messages, KAS has a deficit in *focusing attention* on a specific message to be expressed and subsequent shifting of attention. The perseverations prominent in her speech provide support for this account that suggests a deficit in shifting focus to a different potential message. In this context, her intact performance on word and sentence level generation tasks may reflect the fact that only a single message is required and the way that the task stimulus directs attention to the current focus. Thus, word and sentence level generation tasks place less demands on novel thought generation when compared to discourse level generation.

Would these characteristics of a lack of novelty and perseveration when generating multiple connected sentences also apply to the other dynamic aphasia patients with the *2nd subtype*? The critical discourse level generation tests have not been administered but the plausibility is high given the perseveration noted in the performance of at least one patient reported by Esmonde et al. (1996), similar to KAS.

3.5.3 Conclusion

The pattern of performance documented in KAS, and other patients with propositional language impairments (e.g., ANG and CH), provides evidence for two subtypes of dynamic aphasia that are underpinned by different neuro-cognitive mechanisms. The *1st subtype* is characterised by a propositional language impairment that results in an inability to generate a single response on word and sentence level generation tasks. This deficit is specific to the language production domain and associated with left posterior frontal damage. KAS is an example of the much less documented *2nd subtype* of dynamic aphasia that may not be language specific. This *2nd subtype* is characterised by a propositional language impairment that results in an inability to generate a *fluent sequence of novel thought* on discourse level generation tasks and a preserved ability to generate a single response on word and sentence level generation tasks. The impairments underpinning the *2nd subtype* are associated with bilateral frontal and possibly subcortical involvement.

CHAPTER FOUR: GROUP STUDY

4.1 INTRODUCTION

The investigation of the dynamic aphasic patients ANG, CH, and KAS suggests that propositional language generation involves two functionally and anatomically distinct cognitive mechanisms. One mechanism is involved in the selection of verbal responses at the level of word and sentence generation and is associated with the left inferior frontal region. A second mechanism is involved in the generation of a fluent sequence of novel thought at the level of multiple connected sentences (i.e., discourse) and is associated with bilateral frontal and possibly subcortical damage. The previous chapters demonstrate that patients can present with dynamic aphasia following a failure in either of these cognitive mechanisms. In addition, all of the documented dynamic aphasic patients fail standard verbal fluency tasks requiring the generation of multiple words. The aim of this chapter is to investigate the anatomical correlates of propositional language and the voluntary generation of novel verbal and non-verbal responses in an unselected group of patients with focal frontal lesions.

4.1.1 Imaging Studies of Voluntary Generation

4.1.1.1 Verbal and Non-Verbal Voluntary Generation

PET and fMRI studies have consistently shown associated increased activation of the left dorsolateral prefrontal cortex in word generation tasks, including generation of nouns, verbs and synonyms (e.g., Frith et al., 1991b; Klein et al., 1997; Phelps, Hyder, Blamire, & Shulman, 1997; Warburton et al., 1996). In addition, PET has shown greater left frontal activation (BA 44/46) for phonemic fluency than semantic fluency, which has been associated with more left inferolateral temporal activation (Mummery, Patterson, Hodges, & Wise, 1996).

Frith (2000) identified a tendency for bilateral dorsolateral prefrontal activation when action generation tasks involve non-verbal material, such as using a joystick and finger movements (Deiber et al., 1991; Frith et al., 1991a; Rowe, Toni, Josephs, Frackowiak, & Passingham, 2000). Design fluency has been associated with increased blood flow to bilateral prefrontal cortices (Elfgren & Risberg, 1998). Consistent with this, the dynamic aphasic patients KAS and CO the reported dynamic aphasic patient with a bilateral lesion also had impaired design fluency (Gold et al., 1997). A recent fMRI study found that voluntary action execution was associated with increased bilateral activation of the frontal poles (BA 10) and a simultaneous deactivation of the left dorsolateral prefrontal cortex (BA 46) (Hunter, Green, Wilkinson, & Spence, 2004). By contrast, unilateral left frontal activation of BA 44 has been associated with executing movements in response to objects (Grezes, Armony, Rowe, & Passingham, 2003), although this task is not necessarily a novel voluntary generation task as the action is externally-cued by the object.

Ideational fluency was used in a PET study, although the conventional and unconventional uses conditions were combined (Carlsson, Wendt, & Risberg, 2000). Nevertheless, when contrasted with phonemic word fluency, highly creative individuals showed increased activity in the bilateral prefrontal region, whilst lowly creative individuals showed predominantly left prefrontal activation. Although the focus of this study was creativity, the authors implicated the superior frontal regions in ideational fluency.

4.1.1.2 Propositional Language Generation

There have been several recent neuroimaging studies of propositional language. All of the PET studies involved activation of the left frontal operculum, which is the area of greatest atrophy in dynamic aphasic CH. For example, Indefrey et al (2001) found increased activation in the left operculum (BA 6/44) associated with syntactic encoding during sentence production. Braun and colleagues (Braun, Guillemin, Hosey, & Varga, 2001) investigated internally-generated autobiographical narratives in spoken English and American Sign Language and analysed the common activation which they hypothesised would reflect the conceptual formulation and lexical access stages. They showed a bilateral posterior network and a left lateralised anterior network that included the left operculum (BA 45/47). In a subsequent study, the strength of network activation was found to be associated with the level of linguistic demands (Horwitz & Braun, 2004). Moreover, using probabilistic cytoarchitechtonic maps of BA 44/45, the area in common for bilinguals in both English and sign language is BA 45, not BA 44 (Horwitz et al., 2003). The authors concluded that BA 45 was the conceptual-language area independent of modality-specific information. A PET study comparing narrative production to automatic speech (i.e., propositional vs. nonpropositional) revealed a network that included the anterior left temporal cortex, the left operculum (BA 44), and the left superior frontal gyrus (BA 10) (Blank, Scott, Murphy, Warburton, & Wise, 2002). These authors inferred that disconnection of the left temporal cortex from the left superior frontal gyrus would be associated with impaired propositional speech. The frontal operculum has also implicated in two fMRI studies investigating the rate of connected speech when describing Rorschach inkblot plates (Kircher, Brammer, Levelt, Bartels, & McGuire, 2004; Kircher, Brammer, Williams, & McGuire, 2000). Although the rate of speech and pauses in continuous speech were correlated with activation in the left superior temporal gyrus (BA 39/22), continuous speech was associated with a bilateral frontal, temporal, occipital and cerebellum network that included BA 44/45 (Kircher et al., 2004).

Neuroimaging studies of word and sentence generation have primarily used sentence completion tasks. Two PET studies based on the Hayling Sentence Completion Test have found increased activation in the left inferior frontal region associated with response initiation, that is meaningful sentence completion (Collette et al., 2001; Nathaniel-James, Fletcher, & Frith, 1997). Response suppression was associated with the middle and inferior frontal gyri (BA 9/10/45) (Collette et al., 2001) and the left frontal operculum, LIFG and right anterior cingulate gyrus (Nathaniel-James et al., 1997). Response initiation and suppression were directly compared in the Nathaniel-James et al study which found increased activation in left middle temporal and left inferior frontal regions during response initiation. Nathaniel-James and Frith (2002) adapted the Hayling so that the level of constraint varied, thus varying the number of competing response options as in the test used for CH. For response initiation in the low constraint condition (i.e., many competing response options), and for all levels of constraint in the response suppression part, they found increased activation in the left dorsolateral prefrontal cortex (BA 46/9), which was concluded to reflect the requirement of selection from a set of appropriate words. In a new task similar to the Hayling but incorporating a method for quantifying strategy use, subjects nominated the superordinate category a concrete noun either belonged to (response initiation) or did not belong to (response suppression) (de Zubicaray, Zelaya, Andrew, Williams, & Bullmore, 2000). fMRI failed to find activation of the left frontal or temporal regions for the initiation part, however, left inferior frontal and temporal (as well as right frontopolar and orbitofrontal) activity was seen for the suppression part. Desmond and colleagues used fMRI to compare activity in a word stem completion task using stimuli that had either many or few possible completions (Desmond, Gabrieli, & Glover, 1998). Stem completion in the many condition, thought to activate multiple competing single word options, was associated with increased activity in the left dorsolateral prefrontal cortex (BA 9/10). These studies point to a role of the left prefrontal cortex in response initiation and possibly selection.

4.1.1.3 The Role of the Left Inferior Frontal Gyrus

Recently, based on a series of neuroimaging studies (and 1 lesion study detailed in Footnote 12 below), Thompson-Schill and colleagues have argued that the LIFG has a role in the selection of semantic knowledge from among competing information, rather than its retrieval (Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997; Thompson-Schill et al., 1998; Thompson-Schill, D'Esposito, & Kan, 1999; Thompson-Schill et al., 2002). It was further argued that competition and not repetition demands modulate LIFG activity as increased activity was only associated with increased competition during repetition conditions in a word generation task (Thompson-Schill et al., 1999). With regard to selection, in a fMRI study of healthy controls the selection demands of three different semantic tasks were systematically varied with an associated increase in LIFG activation only found when the selection demands were high (Thompson-Schill et al., 1997). These results were thought consistent with the notion that "left IFG activity reflects the degree of selection among competing alternatives, and not the amount of semantic retrieval per se" (1997; p. 14796).

In a fMRI study that used a verbal working memory task (letter recognition), Nelson and colleagues (2003) explored conflict resolution and distinguished between two sources of conflict. Response-conflict, associated with the anterior cingulate cortex (ACC), occurred at the level of response processing when stimulus-response associations conflicted. High-familiarity conflict, associated with LIFG activation, occurred at an earlier representational level of processing with interference resolved by selecting the most context-appropriate stimulus from among competitors.

Support for a selection role of the LIFG comes from a study investigating memory encoding of word pairs that were first re-paired and, in a second experiment, either closely or distantly related (Fletcher, Shallice, & Dolan, 2000). Increased LIFG activity was found when encoding word pairs that were rearranged with well-learned lists and, second, for the distantly (vs. closely) related word pairs. Fletcher and colleagues concluded this increased activity at encoding "reflects operations necessary to the formation of meaningful associations in the service of optimal learning, a crucial feature being selecting appropriate, and inhibiting inappropriate, semantic attributes of study material" (p. 404).

From another perspective, investigators interested in the role of the ACC have shown early bilateral LIFG activity using fMRI (Barch, Braver, Sabb, & Noll, 2000; Carter et al., 2000). In particular, this activity was found whilst attempting to distinguish between the role of the ACC as either implementing strategic processes to reduce cognitive conflicts (e.g., competition between responses) or monitoring and detecting cognitive states to engage strategic processes. This early bilateral LIFG activity was concluded to be consistent with Thompson-Schill's idea that the selection demands of a task modulate activity in the LIFG. The LIFG role in selection from amongst competing responses would be in keeping with the findings from ANG and CH, the two dynamic aphasic patients reported in Chapter 2.

4.1.2 Lesion Studies of Voluntary Generation

4.1.2.1 Verbal and Non-Verbal Fluency Tasks

Fluency tasks requiring the generation of multiple single responses involve the concepts of *novelty* and *voluntary*, also two key aspects of propositional language (Hughlings Jackson, 1932; Luria, 1973). The most well researched fluency task in relation to the frontal lobes is word fluency. There is an abundance of evidence that phonemic and semantic word fluency is reduced in frontal patients (as detailed in Chapter 1), with a tendency for left frontal patients to be the most severely impaired on phonemic fluency tasks (e.g., Milner, 1964; Stuss et al., 1998). However, there is some conflicting evidence as to whether this is selective for frontal lesions and whether semantic fluency is impaired in both frontal and posterior patients and to what degree. In addition, reduced word fluency has been documented following subcortical lesions (e.g., Laplane et al., 1989). Thus, word fluency has been associated with frontal, posterior and subcortical regions, and frontal-subcortical connections.

The association between design fluency and the right frontal lobe, first reported by Jones-Gotman and Milner (1977), remains controversial as several studies have failed to replicate this finding (e.g., Baldo et al., 2001; Tucha et al., 1999), although one study has corroborated it (Ruff, Allen, Farrow, Niemann, & Wylie, 1994). For the two studies that failed to find a selective right frontal deficit for design fluency both documented a left frontal deficit for phonemic fluency (and semantic fluency for one study), and the design fluency deficit was equally severe for left and right frontal patients.

What pattern is found in dynamic aphasic patients? CH who had a unilateral left lesion supports a word and design fluency dissociation. CH was intact on a series of design fluency tasks whereas he, and all dynamic aphasic patients since those described by Luria including ANG and KAS, was impaired for phonemic and semantic word fluency. Two other dynamic aphasic patients, KAS and CO (Gold et al., 1997), were impaired on design fluency tasks but they had bilateral lesions that were not restricted to the right frontal lobe.

There is little evidence implicating unilateral or bilateral frontal damage in multiple single item generation, apart from words and designs. For example, patients with frontal lobe lesions are impaired when generating unconventional uses of objects (vs. conventional uses) on an Ideational fluency task (Eslinger et al., 1993), although there was no further specification within the frontal lobes. For gesture fluency, there has only been one study investigating the ability of frontal lobe patients to generate meaningful and meaningless gestures and both the left and right frontal lobes were associated with impaired performances (Jason, 1985). In particular, left frontal patients were impaired for both gesture types whilst right frontal patients were only impaired for meaningful gestures. It is not entirely clear how these findings can be interpreted although I note that the dynamic aphasic CH was intact on gesture fluency tasks but impaired on word fluency tasks. This suggests that the generation of gestures is unlikely to be underpinned by the same region as that for words (i.e., left inferior frontal region). Given that KAS was impaired in generating both words and designs on fluency tasks, one could predict that, for these patients with the *2^nd^ subtype* of dynamic aphasia, performance would be similarly impaired on all fluency tasks (verbal and non-verbal) involving the generation of multiple single items. This is in contrast to the generation of a single response on word and sentence generation tasks.

4.1.2.2 Propositional Language Generation

There have been no group lesion studies that specifically investigated the cognitive mechanisms involved in propositional language generation impairments, or the neuronal substrates underpinning these. Although reduced and nonfluent spontaneous speech is characteristic of Broca's and transcortical motor aphasias, studies have tended to characterise these syndromes rather than investigate the cognitive mechanisms responsible. For example, numerous studies of patients with Broca's aphasia focus on different aspects such as agrammatic speech (see for example de Roo, Kolk, & Hofstede, 2003) and studies of transcortical motor aphasia have tended to focus on the heterogeneity of deficits (e.g., Alexander et al., 1990; Freedman et al., 1984).

Dynamic aphasia has been the most fruitful source of information regarding the generation of propositional language. Investigations of these patients provide evidence that propositional language generation can fail for different reasons. In particular, the *1st subtype* of dynamic aphasia, exemplified by patients ANG and CH, has been attributed to a failure in the selection of verbal responses from among competitors. This process is within the domain of language and is associated with damage to the LIFG[12]. The *2nd subtype*, exemplified by dynamic aphasic KAS, has been attributed to a failure in generating a fluent sequence of novel thought. This process encompasses the generation of verbal and non-verbal responses and is associated with bilateral frontal and subcortical damage. Although Raymer and colleagues (2002) suggested that sentence generation deficits may involve a more general verbal and non-verbal response generation impairment, or executive dysfunction, this was not specifically tested. Moreover, as discussed in Chapter 3, not all patients that fail verbal and non-verbal generation tasks (e.g., fluency tests) have a sentence generation deficit (e.g., KAS). Nevertheless, the relationship between the voluntary generation of multiple single items and a single word or sentence is little understood and, thus, both will be explored below.

Apart from dynamic aphasia patients, there are very few single case studies investigating propositional language impairments. Two cases, however, document a dissociation between impaired propositional language and intact nominal language skills (KP - Manning & Warrington, 1996; AM - Marangolo, Basso, & Rinaldi, 1999). KP had severely reduced verbal output and sentence generation abilities in the context of good comprehension. Despite intact naming ability for objects, KP was unable to generate object names in a sentence completion task even when the sentence frames had a high probability for a dominant response[13]. The authors did not classify KP as a dynamic aphasic, given the presence of other language impairments (e.g., verb syntax processing, poor naming of actions) that were speculated as contributing to the sentence completion failure. The authors interpreted this case as supporting two routes

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[12] In line with this, Thompson-Schill et al (1998) compared four patients with LIFG lesions with ten other frontal patients on a single verb generation task. Although it is unclear whether or not these patients had dynamic aphasia, the patients with LIFG lesions were selectively impaired in generating verbs that had high selection demands among competitors (e.g., *cat* - a high demand item – vs. *scissors* - a low demand item). The increased error rate was strongly related to the size of the lesion in BA 44.

[13] There are several cases on record with profound nominal difficulties that perform almost flawlessly on high probability sentence completion tasks (e.g., Zingeser & Berndt, 1990).

to noun-retrieval, a nominal route and a propositional speech route. The second patient, AM, had sparse and agrammatic spontaneous speech but intact naming and mildly impaired comprehension. AM, like KP, was unable to retrieve words to complete high probability sentence frames, despite being able to produce the words on picture naming tasks. AM's performance was also interpreted as supporting a dissociation between the nominal and propositional language systems when generating a single word.

4.1.3 Group Study Methodology

4.1.3.1 Importance of Group Studies

As yet, there has been little attempt to integrate the lesion studies on the role of the left frontal lobe and dynamic aphasia with neuroimaging data. As detailed above, a parallel line of investigation is the recent focus in neuroimaging on the language functions of the inferior left frontal region (for reviews see Noppeney, Phillips, & Price, 2004; Thompson-Schill, Bedny, & Goldberg, 2005), and specifically converging evidence that this area has a role in selection of semantic information (Thompson-Schill et al., 1997; 1999). Shallice (2001) and Stuss and colleagues (2002) point out, however, that there are at least two main difficulties in the interpretation of results from imaging studies. The first concerns the abstract nature of the specific processes such that there is no simple mapping onto either perceptual input or motor output. The second difficulty lies in the number of processes involved in a particular task that are difficult to differentiate in a complex task and to isolate to a stage of normal performance. Thus, these authors, amongst others, have argued for a combination of lesion and neuroimaging studies for more precise specification of cognitive process and the neuroanatomical substrates. As such, lesion research provides additional information as to which brain region is *necessary* for a particular process, whereas neuroimaging can only highlight a group of regions that together are *sufficient* to perform a task.

4.1.3.2 Methodological Issues

The investigation of human subjects with damage to the frontal lobe is fraught with problems. Shallice (1988) highlighted several limitations of Luria's (1973) early lesion studies including that patients often had lesions extending beyond the frontal lobes. Moreover, these patients often passed Luria's tests and their performance was not compared to controls. Recently, Stuss and colleagues (Stuss et al., 2002; Stuss & Alexander, 2000a) elegantly outlined a number of difficulties in the study of frontal lobe functions. For a start, the terms 'frontal lobe function' and 'executive process' are used interchangeable in the literature such that the relationship between them is unclear. For example, some studies refer to a frontal lobe function, such as switching, without relating the process to an anatomical region. A further difficulty is identifying a large number of patients with lesions restricted to, and well-specified within, the frontal lobes as there is no clinical condition that has pathology specifically limited to the frontal cortex (1 exception being focal tumours). Turning to the cognitive processes, these are often complex and may be related to more than one region of the brain, and more than one area within the frontal cortex. In practice, the tests used to investigate cognitive processes thought to reflect frontal lobe functions often tap multiple processes (e.g., Wisconsin Card Sorting Test). This leads to ambiguous conclusions regarding the process responsible for an impaired performance on a test. Although this may be due to the complexity and nature of the processes involved, it means that it is difficult to associate an impaired performance with one process or component of a task. A further difficulty is conceptual in that there are differing camps on whether frontal lobe functions comprise multiple processes that are functionally dissociable (e.g., Shallice, 2001) or whether there is a unitary process (e.g., Duncan, Burgess, & Emslie, 1995).

When lesion studies have been conducted, the basis for grouping patients has been broad. Specifically, it has varied from the basic grouping of 'anterior' versus 'posterior', to the standard anatomical classification of 'left frontal', 'right frontal' and 'bifrontal'. In the context of a wealth of information from imaging studies, Shallice (2001) has pointed out that anatomically based group studies must use a finer localisation grain than the standard approaches if the findings are to be usefully related to imaging.

4.1.3.3 Stuss Method of Lesion Analysis

Recently, Stuss, Alexander and colleagues developed a new method to improve the differentiation of cognitive processes and refine the localisation of regions within the frontal lobe (Stuss et al., 2002; Stuss et al., 2000a). The idea was to improve the identification of gyrus-specific frontal lobe lesions as they argued that damage rarely respects Brodmann Areas. They hypothesised that if an area was relevant to a specific function then patients with damage to that region would be impaired in that function, regardless of damage to surrounding areas. They tested numerous patients with restricted frontal lobe damage and moved from broad and standard anatomical classifications (i.e., anterior/posterior; left/right/bi-frontal) to analysing data based on behavioural performance; that is, performance driven groups based on those who performed well and those who did not (referred to as a modified case study - group approach by Shallice, 1988). The approach is based on the Petrides and Pandya (1994; cited in Stuss et al., 2002) architectonic divisions, which are grouped into more specific subgroups and further clustered into four major anatomical regions (polar, inferior medial, superior medial, lateral). This approach has been useful in precisely localising regions associated with both specific cognitive functions, such as learning and memory, attention and response speed (Alexander, Stuss, & Fansabedian, 2003; Stuss et al., 2000b; Stuss et al., 2005) and subcomponents of standard neuropsychological tests such as the Stroop, Trail Making and Wisconsin Card Sorting Tests (Stuss et al., 2000b; Stuss et al., 2001a; Stuss, Floden, Alexander, Levine, & Katz, 2001b).

The performance driven method can be illustrated through its application to the word fluency task (Stuss et al., 1998; Stuss et al., 2000a). The frontal lobes were divided into the four major anatomical regions with each region identified as being damaged or not. A regression technique, the Classification and Regression Tree, was used to separate patients into anatomical groups that were maximally different in terms of performance. This process identified three of the four anatomical groupings to be maximally different (all but the polar group, i.e., lateral, inferior medial, superior medial). Comparison of the standard anatomical classification to the new performance-based anatomical groupings highlighted how distinct frontal regions can be critical for a process regardless of damage to surrounding regions. Thus, on the phonemic word fluency task the Left Frontal and Bifrontal groups were impaired in the standard classification system. By contrast, the results from the new anatomical groupings showed that only the Left Lateral and Superior Medial groups were impaired and not the Inferior Medial group (Stuss et al., 2000a).

4.1.4 Aims of This Chapter

This chapter aims to investigate the functional and anatomical contribution of the frontal lobes to the voluntary generation of novel responses (verbal, non-verbal, propositional language) in a sample of 39 patients with focal frontal lesions. The overall predictions are as follows:

1. Based on the fluency literature and the performance of dynamic aphasic patients it is predicted that: word fluency will be associated with the left frontal

region, particularly for phonemic fluency whilst semantic fluency will be associated with all frontal regions and the left posterior region; and design fluency will be associated with the frontal region, and tentatively the right frontal region. Ideational and gesture fluency are predicted to be associated with the frontal lobes as they involve voluntary generation, although no further lesion specification is made given the limited previous results. However, gesture fluency is not expected to be associated with the same frontal lobe regions as word fluency based on the performance of CH. The pattern of association and dissociation between fluency tasks will be examined. These will be addressed in the Verbal and Non-Verbal Fluency Investigation.

2. Based on the performance of ANG and CH for single word and sentence generation tests, it is predicted that number of competing response options will affect performance but only for patients with lesions to the LIFG. For these patients with LIFG damage, word and sentence generation will be impaired when stimuli activate many competing response options. By contrast, word and sentence generation will be unimpaired when stimuli activate a dominant response option. It is predicted that this stimulus feature will not affect the word and sentence generation performance of patients who do not have LIFG damage. It is predicted that verbal and pictorial stimuli will result in the same pattern of word and sentence generation performance. This will be addressed in the Word and Sentence Level Generation Investigation.
3. Based on the performance of KAS for the generation of multiple connected sentences, it is predicted that discourse generation performance will be impaired for patients with frontal damage. Thus, for these patients, discourse generation will be both reduced in quantity (i.e., low production of words and sentences) and lacking in novel content. In terms of associated anatomical damage, bilateral frontal damage is predicted, however implicit is the absence of focal and lateralised frontal damage. As tasks involving multiple connected sentences are relatively unexplored, one aim is to systematically analyse and quantify discourse generation. This will be addressed in the Discourse Level Generation Investigation.

4.1.4.1 Method of Analysis

The method of lesion localisation will include the standard anatomical classifications as well as the lesion localisation and statistical procedures developed by

Stuss and colleagues (2002). Thus, four levels of analysis are included in the study as follows:

1. The Level 1 Analysis compares Frontal patients, Posterior patients and healthy Controls. This analysis will be used to establish whether there is a general frontal effect for baseline and experimental tests (i.e., does a task tap a frontal process).
2. The Level 2 Analysis compares Left Frontal and Right Frontal patients only. This has been the standard anatomical classification used for grouping frontal patients and, thus, will allow for a comparison between our findings and those in the literature, and to address left/right lateralisation.
3. The Level 3 Analysis investigates the frontal subgroups recently proposed by Stuss et al. (2002). This level of analysis is only conducted if a frontal effect was revealed at the first level of analysis (i.e., significant Level 1 result). If this was the case, patients with Left Lateral, Right Lateral, Superior Medial and Inferior Medial lesions were compared to the Control group. This allows for a fine-grained analysis of lesion location within the frontal regions that is more in line with recent subdivisions, and also enables direct comparison with neuroimaging results. In addition, a comparison can be made between grouping methods (i.e., standard anatomical classification vs. new fine-grained frontal subgroups).
4. The Level 4 Analysis specifically compares patients with and without LIFG lesions. These two frontal groups (LIFG, Non-LIFG) are compared with the Control group. This analysis is designed to investigate the cognitive mechanism involved in the selection of verbal responses from amongst competitors, which was found to be the critical deficit for the propositional language impairment of ANG and CH. This analysis is theoretically driven and only applied to word and sentence generation tests that manipulate the number of possible response options (i.e., many vs. one or few). It is also conducted for the language baseline to ensure there are no group differences that could confound other findings and it is applied to the verbal and non-verbal fluency tests to explore whether this is a critical region for the generation of multiple single items.

In order to address these questions the chapter proceeds in the following manner. The overall method details the characteristics of the sample, the procedure for lesion analysis and the statistical methods employed (4.2). The results for the group's performance on baseline cognitive, language and frontal 'executive' tests is presented in the next three sections (4.3 – 4.5). The first experimental section investigates the pattern of performance on a series of verbal and non-verbal fluency tests and addresses the question of critical frontal lobe regions associated with the generation of multiple single verbal and non-verbal items (4.6). The second experimental section presents the results from word and sentence generation tests devised to assess the effect of competing response options (4.7). The third experimental section details the results of an in-depth quantitative production analysis of discourse level generation (4 .8).

4.2 OVERALL METHOD

4.2.1 Subjects

4.2.1.1 Patients

Fifty-nine patients with focal lesions were recruited from the National Hospital for Neurology and Neurosurgery. Patients met the following *inclusion* criteria:

1. The presence of a focal frontal or non-frontal lesion (see 4.2.3 for definition of Frontal and Posterior lesions). A number of different aetiologies resulting in a focal acute or chronic lesion were included; brain tumour, stroke, haemorrhage, subdural haematoma and 1 traumatic brain injury patient (see Table 18).

2. The availability of a MRI or CT scan.

3. No prior neurological or psychiatric history.

4. English as the primary language.

5. No history of learning disability.

Patients were *excluded* if:

1. Significant cognitive impairments (receptive aphasia, alexia, neglect) or behavioural problems confounded the ability to participate in testing.
2. Scans showed concomitant widespread pathology (e.g. diffuse cerebral vascular disease) or more than two hyperintense areas with a diameter $\geq$ 10 mm or more than eight hyperintense areas with a diameter between 5-9 mm on DE images (in addition to the single focal lesion), as these might be, at least partially, responsible for the observed cognitive deficits. For the

traumatic brain injury patient care was taken to ensure no significant diffuse axonal damage was evident on neuroradiological examination.

Of the fifty-nine patients, five were excluded at the lesion analysis stage due to significant posterior involvement. This left thirty-nine patients with focal frontal lesions and fifteen patients with posterior lesions. Of note, only two patients had left temporal lobe lesions and very few patients with left posterior lesions presented with language deficits. A description of patients' lesion location, aetiology and chronicity is presented in Table 18.

Table 18. *Imaging, Aetiology and Chronicity within Frontal and Posterior Patient Groups*

Patient Number	Imaging (MRI/CT)	Aetiology	Number of Months Post Lesion~
Left Frontal			
1	MRI	Psuedotumour	4.00
3	MRI	Astrocytoma	.10
7	MRI	Glioma	16.0
9	CT	Traumatic Brain Injury	1.00
10	MRI	Astrocytoma	36.2
11	CT	ACoA	9.57
12	CT	Glioma	11.2
13	MRI	Stroke	16.2
14	MRI	Glioma	1.40
15	MRI	Astrocytoma	17.2
16	MRI	Lobectomy	96.5
17	MRI	Astrocytoma	60.3
18	CT	ACoA	20.2
59	MRI	Meningioma	.83
60	MRI	Glioma	.47
61	MRI	Glioma	.17
n=16			
Right Frontal			
19	CT	Chronic Subdural Haematoma	67
20	MRI	Meningioma	181
22	MRI	Stroke	14.0
24	MRI	Stroke	2.97
25	CT	Chronic Subdural Haematoma	.67
26	CT	Meningioma	12.0
27	MRI	Glioma	15.0
28	MRI	Meningioma	5.83
30	CT	Meningioma	28.0
34	CT	Astrocytoma	.17
53	CT	Stroke	1.67
54	CT	Glioma	.47
55	MRI	Meningioma	.23
51	MRI	Stroke	3.03
63	MRI	Meningioma	.27
55	MRI	ACoA	.17
21	CT	Meningioma	.40
29	MRI	Meningioma	52.6
n=18			

Bilateral: Lateral			
32	CT	Meningioma	1.00
62	MRI	Stroke	11.1
n=2			
Bilateral: Medial			
5	CT	Brain abscess	.33
n=1			
Bilateral: Orbital			
6	MRI	Meningioma	.80
8	MRI	Glioma	.47
n=2			
Posterior			
2	MRI	Glioma	.73
33	MRI	Glioma	.07
65	MRI	Meningioma	.40
66	MRI	Stroke	.67
67	MRI	Glioma	.17
68	MRI	Meningioma	.23
69	MRI	Stroke	.73
70	MRI	Stroke	42.6
71	MRI	Glioma	.10
76	MRI	Meningioma	.20
77	MRI	Meningioma	.13
78	MRI	Meningioma	12.7
79	MRI	Glioma	.23
80	MRI	Meningioma	21.2
82	MRI	Meningioma	.13
n = 15			

~ e.g., 1.00 = 30 days

4.2.1.2 Controls

Thirty-five healthy adult controls with no neurological or psychiatric history were recruited to match the patient group as closely as possible for age, gender and education.

All subjects (patients and controls) were administered the National Adult Reading Test (Nelson et al., 1991) as a measure of estimated pre-morbid level of intelligence.

4.2.2 Materials and Procedure

All subjects were assessed on six batteries of tests, 3 baselines and 3 investigations: 1. Cognitive Function Baseline; 2. Language Function Baseline; 3. Frontal 'Executive' Function Baseline; 4. Verbal and Non-Verbal Fluency Investigation; 5. Word and Sentence Level Generation Investigation; 6. Discourse

Level Generation Investigation. The tests within the six batteries were completed in a pseudorandom order over at least two sessions or more if fatigue was a factor. Patients were tested either at hospital whilst an inpatient or outpatient, or in their home. Approval for the study was granted by the National Hospital for Neurology and Neurosurgery and the Institute of Neurology Joint Research Ethics Committee and the University College London Hospitals NHS Trust Research and Development Directorate. All subjects gave informed written consent to take part in the study, and were allowed to withdraw at any time.

4.2.3 Lesion Analysis

A single Neurologist who was blind to the neurological history of each patient, and unaware to whom each scan belonged, reviewed the hard copies of the MRI scans for each patient. Brain MRI was obtained on systems operated at 1.5 T, and included, for each patient, the acquisition of an axial dual-echo, and an axial and coronal T1-weighted scan. The position of every lesion was labelled using standard atlases (Duvernoy, 1991). A subgroup of patients (n = 14) with no MRI scans available was also included in the analysis, their focal lesion being evaluated on CT scan.

Frontal patients were identified as those with a lesion in any part of the cortex anterior to the central sulcus and superior to the lateral fissure, including cases with dorsal striatum lesions. For two patients with vascular lesions to the right lateral frontal lobe, damage extended to the postcentral gyrus. The classification system was based on a method devised by Stuss and colleagues (Stuss et al., 2002). Each patient was therefore coded for the absence or presence of lesion and surrounding oedema in 12 a priori selected regions in each hemisphere (24 areas in total; see Appendix 3). These could be broadly grouped into three surface areas of the frontal lobes: Lateral, Superior Medial and Inferior Medial. The structures of the striatum (Caudate nucleus, Putamen, Globus Pallidus) were coded as the fourth region, although these did not form the basis for subsequent grouping.

Posterior lesions were coded as broadly falling within the temporal, parietal and/or occipital lobes in either hemisphere (left or right). A dimensional index was also assigned to each lesion, providing a numerical rating scale (ranging from 0 to 4) accounting for the percentage of tissue damage to the lobe where the focal lesion was located.

4.2.4 Statistical Analysis

There were four levels of analyses:

4.2.4.1 Level 1 Analysis: Frontal versus Posterior

The first analysis compared Frontal patients, Posterior patients and Controls, using one-way analysis of variance (ANOVA).

4.2.4.2 Level 2 Analysis: Frontal Lateralisation

The second analysis compared Left with Right Frontal patients only, using univariate analysis of covariance (ANCOVA). 16 Left Frontal and 17 Right Frontal patients were entered into this analysis (see Appendix 4). 1 Right Frontal patient (#20) was excluded due to an extensive lesion that compressed the left frontal medial region. Age was entered as a covariate.

4.2.4.3 Level 3 Analysis: Localisation within the Frontal Lobes

The third analysis compared four different frontal subgroups according to the primary site of their lesion: Left Lateral, Right Lateral, Superior Medial, and Inferior Medial (for grouping details see Table 19) with Controls using one-way ANOVA. 7 Left Lateral, 6 Right Lateral, 8 Superior Medial (3 of these had SMIM, 5 SM only) and 5 Inferior Medial only patients were entered into this analysis (see Appendix 4). This level of analysis was only undertaken if the Level 1 analysis found the Frontal group to be significantly different from the Control group.

4.2.4.4 Level 4 Analysis: Left Inferior Frontal Gyrus Lesions

The fourth analysis compared Frontal patients with lesions that included the LIFG to Frontal patients whose lesions did not (for grouping details see Table 19) using one-way ANOVA. 9 LIFG and 29 Non-LIFG patients were entered into this analysis (see Appendix 4) only for critical tests in terms of hypotheses.

The Level 1 and 2 Analyses were conducted on each test in all six batteries. The Level 3 Analysis was only undertaken if a significant Frontal effect was found in the Level 1 Analysis in order to investigate finer-grained frontal effects. The Level 4 Analysis was conducted only when hypotheses predicted specific LIFG involvement (Word and Sentence Level Generation Tests) and for fluency tests to see if this region plays a role in verbal and non-verbal generation generally.

Table 19. *Localisation and Lesion Specification within the Frontal Lobes*

Region		**Grouping Level 3**	**Grouping Level 4**
Inferior Frontal Gyrus:	Anterior Section Posterior Section	**Lateral (Left/Right)**	**Left Inferior Frontal Gyrus (LIFG)** **Right IFG (Non-LIFG)**
Middle Frontal Gyrus:	Anterior section Posterior Section	**Lateral (Left/Right)**	**Non -LIFG**
Superior Frontal Gyrus:	Anterior Section Posterior Section	**Superior Medial**	**Non -LIFG**
Cingulate Cortex:	Anterior Section Posterior Section	**Inferior Medial**	**Non -LIFG**
Orbital Cortex		**Inferior Medial**	**Non -LIFG**

4.2.4.5 Transformations of data and Statistical tests:

In all instances where Levene's test for equality of variances between groups revealed significant differences, data were transformed using the logarithm (or reflect and logarithm). If normality assumptions were met and Levene's test was not significant, one-way analysis of variance was used (or univariate analysis of covariance for Level 2 analyses). When error variances remained unequal (i.e., Levene's test remained significant), non-parametric statistics were applied (Kruskal-Wallis Test when comparing 3 or more groups, Mann-Whitney U when comparing 2 groups). For select tasks mixed model analysis of variance (with group as the between-subject factor and stimulus type or condition as the within-subject factor) was used to investigate interactions. Unfortunately, on each occasion this test was used in the Word and Sentence Generation Investigation the normality assumption of homogeneity of intercorrelations was violated (i.e., Box's M was significant), and remained so following data transformation. Thus, mixed model analysis of variance was only used for one task (Ideational Fluency). Chi-square test of independence was used for categorical data.

4.2.4.6 Post Hoc Testing and Correction for Multiple Comparisons:

In order to investigate differences between groups following significant analysis of variance tests, Fischer's least significant difference (LSD) pairwise comparisons were used. Significant Kruskal-Wallis Tests were followed by Mann-Whitney U Tests (Dytham, 2003).

Adjustment for multiple comparisons was made according to the following rule. In the Level 1 Analysis (Frontal vs. Posterior vs. Control) the Bonferroni correction method was used and, thus, results were only considered significant if $p \leq 0.017$. If the Level 1 Analysis shows a significant Frontal effect, then Bonferroni corrections are not applied to the analyses that further explore frontal effects (i.e., Level 3 - Left Lateral vs. Right Lateral vs. Superior Medial vs. Inferior Medial vs. Control; Level 4 - LIFG vs. Non-LIFG vs. Control). This is because the aim of these levels of analyses is to be more specific anatomically about a lesion effect already established in the Level 1 Analysis (for example of method see Picton, Stuss, Shallice, Alexander, & Gillingham, 2005). Of note, the Level 3 Analysis was only conducted if a significant Frontal effect was established at the Level 1 Analysis. If the Level 4 Analysis gives significant results in the absence of a significant Frontal deficit in the Level 1 Analysis, Bonferroni correction for 3 comparisons is applied (i.e., $p \leq 0.017$).

4.2.5 Descriptive Characteristics

Level 1 Analysis

The Frontal, Posterior and Control groups did not differ significantly in terms of sex ($\chi^2_{(2)} = 1.238$, $p = 0.538$), chronicity (i.e., time since damage for Frontal and Posterior groups; $t_{(52)} = 1.195$, $p = 0.\ 237$), age ($F_{(2,86)} = 1.391$, $p = 0.254$), or pre-morbid level of intelligence which was average across groups ($F_{(2.86)} = 2.957$, $p = 0.057$; see Table 20a).

Level 2 Analysis

The difference between the Left and Right Frontal patients did not reach significance for sex ($\chi^2_{(1)} = 3.622$, $p = 0.057$), chronicity ($t_{(1)} = 0.039$, $p = 0.969$) or average estimated pre-morbid level of intelligence ($t_{(1)} = -0.772$, $p = 0.446$; see Table 20a). By contrast, independent t-test revealed a significant effect of age ($t_{(1)} = -3.780$, $p = 0.001$; see Table 20a), with the Right Frontals older than the Left Frontals. Thus, age was entered as a covariate in all analyses between these two groups (i.e., Level 2).

Table 20a. *Descriptive Characteristics of Patient and Control Groups: Sex, Chronicity, Age and NART IQ*

Level 1 Analysis		**Frontal** **N = 39**	**Posterior** **N = 15**	**Control** **N = 35**
Sex	Male	25	9	18
	Female	14	6	17
Chronicity (in months)	Mean (SD)	16.0 (33.6)	5.3 (11.9)	-
Age	Mean (SD)	52.9 (14.2)	53.1 (10.7)	47.8 (15.5)
	Range	30-77	30-68	18-70
NART-Derived Full Scale IQ	Mean (SD)	102.9 (13.6)	108.6 (8.2)	109.5 (12.4)
	Range	70-124	89-120	80-127

Level 2 Analysis		**Left Frontal** **N = 16**	**Right Frontal** **N = 18**
Sex	Male	13	9
	Female	3	9
Chronicity (in months)	Mean (SD)	18.2 (26.4)	17.7 (42.9)
Age (in years)	Mean (SD)	42.9 (9.3)**	58.0 (13.3)
	Range	30-61	31-77
NART-Derived Full Scale IQ	Mean (SD)	100.2 (15.2)	104.0 (13.6)
	Range	70-122	75-124

NART = National Adult Reading Test; ** = p<0.01; SD = standard deviation

Level 3 Analysis

The Left Lateral, Right Lateral, Superior Medial, Inferior Medial and Control groups did not differ significantly in terms of sex ($\chi^2_{(4)}$ = 4.330, p = 0.363), chronicity ($F_{(3,22)}$ = 0.502, p = 0.685), age ($F_{(4,56)}$ = 0.830, p = 0.512) or average pre-morbid levels of intelligence ($F_{(4,56)}$ = 1.696, p = 0.164; see Table 20b).

Table 20b. *Descriptive Characteristics of Patient and Control Groups: Sex, Chronicity, Age and NART IQ*

Level 3 Analysis		**Left Lateral N = 7**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 5**	**Control N = 35**
Sex	Male	6	2	4	2	18
	Female	1	4	4	3	17
Chronicity (in months)	Mean (SD)	11.4 (13.5)	3.0 (4.5)	13.2 (20.4)	12.8 (22.6)	-
Age (in years)	Mean (SD)	46.3 (11.3)	50.5 (14.9)	48.1 (13.3)	59.8 (12.6)	47.8 (15.5)
	Range	31-61	31-67	30-70	44-76	18-70
NART-Derived Full Scale IQ	Mean (SD)	105.6 (14.8)	106.8 (11.1)	96.6 (15.6)	107.0 (8.0)	109.5 (12.4)
	Range	86-122	92-124	75-115	95-117	80-127

NART = National Adult Reading Test.

Level 4 Analysis

There was no difference between the LIFG, Non-LIFG and Control groups in terms of sex ($\chi^2_{(2)} = 2.058$, $p = 0.357$), chronicity ($t_{(36)} = 0.346$, $p = 0.732$), age ($F_{(2.70)} = 2.656$, $p = 0.077$) or the pre-morbid level of intelligence that was average ($F_{(2.70)} = 2.423$, $p = 0.096$; see Table 20c).

Table 20c. *Descriptive Characteristics of Patient and Control Groups: Sex, Chronicity, Age and NART IQ*

Level 4 Analysis		**LIFG N = 9**	**Non-LIFG N = 28**	**Control N = 35**
Sex	Male	7	17	18
	Female	2	12	17
Chronicity (in months)	Mean (SD)	19.9 (31.1)	15.4 (35.2)	-
Age (in years)	Mean (SD)	45.3 (14.2)	55.2 (13.9)	47.8 (15.5)
	Range	34-76	30-77	18-70
NART-Derived Full Scale IQ	Mean (SD)	101.6 (14.8)	103.2 (13.6)	109.5 (12.4)
	Range	70-118	75-124	80-127

NART = National Adult Reading Test.

4.3 COGNITIVE FUNCTION BASELINE

4.3.1 Tests and Procedure

A number of standardised tests were administered to assess baseline cognitive functioning. These included measures of intellectual ability (Raven, 1976a), memory (Warrington, 1984) and visual perception (Warrington et al., 1991). Each test was administered according to the standard instructions provided in each manual.

4.3.2 Results

4.3.2.1 Current Level of General Intellectual Function

Level 1 Analysis

The Frontal, Posterior and Control groups all obtained average scores on the Advanced Progressive Matrices (APM) (See Table 21 and Appendix 5 ref 1.1)[14]. Thus, current intellectual functioning was intact and equivalent across groups.

Level 2 Analysis

Similarly, using univariate ANCOVA, there was no significant difference between the average APM scores of the Left and Right Frontal groups. Age was, however, revealed as a significant covariate (See Table 21 and Appendix 5 ref 2.1). Of note, the Left Frontal score places just above the 50th percentile for their age whilst the Right Frontal score places them just below the 50th percentile for their age.

Table 21. *Mean Advanced Progressive Matrices Score (Max = 12) and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 38**	**Posterior N = 15**	**Control N = 27**
Number Correct (SD)	6.24 (2.9)	7.00 (2.4)	7.56 (3.0)
Level 2 Analysis	**Left Frontal N = 15**		**Right Frontal N = 17**
Number Correct (SD)	8.13 (2.4)		5.47 (2.5)

[14] Insignificant results will be referenced in the Appendices, including results that reveal Age as a significant covariate.

4.3.2.2 Memory Function

Level 1 Analysis

Performance on the Recognition Memory Test was within normal limits and, specifically, it was average for verbal material and low average for visual material. For comparison purposes, the 50^{th} percentile score from the standardised sample for a similar age (40-54yrs) is reported in Table 22. In particular, there was no difference between the Frontal and Posterior patient groups for Words or Faces (See Table 22 and Appendix 5 ref 1.2).

Table 22. *Mean Recognition Memory Test Score (Max = 50) and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 35**	**Posterior N = 9**	**Standardised Sample 50^{th}%ile (40-54yrs)**
Mean Word Score (SD)	44.1 (5.1)	45.1 (4.20)	45
Mean Faces Score (SD)	39.6 (6.2)	40.9 (6.19)	44
Level 2 Analysis	**Left Frontal N = 14**		**Right Frontal N = 16**
Mean Word Score (SD)	46.2 (3.3)		42.9 (5.7)
Mean Faces Score (SD)	42.9 (3.6)		36.3 (6.7)**

** = p<0.01

Level 2 Analysis

There was no difference in the average scores obtained for Words by the Left and Right Frontal groups, using univariate ANCOVA (See Table 22 and Appendix 5 ref 2.2). By contrast, the Right Frontal group's borderline impaired score for Faces was significantly lower than the average score obtained by the Left Frontal group ($F_{(1,27)}$ = 13.434, p = 0.001; see Table 22).

4.3.2.3 Visual Perceptual Function

Level 1 Analysis

All subjects (patients and controls) performed above the 5% cut-off on the Incomplete Letters Test, indicating that each subject had intact visual perception. One-way ANOVA, however, revealed a significant difference between the intact scores of the Frontal, Posterior and Control groups ($F_{(2,73)} = 3.646$, p = 0.031; see Table 23). As Levene's test indicated unequal error variances ($F_{(2,73)} = 8.787$, p<0.001), subsequent Kruskal-Wallis Test was used to confirm the result ($\chi^2_{(2)} = 7.207$, p = 0.027). Pairwise Mann-Whitney U comparisons found that Posteriors scored significantly lower than Controls (U = 95.000, p = 0.007). The Posterior group's score, however, is within normal limits and above the 5% cut-off reported in the test manual.

Level 2 Analysis

No frontal group effects were found for visual perception (See Table 23 and Appendix 5 ref 2.3).

Table 23. *Mean Incomplete Letters Test Score (Max = 20) and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 39**	**Posterior N = 15**	**Controls N = 22**
Mean (SD)	19.46 (.85)	19.20 (.94)**	19.86 (.35)
Level 2 Analysis	**Left Frontal N = 16**	**Right Frontal N = 17**	
Mean (SD)	19.75 (0.6)	19.29 (0.8)	

** = p<0.01

4.3.3 Cognitive Function Baseline Summary and Discussion

Baseline cognitive testing found that the Frontal group performed normally on intellectual, verbal recognition memory and visual perceptual tests. The normal intellectual ability of the Frontals is slightly surprising given reports of frontal patients being impaired on tests of fluid intelligence like the APM (e.g., Duncan et al., 1995) and imaging findings that lateral prefrontal and parietal regions are associated with fluid intelligence and specifically the APM (Gray, Chabris, & Braver, 2003). Within the Frontal group, fluid intelligence was found to be poorer in the older Right Frontal group, which concurs with the literature that demonstrates fluid intelligence declines with age (Gong et al., 2005). Frontal and Posterior patients performed weakly on the visual recognition memory test (Faces). This is consistent with the results reported in the test manual (Warrington, 1984) and reports of frontal patients being impaired on tests of recognition memory (e.g., Daum & Mayes, 2000). Within the frontal group, mild-moderate visual recognition memory impairment was selectively present in the Right Frontal group, a finding also reported by Warrington. On the whole, the Frontal group performed almost normally on baseline cognitive tests. This suggests that the Frontal group overall presents with relatively mild global deficits.

4.4 LANGUAGE FUNCTION BASELINE

4.4.1 Tests and Procedure

Four tests were administered to assess baseline language skills. These included measures of spontaneous speech (complex scene description), repetition (sentences), naming (Graded Naming Test; McKenna et al., 1980) and word comprehension (Synonym Test; Warrington et al., 1998).

Each subject was asked to describe the contents of a complex scene (Beach Scene). A maximum of 1 minute was allowed. Responses were recorded for the purpose of analysis. Each speech sample was characterised clinically along three dimensions: fluency (fluent or nonfluent within 1 sentence – structure and grammar); quantity produced (adequate or reduced for the total number of sentences produced overall); and dysphasic errors (none, semantic, or phonological). The repetition test consisted of ten sentences (3-6 words in length). The sentences were orally presented and subjects were required to repeat them. The total score was the number of sentences correctly repeated. The Graded Naming Test and Synonym Test were administered according to the standard instructions provided in each manual.

4.4.1 Results

4.4.1.1 Spontaneous Speech

Level 1 Analysis

Using the Chi-square test, a significant difference was found between the Frontal, Posterior and Control groups for fluency ($\chi^2_{(2)} = 11.269$, p = 0.004), quantity produced ($\chi^2_{(2)} = 17.782$, p<0.001) and errors ($\chi^2_{(4)} = 10.851$, p = 0.028) (see Table 24a). Further analysis showed that the Frontal group contained more patients with nonfluent and reduced spontaneous speech than the Control group ($\chi^2_{(1)} = 8.050$, p = 0.005 and $\chi^2_{(1)} = 12.854$, p<0.001, respectively) and Posterior group for quantity ($\chi^2_{(1)}$

= 5.934, p = 0.015), although this just failed to reach significance for fluency ($\chi^2_{(1)}$ = 3.612, p = 0.057). For errors, the difference between the Frontal and Control groups just failed to reach significance ($\chi^2_{(2)}$ = 5.860, p = 0.053) and there was no difference between the Frontal and Posterior groups ($\chi^2_{(2)}$ = 2.658, p = 0.265).

All Posterior patients and Controls were classified as having fluent speech that was adequate in quantity, however the Posteriors produced more errors than Controls ($\chi^2_{(2)}$ = 7.447, p = 0.006).

Level 2 Analysis

Fluency and quantity produced did not differ significantly between Left and Right Frontals (See Table 24a and Appendix 5 ref 2.4). Of note, all patients except for 1 with non-fluent speech were in the left Frontal group. In addition, only Left Frontal patients produced errors, with the difference between left and Right Frontals reaching significance ($\chi^2_{(2)}$ = 6.261, p = 0.044).

Table 24a. *Complex Scene Description: Fluency, Quantity Produced and Errors*

Level 1 Analysis		**Frontal N = 39**	**Posterior N = 15**	**Control N = 35**
*Fluency***	Fluent	31	15	35
	Non-fluent	8**	0	0
*Quantity Produced****	Adequate	27	15	35
	Reduced	12***	0	0
*Errors**	None	33	12	35
	Semantic	3	3**	0
	Phonological	3	0	0

Level 2 Analysis		**Left Frontal N = 16**	**Right Frontal N = 17**
Fluency	Fluent	11	16
	Non-fluent	5	1
Quantity Produced	Adequate	12	13
	Reduced	4	4
*Errors**	None	11	17
	Semantic	3*	0
	Phonological	2*	0

* = p<0.05, ** = p<0.01, *** = p<0.001

Level 3 Analysis

Chi-square revealed a significant frontal effect for fluency ($\chi^2_{(4)} = 17.098$, p = 0.002) and quantity produced ($\chi^2_{(4)} = 10.366$, p = 0.035), but not errors ($\chi^2_{(4)} = 6.379$, p = 0.173; see Table 24b). Further analysis revealed that more Left Lateral and Superior Medial patients presented with nonfluent speech than Controls ($\chi^2_{(1)} = 10.500$, p = 0.001 and $\chi^2_{(1)} = 14.109$, p<0.001, respectively). All Frontal groups had a higher number of patients with reduced speech compared to Controls (Left Laterals: $\chi^2_{(1)} = 5.122$, p = 0.024; Right Laterals: $\chi^2_{(1)} = 12.265$, p<0.001; Superior Medials: $\chi^2_{(1)} = 9.177$, p = 0.002; Inferior Medials: $\chi^2_{(1)} = 7.179$, p = 0.007).

Table 24b. *Complex Scene Description: Fluency, Quantity Produced and Errors*

Level 3 Analysis		**Left Lateral N = 7**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 5**	**Control N = 35**
*Fluency***	Fluent	5	6	5	5	35
	Non-fluent	2**	0	3***	0	0
*Quantity produced**						
	Adequate	6	4	6	4	35
	Reduced	1*	2***	2**	1**	0
Errors	None	6	6	7	5	35
	Semantic	1	0	1	0	0
	Phonological	0	0	0	0	0

* = p<0.05, ** = p<0.01, *** = p<0.001

Level 4 Analysis

Using the Chi-square test, a significant difference was found between the LIFG, Non-LIFG and Control groups for fluency ($\chi^2_{(2)} = 8.292$, p = 0.016), quantity produced ($\chi^2_{(2)} = 12.106$, p = 0.002) and errors ($\chi^2_{(4)} = 25.943$, p<0.001) (see Table 24c). Further analysis showed that more LIFG and Non-LIFG patients had nonfluent and reduced spontaneous speech than Controls (LIFG: $\chi^2_{(1)} = 7.990$, p = 0.005 and $\chi^2_{(1)} = 11.034$, p = 0.001; Non-LIFG: $\chi^2_{(1)} = 8.148$, p = 0.004 and $\chi^2_{(1)} = 12.520$, p<0.001, respectively). Significantly more LIFG patients made errors than both Non-LIFG patients and Controls ($\chi^2_{(2)}$ = 10.971, p = 0.004 and $\chi^2_{(2)}$ = 17.111, p<0.001, respectively).

Table 24c. *Complex Scene Description: Fluency, Quantity Produced and Errors*

Level 4 Analysis		**LIFG N = 9**	**Non-LIFG N = 28**	**Control N = 35**
*Fluency**	Fluent	7	23	35
	Non-fluent	2**	6**	0
*Quantity produced***				
	Adequate	6	21	35
	Reduced	3**	8***	0
*Errors****	None	5	27	35
	Semantic	3***	0	0
	Phonological	1***	2	0

* = p<0.05, ** = p<0.01, *** = p<0.001

4.4.1.2 Repetition

Level 1 Analysis

Sentence repetition ability did not differ between the Frontal, Posterior and Control groups ($F_{(2,86)}$ = 2.799, p = 0.066). However, as Levene's test of homogeneity of error variances was significant ($F_{(2,86)}$ = 10.958, p<0.001), a Kruskal-Wallis Test was used and found a significant difference between groups ($\chi^2_{(2)}$ = 9.614, p = 0.008; see Table 25a). Frontals performed worse than the Controls on the sentence repetition task (Mann-Whitney U = 560.000, p = 0.009).

Level 2 Analysis

Although there was no difference between the Left and Right Frontal groups (See Table 25a and Appendix 5 ref 2.5), 5 Left Frontal patients scored below ceiling whilst only 1 Right Frontal patient did not achieve a perfect score.

Table 25a. *Repetition: Number Correct (Max = 10), Standard Deviation (SD) and Range*

Level 1 Analysis	**Frontal N = 39**	**Posterior N = 15**	**Control N = 35**
Sentence Repetition (SD)	9.54 (1.4)**	10 (0)	10 (0)
Range	4-10	10-10	10-10
Level 2 Analysis	**Left Frontal N = 16**	**Right Frontal N = 17**	
Sentence Repetition (SD)	9.31 (1.5)	9.94 (0.2)	
Range	4-10	9-10	

** = p<0.01

Level 3 Analysis

The difference between frontal groups did not reach significance ($F_{(4,56)}$ = 1.991, p = 0.108), although Levene's test showed that the error variances were unequal ($F_{(4,56)}$ = 11.521, p<0.001). Subsequent Kruskal-Wallis Test revealed a significant difference between groups ($\chi^2_{(4)}$ = 10.269, p = 0.036; see Table 25b). Pairwise Mann-Whitney U comparisons found that only the Left Laterals and Superior Medials performed worse than Controls on the sentence repetition task (U = 105.000, p = 0.025 and U = 105.000, p = 0.003, respectively).

Table 25b. *Repetition: Number Correct (Max = 10), Standard Deviation (SD) and Range*

Level 3 Analysis	**Left Lateral N = 7**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 5**	**Control N = 35**
Sentence Repetition Total (SD)	9.14 (2.3)*	10 (0)	9.63 (0.7)**	10 (0)	10 (0)
Range	4-10	10-10	8-10	10-10	10-10

* = p<0.05, ** = p<0.01

Level 4 Analysis

The ability to repeat sentences did not differ between the LIFG, Non-LIFG and Control groups ($F_{(2,70)} = 2.463$, p = 0.093). As Levene's test was significant ($F_{(2,70)}$ = 9.435, p<0.001), a Kruskal-Wallis Test was used and a significant difference between groups was found ($\chi^2_{(2)} = 6.594$, p = 0.037; see Table 25c). A poorer sentence repetition performance was given by both the LIFG and Non-LIFG groups, compared to Controls (U = 122.500, p = 0.005 and U = 437.500, p = 0.024, respectively).

Table 25c. *Repetition: Number Correct (Max = 10), Standard Deviation (SD) and Range*

Level 4 Analysis	**LIFG** **N = 9**	**Non-LIFG** **N = 28**	**Control** **N = 35**
Sentence Repetition (SD)	9.22 (2.0)**	9.66 (1.2)*	10 (0)
Range	4-10	4-10	10-10

* = p<0.05; ** = p<0.01.

4.4.1.3 Naming

Level 1 Analysis

The Frontal, Posterior and Control groups all obtained average scores on the Graded Naming Test. One-way ANOVA, however, did reveal a significant difference between these groups ($F_{(2,84)} = 5.321$, p = 0.007; see Table 26a). Pairwise comparisons indicated that Frontals named fewer pictures than Controls (p = 0.003). Given the Frontal group performed within the average range, they cannot be classed as impaired. Upon examination of individual scores, impaired performances (< 5^{th}%ile) were given by 2 Left Frontal and 3 Right Frontal patients. Interestingly, 1 Posterior and 2 Controls performed below the 5% cut-off. Thus, impaired nominal function cannot explain any further group differences.

Level 2 Analysis

Nominal ability of the Left and Right Frontal groups was equivalent (See Table 26a and Appendix 5 ref 2.6).

Table 26a. *Naming: Mean Number Correct (Max = 30) and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 39**	**Posterior N = 15**	**Control N = 33**
Graded Naming Test (SD)	18.3 (5.7)**	18.5 (6.2)	22.3 (4.9)
Level 2 Analysis	**Left Frontal N = 16**	**Right Frontal N = 17**	
Graded Naming Test (SD)	18.1 (4.9)	18.1 (6.1)	

** = p<0.01

Level 3 Analysis

No further frontal effects were evident (See Appendix 5 ref 3.1). Thus, any differences on generation tests cannot be explained by a difference in nominal ability.

Level 4 Analysis

A significant difference between the LIFG, Non-LIFG and Control groups was revealed by a one-way ANOVA ($F_{(2,68)}$ = 5.481, p = 0.006; see Table 26b). Pairwise comparisons indicated that the LIFG and Non-LIFG frontal groups named fewer pictures than Controls (p = 0.007 and p = 0.012, respectively), although there was no difference between the LIFG and Non-LIFG groups.

Table 26b. *Naming: Mean Number Correct (Max = 30) and Standard Deviation (SD)*

Level 4 Analysis	**LIFG N = 9**	**Non-LIFG N = 29**	**Control N = 33**
Graded Naming Test (SD)	16.7 (5.8)**	18.8 (5.7)*	22.3 (4.9)

* = p<0.05, ** = p<0.01

4.4.1.4 Word Comprehension

Level 1 Analysis

The Frontal, Posterior and Control groups all obtained average scores on the Synonyms Test of word comprehension ability, with no significant difference found (See Table 27a and Appendix 5 ref 1.3).

Level 2 Analysis

Word comprehension ability was equivalent across the Left and Right Frontal groups (See Table 27a and Appendix 5 ref 2.7).

Table 27a. *Word Comprehension: Mean Number Correct (Max = 50) and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 37**	**Posterior N = 14**	**Control N = 32**
Synonyms Test Score (SD)	39.6 (7.4)	43.6 (4.4)	43.1 (6.8)
Level 2 Analysis	**Left Frontal N = 16**	**Right Frontal N = 16**	
Synonyms Test Score (SD)	37.1 (7.9)	40.9 (7.2)	

Level 4 Analysis

Word comprehension ability did not differ significantly between the LIFG, Non-LIFG and Control groups ($F_{(2,65)} = 2.423$, $p = 0.097$; see Table 27b).

Table 27b. *Word Comprehension: Mean Number Correct (Max = 50) and Standard Deviation (SD)*

Level 4 Analysis	**LIFG N = 9**	**Non-LIFG N = 27**	**Control N = 32**
Synonyms Test Score (SD)	37.6 (10.1)	40.3 (6.6)	43.06 (6.8)

4.4.2 Language Function Baseline Summary and Discussion

Baseline language tests showed that the spontaneous speech and sentence repetition skills of the Frontal group were impaired. Nonfluent speech was noted in more Left Lateral and Superior Medial patients, as was poorer repetition ability. Of note, the specific Superior Medial patients showing these deficits all had left lateralised lesions. In addition, only Left Frontal patients produced errors. Given the nonfluent measure reflects sentence structure (i.e., encompassing agrammatical speech), the findings for fluency, repetition and errors are consistent with the typical aphasic impairments associated with the left frontal lobe (e.g., Alexander et al., 1989; Cappa et al., 1999; Goodglass et al., 1983). All Frontal subgroups produced a reduced amount of speech that would fit broadly with decreased generation and initiation. Nominal ability of the Frontal group was poorer than Controls; however, their performance was within normal limits with no specific frontal deficit when directly compared to Controls. Comprehension skills were normal and, as noted in the Descriptive Characteristics above, no reading deficit was found in any group (NART). The absence of significant nominal, comprehension and reading deficits in Frontal patients concurs with previous lesion studies (for review see McCarthy & Warrington, 1990). Overall, apart from spontaneous speech and sentence production difficulties evident in left lateralised patients, the Frontal group performed well on baseline language tests.

4.5 FRONTAL EXECUTIVE FUNCTION BASELINE

4.5.1 Tests and Procedure

Five standardised measures were used to assess frontal executive function. These were the Cognitive Estimates Test (Shallice et al., 1978), Trail Making Test (Army Individual Test Battery, 1944), Stroop Test (1935), Proverb Interpretation task and Hayling Sentence Completion Test (Burgess et al., 1996b).

The Cognitive Estimates Test was designed to assess judgement. Shallice and Evans (1978) found that patients with frontal lobe lesions tended to give more bizarre estimations than patients with posterior lesions. In the current study, 10 questions from the Shallice and Evans test were given and the total error score was recorded. Each subject's performance was then categorised as a 'Pass' or 'Fail' based on the 5% cut-off score calculated from the performance of the Controls.

The Trail Making Test is thought to assess cognitive flexibility, divided attention, scanning and visuomotor ability (Lezak et al., 2004; Olivera-Souza et al., 2000). The original version was used with errors corrected and the total time taken to complete each part recorded.

The Stroop Test is widely used to assess executive function as it provides a measure of selective attention and ability to suppress an automatic response in favour of an unusual one (Spreen et al., 1998). The version of the Stroop Test used in this study contains two conditions, each with 112 items (reading of colour words printed in different colours, naming of ink colours; Trenerry, Crosson, DeBoe, & Leber, 1989). The total number correct in two minutes for both conditions was recorded. When subjects completed either task (i.e., 112 items) in less than two minutes, scores were prorated to be equivalent to two minutes. In addition, number of errors in the conflict naming of ink colours condition was recorded.

Proverb Interpretation tasks assess abstraction (Lezak et al., 2004). In this study, four standard proverbs were orally presented to subjects who were asked what each proverb really meant. Each proverb interpretation was scored on a 3-point scale. A score of 2 was given if a response was a complete abstract interpretation. A score of 1 was given if the response was partially correct. A score of 0 was given if the response was concrete or incorrect. The total score for the four proverbs was recorded.

The Hayling Sentence Completion Test involves verbal response initiation and suppression, as well as strategy formation and use. Burgess and Shallice (1996b) showed that patients with frontal lobe lesions (no lateralisation) had longer response latencies in the verbal initiation condition and performed worse on the response suppression condition. This test was administered as detailed in the manual. Overall and individual scaled scores were recorded and analysed: Overall scaled score; Section 1 (Meaningful Completion) response time [RT]; Section 2 (Unrelated Completion) RT; and Section 2 Errors. Level 4 Analysis was applied to this test given the findings reported in Chapter 2 for the dynamic aphasic patient CH whose performance was impaired only on the meaningful completion condition (verbal initiation).

4.5.2 Results

4.5.2.1 Cognitive Estimates Test

Level 1 Analysis

The difference between the mean error scores obtained by the Frontal, Posterior and Control groups did not reach significance (See Table 28 and Appendix 5 ref 1.4). The 5% cut-off score, based on the performance of the Controls, was calculated to be 7. Thus, error scores between 0-6 were assigned a 'Pass' whilst error scores of 7 or higher were assigned a 'Fail'. The difference between groups for the number of subjects that passed or failed was significant ($\chi^2_{(2)} = 6.892$, p = 0.032). Further analysis revealed that more Frontal patients failed the Cognitive Estimates Test than Control subjects ($\chi^2_{(1)} = 5.889$, p = 0.015).

Level 2 Analysis

The Left and Right Frontal groups did not differ significantly (See Table 28 and Appendix 5 ref 2.8).

Table 28. *Mean Cognitive Estimates Error Score and Standard Deviation (SD) and Number of Subjects who Passed/Failed*

Level 1 Analysis	**Frontal N = 34**	**Posterior N = 10**	**Control N = 28**
Mean Error Score (SD)	4.82 (3.5)	3.60 (1.6)	3.04 (2.4)
Pass (Score 0-6)	23	9	26
Fail (Score 7+)	11*	1	2
Level 2 Analysis	**Left Frontal N = 13**		**Right Frontal N = 17**
Mean Error Score (SD)	5.00 (4.3)		4.53 (3.2)
Pass (Score 0-6)	8		12
Fail (Score 7+)	5		5

* = p<0.05

Level 3 Analysis

No further Frontal group effects were revealed for the number of subjects that passed or failed (See Appendix 5 ref 3.2).

4.5.2.2 Trail Making Test

Level 1 Analysis

The difference in time taken to complete Trail Making A between Frontal, Posterior and Control groups just failed to reach significance ($p = 0.056$; See Table 29 and Appendix 5 ref 1.5). One-way ANOVA revealed a significant difference between groups for the Trail Making B time ($F_{(2,64)} = 4.858$, $p = 0.011$). As Levene's test of homogeneity of error variances was significant ($F_{(2,64)} = 6.284$, $p = 0.003$), a Kruskal-Wallis Test was used to confirm the difference was significant ($\chi^2_{(2)} = 10.063$, $p = 0.007$). Pairwise Mann-Whitney U comparisons found that Frontals were significantly slower to complete part B than Controls ($U = 184.50$, $p = 0.002$).

Level 2 Analysis

There was no difference between the Left and Right Frontal groups for the Trail Making A time (See Table 29 and Appendix 5 ref 2.9). Although no significant difference was found between groups for Trail Making B time, using univariate ANCOVA, age was a significant covariate (See Table 29 and Appendix 5 ref 2.10).

Table 29. *Trail Making Test: Mean Time and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 36~**	**Posterior N = 11**	**Control N = 21**
Trail Making A time (SD)	51.6 (35.3)	53.0 (21.6)	33.7 (13.7)
Trail Making B time (SD)	141.6 (95.1)**	109.6 (70.0)	76.1 (30.3)

Level 2 Analysis	**Left Frontal N = 14**	**Right Frontal N = 17**
Trail Making A time (SD)	37.5 (14.9)	57.0 (45.4)
Trail Making B time (SD)	98.2(45.7)	158.5 (99.2)

~ = 1 Frontal patient was unable to complete the Trail Making B Test; ** = p<0.01.

Level 3 Analysis

No further Frontal group effects were revealed for the Trail Making B time (See Appendix 5 ref 3.3).

4.5.2.3 Stroop Test

Level 1 Analysis

The colour word reading scores obtained by the Frontal, Posterior and Control groups were revealed to be significantly different using one-way ANOVA ($F_{(2,76)}$ = 4.348, p = 0.016; see Table 30). Pairwise comparisons confirmed that the colour word reading score of the Frontals was lower than Controls (p = 0.005). The groups also differed significantly in the conflict condition in terms of colour ink naming scores ($F_{(2,74)}$ = 4.783, p = 0.011), although the error variances were unequal using Levene's test ($F_{(2,74)}$ = 4.539, p = 0.014). Subsequent Kruskal-Wallis Test confirmed the significant difference ($\chi^2_{(2)}$ = 6.557, p = 0.038). Pairwise Mann-Whitney U comparisons found that the colour ink naming score of the Frontals was lower than

Controls (U = 329.00, p = 0.009). There was no difference between groups for errors in the colour ink naming condition (See Table 30 and Appendix 5 ref 1.6).

Level 2 Analysis

The Left and Right Frontal groups did not differ significantly on the three Stroop Test measures (See Table 30 and Appendix 5 refs 2.11 - 2.13).

Level 3 Analysis

For the three Stroop Test measures, no further frontal effects were revealed (See Appendix 5 refs 3.4 - 3.6).

Table 30. *Stroop Test: Mean Score (in 2 minutes) and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 35~**	**Posterior N = 12**	**Control N = 32**
Colour Word Reading Score (SD)	180.5 (70.1)**	217.4 (70.5)	229.3 (67.8)
Colour Ink Naming Score (SD)	83.3 (33.6)**	98.3 (38.7)	106.2 (21.5)
Colour Ink Naming Error Score (SD)	2.36 (4.2)	0.42 (0.7)	1.38 (1.8)
Level 2 Analysis	**Left Frontal N = 14~**	**Right Frontal N = 17~**	
Colour Word Reading Score (SD)	172.8 (69.7)	185.7 (50.8)	
Colour Ink Naming Score (SD)	87.4 (39.3)	84.1 (26.0)	
Colour Ink Naming Error Score (SD)	1.54 (2.9)	3.13 (5.2)	

~ = 1 Left Frontal and 1 Right Frontal patient were unable to complete the Colour Ink Naming Condition; ** = p<0.01.

4.5.2.4 Proverbs Test

Level 1 Analysis

The total score obtained by the Frontal, Posterior and Control groups was significantly different, as revealed by one-way ANOVA ($F_{(2,75)}$ = 7.900, p = 0.001; see Table 31a). Pairwise comparisons confirmed that Frontals gave poorer proverb interpretations than both Posteriors (p = 0.007) and Controls (p = 0.001).

Level 2 Analysis

Left and Right Frontal groups did not differ in the total score obtained on the proverbs task (See Table 31a and Appendix 5 ref 2.14).

Table 31a. *Mean Proverb Test Score (Max = 8) and Standard Deviation (SD)*

Level 1 Analysis	Frontal N = 38	Posterior N = 13	Control N = 27
Mean Score (SD)	4.16 (1.9)**	5.69 (1.3)	5.63 (1.3)
Level 2 Analysis	**Left Frontal N = 15**	**Right Frontal N = 17**	
Mean Score (SD)	4.00 (2.4)	4.59 (1.5)	

** = p<0.01

Level 3 Analysis

One-way ANOVA revealed significant frontal effects for the proverbs total score ($F_{(4,47)}$ = 2.694, p = 0.042; see Table 31b). Pairwise comparisons confirmed that only the Superior Medial and Inferior Medial groups gave poorer proverb interpretations than Controls (p = 0.038 and p = 0.007, respectively).

Table 31b. *Mean Proverb Test Score (Max = 8) and Standard Deviation (SD)*

Level 3 Analysis	Left Lateral N = 6	Right Lateral N = 6	Superior Medial N = 8	Inferior Medial N = 5	Control N = 27
Mean Score (SD)	4.83 (2.5)	5.00 (2.2)	4.13 (2.0)*	3.20 (2.2)**	5.63 (1.3)

* = p<0.05, ** = p<0.01

4.5.2.5 Hayling Sentence Completion Test

Level 1 Analysis

For the Hayling overall and individual scaled scores, there was a significant difference between the Frontal, Posterior and Control groups, as revealed by one-way ANOVA's ($F_{(2,78)}$ = 20.298, p<0.001, $F_{(2,78)}$ = 5.545, p = 0.006, $F_{(2,78)}$ = 6.502, p = 0.002, $F_{(2,78)}$ = 19.613, p<0.001, respectively) (See Table 32a). However, for each analysis Levene's test of homogeneity of error variances was significant ($F_{(2,78)}$ = 18.897, p<0.001, $F_{(2,78)}$ = 4.083, p = 0.021, $F_{(2,78)}$ = 4.978 = 0.009, $F_{(2,78)}$ = 47.223, p<0.001, respectively). Subsequent Kruskal-Wallis Tests confirmed the differences in each analysis was significant ($\chi^2_{(2)}$ = 25.152, p<0.001, $\chi^2_{(2)}$ = 11.712, p = 0.003, $\chi^2_{(2)}$ = 13.941, p = 0.001, $\chi^2_{(2)}$ = 23.038, p<0.001, respectively). Pairwise Mann-Whitney U comparisons found that the overall scaled score obtained by Frontals was significantly lower than both Posteriors (U = 204.50, p<0.001) and Controls (U = 104.50, p = 0.003). For the two RT scaled scores, Frontals were impaired compared to Controls indicating they were significantly slower to complete sentences with both a meaningful and an unrelated word (U = 335.00, p = 0.001 and U = 307.00, p<0.001, respectively). Finally, pairwise Mann-Whitney U comparisons found that Frontals made significantly more errors in the unrelated condition than both Posteriors (U = 108.50, p = 0.004) and Controls (U = 214.50, p<0.001).

Table 32a. *Mean Hayling Sentence Completion Test Scaled Scores# and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 36**	**Posterior N = 13**	**Control N = 32**
Overall SS (SD)	3.83 (2.1)**	5.85 (0.9)	6.19 (1.1)
Meaningful Completion SS - RT (SD)	4.75 (1.6)**	5.69 (0.9)	5.72 (1.1)
Unrelated Completion SS - RT (SD)	4.47 (1.7)***	5.31 (0.9)	5.69 (1.2)
Unrelated Completion SS - Errors (SD)	4.03 (2.8)***	6.69 (1.0)	6.94 (1.1)
Level 2 Analysis	**Left Frontal N = 15**	**Right Frontal N = 17**	
Overall SS (SD)	4.27 (2.2)	3.41 (1.9)	
Meaningful Completion SS - RT (SD)	4.40 (1.8)	5.06 (1.3)	
Unrelated Completion SS - RT (SD)	4.93 (1.7)	4.24 (1.6)	
Unrelated Completion SS - Errors (SD)	4.67 (2.8)	3.18 (2.6)	

SS = Scaled Score; # = SS is from 1-10 with 6 being average; ** p<0.01, *** = p<0.001.

Level 3 Analysis

One-way ANOVA revealed a significant frontal effect for the overall scaled score ($F_{(4,52)}$ = 7.473, p<0.001). As Levene's test was significant ($F_{(4,52)}$ = 4.337, p = 0.004), Kruskal-Wallis Test was used to confirm the difference ($\chi^2_{(4)}$ = 20.727, p<0.001; see Table 32b). Left and Right Laterals obtained significantly lower overall scaled scores than Controls, using pairwise Mann-Whitney U comparisons (U = 32.500, p = 0.002 and U = 8.5000, p<0.001, respectively). For the meaningful completion RT scaled score, the difference just failed to reach significance using one-way ANOVA (p = 0.063; see Appendix 5 ref 3.7). For the unrelated completion RT scaled score, one-way ANOVA revealed a significant difference ($F_{(4,52)}$ = 3.160, p = 0.021). Pairwise comparisons found that the Right Lateral and Superior Medial groups were significantly slower to complete sentences with an unrelated word than Controls (p = 0.004 and p = 0.033, respectively). Although a significant difference was found for the unrelated completion error scaled score ($F_{(4,52)}$ = 8.430, p<0.001), Levene's test was significant ($F_{(4,52)}$ = 9.490, p<0.001). Subsequent Kruskal-Wallis Test confirmed the significant difference ($\chi^2_{(4)}$ = 20.273, p<0.001). Pairwise Mann-Whitney U comparisons found that the Left Lateral and Right Lateral groups made significantly more errors when completing sentences with an unrelated word than Controls (U = 31.000, p = 0.002 and U = 7.500, p<0.001, respectively).

Table 32b. *Mean Hayling Sentence Completion Test Scaled Scores[#] and Standard Deviation (SD)*

Level 3 Analysis	**Left Lateral N = 7**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 4**	**Control N = 32**
Overall SS (SD)	4.00** (1.9)	3.17*** (1.8)	4.63 (2.3)	4.50 (1.7)	6.19 (1.1)
Meaningful Completion SS - RT (SD)	4.57 (1.5)	5.50 (0.5)	4.63 (1.8)	4.75 (1.5)	5.72 (1.1)
Unrelated Completion SS - RT (SD)	5.43 (0.8)	3.83** (1.7)	4.50* (1.6)	4.75 (2.5)	5.69 (1.2)
Unrelated Completion SS - Errors (SD)	4.00** (2.8)	2.83*** (2.1)	4.88 (2.9)	5.25 (2.9)	6.94 (1.1)

SS = Scaled Score; # = SS is from 1-10 with 6 being average; * = p<0.05, ** = p<0.01, *** = p<0.001.

Level 4 Analysis

The LIFG, Non-LIFG and Control groups differed significantly on all 4 Hayling measures, as revealed by one-way ANOVA's: overall scaled score ($F_{(2,64)}$ = 16.682, p<0.001); meaningful completion RT scaled score ($F_{(2,64)}$ = 4.153, p = 0.020); unrelated completion RT scaled score ($F_{(2,64)}$ = 6187, p = 0.003); and unrelated completion error scaled score ($F_{(2,64)}$ = 16.172, p<0.001) (see Table 32c). For all 4 measures Levene's test was significant ($F_{(2,64)}$ = 12.376, p<0.001, $F_{(2,64)}$ = 3.484, p = 0.037, $F_{(2,64)}$ = 3.569, p = 0.034, $F_{(2,64)}$ = 34.952, p<0.001, respectively). However, the significant differences were confirmed by Kruskal-Wallis Tests ($\chi^2_{(2)}$ = 23.029, p<0.001; $\chi^2_{(2)}$ = 10.191, p = 0.006; $\chi^2_{(2)}$ = 14.329, p = 0.001; $\chi^2_{(2)}$ = 20.101, p<0.001, respectively). Pairwise Mann-Whitney U comparisons found that for the overall scaled score the Non-LIFG group scored significantly lower than Controls (U = 134.000, p<0.001). For the meaningful and unrelated completion RT scaled scores, the LIFG and Non-LIFG groups were found to be significantly slower than Controls (Meaningful Completion: U = 62.500, p = 0.034 and U = 269.000, p = 0.003; Unrelated Completion: U = 66.000, p = 0.039 and U = 223.000, p<0.001). For the unrelated completion condition, the LIFG and Non-LIFG groups made significantly more errors than Controls (U = 46.500, p = 0.012 and U = 168.000, p<0.001).

Table 32c. *Mean Hayling Sentence Completion Test Scaled Scores# and Standard Deviation (SD)*

Level 4 Analysis	**LIFG N = 7**	**Non-LIFG N = 28**	**Control N = 35**
Overall SS (SD)	4.57 (2.5)	3.68 (2.0)***	6.19 (1.1)
Meaningful Completion SS - RT (SD)	4.57 (1.9)*	4.82 (1.5)**	5.72 (1.1)
Unrelated Completion SS - RT (SD)	4.71 (1.8)*	4.36 (1.7)***	5.69 (1.2)
Unrelated Completion SS - Errors (SD)	5.29 (2.1)*	3.82 (2.9)***	6.94 (1.1)

SS = Scaled Score; # = SS is from 1-10 with 6 being average; * = p<0.05, ** = p<0.01, *** = p<0.001.

4.5.3 Frontal Executive Function Summary and Discussion

Frontal executive testing confirmed a selective Frontal deficit, without left/right lateralisation, on all five tests (Cognitive Estimates, Trail Making, Stroop, Proverbs, Hayling). First, more Frontal patients failed the Cognitive Estimates Test in comparison to Controls. Thus, Frontals tended to give more bizarre responses indicating poor judgement. No further frontal localisation or lateralisation was revealed. This finding is consistent with the original findings of Shallice and Evans (1978). In a sample of older normal adults (> 55 years), performance on the Cognitive

Estimates test was found to correlate with verbal intelligence (Gillespie, Evans, Gardener, & Bowen, 2002). Studies of neurological patients have been equivocal. For example, Taylor and O'Carroll (1995) failed to find a difference between patients with focal frontal and non-frontal lesions, although they did report an impairment in Korsakoff's patients. By contrast, an earlier study found that Korsakoff's patients performed normally but postencephalitic patients performed poorly (Leng & Parkin, 1988). Patients with both frontotemporal degeneration and Alzheimer's Disease have been reported to give significantly more extreme cognitive estimates than controls, and the Alzheimer's Disease patients gave poorer estimates than the frontotemporal patients (Mendez, Doss, & Cherrier, 1998). Perhaps one reason for the disparity in findings is the measure used to indicate impairment. For example, in this study no difference was found between groups for overall mean error score; however, the number of Frontal patients that scored below the Control groups' 5% cut-off was significant. This study confirms the usefulness of the Cognitive Estimates Test as a frontal lobe measure of poor judgement.

Compared to Controls, Frontal patients were impaired for the time taken to complete the Trail Making B Test. The main difference between part A and B of this test is that part B involves cognitive flexibility (i.e., switching) and divided attention; hence, this study supports a role for the frontal lobes in these abilities. No further localisation within the frontal region was evident. The Frontal deficit is consistent with previous lesion studies (Stuss et al., 2001a) and confirms a selective Frontal deficit that has been questioned (e.g., Anderson, Bigler, & Blatter, 1995). However, Stuss and colleagues (2001a) also found that patients with dorsolateral lesions were more impaired than patients with inferior medial lesions. This was not confirmed by the present study, nor was specific involvement of the left dorsolateral and medial areas as suggested by recent neuroimaging data (Moll, Oliveira-Souza, Moll, Bramati, & Andreiuolo, 2002).

For the Stroop Test, Frontal patients were impaired on both the reading and ink naming conditions, in comparison to Controls. This test taps selective attention and ability to suppress automatic responses, a failure of which is measured by errors. Although, the error measure was not significant, the time cost (i.e., lower score) for ink colour naming does show this process is less efficient for Frontal patients. No further frontal localisation was revealed. Although these findings support a role of the frontal lobes in this task, they contrast with previous findings for the conflict ink colour naming condition that specifically implicated the left frontal region (e.g., Perret, 1974), right frontal region (Vendrell et al., 1995) or superior medial region (Stuss et al., 2001b). The absence of fine-grained frontal effects in this study for the Trail Making and Stroop Tests may be due to the small numbers of patients in the frontal subgroups.

The selective Medial (Superior and Inferior) deficit for Proverb Interpretations is the first report suggesting a role for this frontal region in the process of abstraction. Benton (1968) reported that patients with bilateral frontal lesions gave the poorest proverb interpretations, patients with right frontal lesion performed somewhat better, and patients with left frontal lesions were relatively intact. If a comparison is made with the Level 2 Analysis (i.e., Left vs. Right Frontal) in this study, the findings differ in that no left/right lateralisation was revealed. Further, it is unlikely that the Medial deficit documented in this study completely overlaps with the bilateral deficit in Benton's (1968) group as presumably patients with lateral damage as well as medial damage were included. This highlights the need for fine-grained lesion studies, as the current study clearly demonstrates it is the Medial and not Lateral lesions that have a role in abstraction.

For the fifth frontal executive test, the Hayling Sentence Completion Test, a Frontal deficit was found on all 4 measures in comparison to Controls. In comparison to Posterior patients, Frontals performed significantly more poorly overall and they made more errors in the unrelated completion condition involving response suppression. For the Hayling overall score, Left and Right Lateral deficits were revealed. Both Lateral groups were also impaired in the unrelated completion condition in terms of errors (i.e., failure to suppress an automatic response). In addition, the response times of Right Laterals and Superior Medials were significantly slower than Controls for the unrelated condition. Imaging studies have only implicated left regions in the response suppression condition (left operculum, left inferior and middle frontal gyrus), although this method has not allowed for separation of errors and response times (Collette et al., 2001; Nathaniel-James et al., 1997; Nathaniel-James & Frith, 2002). Thus, for response suppression, convergence between lesion and imaging data only occurs for the Left Lateral involvement. There was a strong trend for Left Frontal patients to take longer to complete sentences with a meaningful word (i.e., response initiation). This trend would be in keeping with the performance of the dynamic aphasic CH as he was only impaired for the meaningful completion condition and his damage was confined to the left frontal region. This trend for response initiation is also consistent with imaging findings that have implicated the left inferior frontal region (Nathaniel-James et al., 1997). This is the first time fine-grained frontal effects have been revealed for the Hayling Test.

4. 6 VERBAL AND NON-VERBAL FLUENCY INVESTIGATION

This battery consisted of four fluency tests designed to explore the generation of multiple single items from a given cue or prompt; word fluency, design fluency, ideational fluency, and gesture fluency. The four fluency tests are thought to tap verbal and non-verbal voluntary generation of both stored and novel responses. Specifically, verbal based tasks include word fluency and possibly ideational fluency although little is understood about the latter task. Non-verbal based tasks include design fluency. Gesture fluency could be argued to tap both verbal and non-verbal processes.

4.6.1 Word Fluency

Standard phonemic and semantic word fluency tasks were administered (Benton, 1968; Hodges, Salmon, & Butters, 1990; Milner, 1964). Subjects were asked to generate as many words as possible in 1 minute in 2 Conditions: *Phonemic* – beginning with a letter (S, J); and *Semantic* – from a category (Living things, Fruit/Vegetables). Subjects were asked not to produce proper nouns or numbers (phonemic fluency) or to repeat words. The total number of correct words generated, perseverative errors and rule breaks (i.e., inappropriate errors) were recorded. The total from the two phonemic tasks was analysed together whilst each semantic task was analysed separately.

4.6.1.1 Phonemic Fluency

Level 1 Analysis

The Frontal, Posterior and Control groups generated a significantly different number of words, as revealed by one-way ANOVA ($F_{(2,86)} = 20.242$, $p<0.001$; see Table 33a). Pairwise comparisons found that Frontals and Posteriors generated fewer words than Controls ($p<0.001$ and $p = 0.012$, respectively). The difference between groups did not reach significance for perseverative errors (See Table 33a and Appendix 6 ref 1.1), although one-way ANOVA revealed a significant difference between groups for inappropriate errors ($F_{(2,86)} = 6.668$, $p = 0.002$). As Levene's test found the error variances to be unequal ($F_{(2,86)} = 3.427$, $p = 0.037$), Kruskal-Wallis Test was used to confirm the difference was significant ($\chi^2_{(2)} = 13.832$, $p = 0.001$). Pairwise Mann-Whitney U comparisons found that Frontals and Posteriors made more inappropriate errors than Controls (U = 376.500, $p<0.001$ and U = 163.000, $p = 0.015$, respectively).

Table 33a. *Word Fluency: Phonemic Fluency; Mean Number and Standard Deviation (SD) of Total Words Generated, Perseverative Errors and Inappropriate Errors*

Level 1 Analysis		**Frontal** N = 39	**Posterior** N = 15	**Control** N = 35
S & J	Mean Total No. (SD)	13.92 (8.8)***	19.60 (7.9)*	26.11 (7.7)
	Errors – Perseverative (SD)	.44 (.72)	.67 (.98)	.31 (.63)
	Errors – Inappropriate (SD)	1.31 (1.22)***	1.00 (1.00)*	.43 (.82)
Level 2 Analysis		**Left Frontal** N = 16	**Right Frontal** N = 17	
S & J	Mean Total No. (SD)	10.31 (8.3)**	18.12 (6.0)	
	Errors – Perseverative (SD)	.56 (.73)	.24 (.44)	
	Errors – Inappropriate (SD)	1.50 (1.10)	1.35 (1.41)	

* = p<0.05, *** = p<0.001.

Level 2 Analysis

Left Frontals generated significantly fewer words than Right Frontals, using univariate ANCOVA ($F_{(1,30)} = 11.746$, $p = 0.002$; see Table 33a). The difference between groups for perseverative and inappropriate errors did not reach significance (See Table 33a and Appendix 6 ref 2.1 and 2.2).

Level 3 Analysis

Using one-way ANOVA, a significant difference in the number of words generated was found between frontal subgroups ($F_{(4,56)} = 7.121$, $p<0.001$; see Table 33b). Pairwise comparisons revealed that Left Laterals, Superior Medials and Inferior Medials generated significantly fewer words than Controls ($p<0.001$, $p = 0.001$ and $p = 0.008$, respectively). One-way ANOVA revealed a significant difference between groups for inappropriate errors ($F_{(4,56)} = 3.800$, $p = 0.008$). Levene's test found unequal error variances ($F_{(4,56)} = 4.676$, $p = 0.003$), thus, Kruskal-Wallis Test was used to confirm the significant difference ($\chi^2_{(4)}$ = 13.702, p = 0.008). Pairwise Mann-Whitney U comparisons found that Left Laterals, Right Laterals and Superior Medials made more inappropriate errors than Controls (U = 45.500, p = 0.002, U = 52.000, p = 0.018 and U = 71.000, p = 0.011, respectively).

Table 33b. *Word Fluency: Phonemic Fluency; Mean Number and Standard Deviation (SD) of Total Words Generated, Perseverative Errors and Inappropriate Errors*

Level 3 Analysis		**Left Lateral N = 7**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 5**	**Control N = 35**
S & J	Mean Total No.	12.9 ***	20.0	15.8 **	16.0 **	26.1
	(SD)	(10.1)	(2.4)	(6.1)	(9.8)	(7.7)
	Errors – Inappropriate	1.57 **	1.83 *	1.38 *	1.20	0.43
	(SD)	(1.0)	(1.7)	(1.3)	(1.8)	(0.8)

* = p<0.05, ** = p<0.01, *** = p<0.001.

Level 4 Analysis

A significant difference was found between the LIFG, Non-LIFG and Control groups for number of words generated using one-way ANOVA ($F_{(2,70)}$ = 22.796, p<0.001; see Table 33c). Pairwise comparisons found that the LIFG and Non-LIFG groups generated significantly fewer words than Controls (both p<0.001) and that the LIFG group also generated fewer than the Non-LIFG group (p = 0.024). The difference between groups for perseverative errors did not reach significance (See Table 33c and Appendix 6 ref 4.1). One-way ANOVA revealed a significant difference between groups for inappropriate errors ($F_{(2,70)}$ = 6.901, p = 0.002). As Levene's test found the error variances to be unequal ($F_{(2,70)}$ = 6.260, p = 0.003), Kruskal-Wallis Test was used to confirm the difference was significant ($\chi^2_{(2)}$ = 14.222, p = 0.001). Pairwise Mann-Whitney U comparisons found that the LIFG and Non-LIFG groups made more inappropriate errors than Controls (U = 62.000, p = 0.001 and U = 292.500, p = 0.001).

Table 33c. *Word Fluency: Phonemic Fluency; Mean Number and Standard Deviation (SD) of Total Words Generated, Perseverative Errors and Inappropriate Errors*

Level 4 Analysis		**LIFG N = 9**	**Non-LIFG N = 29**	**Control N = 35**
S & J	Mean Total No. (SD)	8.78 (9.0)***#	15.86 (8.1)***	26.11 (7.7)
	Errors – Perseverative (SD)	.78 (1.09)	.34 (.55)	.31 (.63)
	Errors – Inappropriate (SD)	1.33 (.71)**	1.34 (1.34)**	.43 (.82)

** = p<0.01, *** = p<0.001, # - significant compared to both Non-LIFG and Controls

4.6.1.2 Semantic Fluency

Level 1 Analysis

One-way ANOVA's revealed a significant difference in the number of living things and fruit/vegetables generated by the Frontal, Posterior and Control groups ($F_{(2,86)}$ = 9.026, p<0.001 and $F_{(2,86)}$ = 17.999, p<0.001, respectively; see Table 34a). Using pairwise comparisons, Frontals generated fewer living things than Controls (p<0.001) with a trend for Posteriors to generate fewer living things than Controls, although this failed to reach significance after Bonferroni adjustment (p = 0.021). Both Frontals and Posteriors generated significantly fewer fruit/vegetables than Controls (p<0.001 and p<0.001, respectively). For both semantic categories, the difference between groups failed to reach significance for perseverative errors and, for fruit/vegetables, the groups did not differ for inappropriate errors (See Table 34a and Appendix 6 refs 1.2 - 1.4). However, for living things, the groups did differ significantly for inappropriate errors ($F_{(2,86)}$ = 4.888, p = 0.010). As Levene's test revealed unequal error variances ($F_{(2,86)}$ = 23.810, p<0.001), subsequent Kruskal-Wallis Test was used to confirm the difference ($\chi^2_{(2)}$ = 11.168, p = 0.004). Pairwise Mann-Whitney U comparisons found that Frontals and Posteriors made more inappropriate errors for the living things task than Controls (U = 490.000, p = 0.001 and U = 210.000, p = 0.007, respectively).

Level 2 Analysis

For both semantic categories, there was no difference between the Left and Right Frontal groups in terms of the number generated, perseverative errors and inappropriate errors (See Table 34a and Appendix 6 refs 2.3 - 2.8).

Table 34a. *Word Fluency: Semantic Fluency; Mean Number and Standard Deviation (SD) of Total Words Generated, Perseverative Errors and Inappropriate Errors*

Level 1 Analysis		**Frontal N = 39**	**Posterior N = 15**	**Control N = 35**
Living Things	Mean Total No. (SD)	13.21 (7.2)***	15.00 (7.6)	20.26 (7.1)
	Errors – Perseverative (SD)	.26 (.60)	.60 (.99)	.29 (.67)
	Errors – Inappropriate (SD)	.46 (.88)**	.27 (.59)**	.00 (.00)
Fruit/Vegetables	Mean Total No. (SD)	12.82 (6.3)***	13.33 (5.0)***	20.49 (5.5)
	Errors – Perseverative (SD)	.38 (.75)	.27 (.46)	.34 (1.1)
	Errors – Inappropriate (SD)	.15 (.37)	.80 (2.83)	.00 (.00)

Level 2 Analysis		**Left Frontal N = 16**	**Right Frontal N = 17**
Living Things	Mean Total No. (SD)	13.13 (7.4)	14.00 (6.3)
	Errors – Perseverative (SD)	.19 (.40)	.41 (.80)
	Errors – Inappropriate (SD)	.25 (.45)	.82 (1.19)
Fruit/Vegetables	Mean Total No. (SD)	12.75 (6.2)	13.76 (5.2)
	Errors – Perseverative (SD)	.25 (.58)	.53 (.87)
	Errors – Inappropriate (SD)	.19 (.40)	.18 (.39)

** = p<0.01, *** = p<0.001.

Level 3 Analysis

For the number of living things generated, the difference between frontal subgroups just failed to reach significance using one-way ANOVA ($F_{(4,56)}$ = 2.439, p = 0.057; see Table 34b). However, one-way ANOVA revealed a significant difference between frontal subgroups for number of fruit/vegetables generated ($F_{(4,56)}$ = 4.777, p = 0.002). Pairwise comparisons found that all groups generated significantly fewer fruit/vegetables than Controls (Left Laterals: p = 0.025; Right Laterals: p = 0.016; Superior Medials: p = 0.027; Inferior Medials: p = 0.002). Although, a significant difference between frontal groups was revealed for inappropriate errors in the living things task ($F_{(4,56)}$ = 4.325, p = 0.004), Levene's test was significant ($F_{(4,56)}$ = 16.559, p<0.001). The significant difference between groups was confirmed using a Kruskal-Wallis Test ($\chi^2_{(4)}$ = 16.068, p = 0.003). Pairwise Mann-Whitney U found that all groups made more inappropriate errors than Controls (Left Laterals: U = 87.500, p =

0.001; Right Laterals: U = 52.500, p<0.001; Superior Medials: U = 105.000, p = 0.003; Inferior Medials: U = 52.500, p<0.001).

Table 34b. *Word Fluency: Semantic Fluency; Mean Number and Standard Deviation (SD) of Total Words Generated, Perseverative Errors and Inappropriate Errors*

Level 3 Analysis		**Left Lateral N = 7**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 5**	**Control N = 35**
Living Things						
	Mean Total No.	15.6	15.2	14.5	13.0	20.3
	(SD)	(9.2)	(5.6)	(4.8)	(7.9)	(7.1)
	Errors – Inappropriate	.29**	.83***	.38**	.80***	.00
	(SD)	(.49)	(1.17)	(.74)	(1.30)	(.00)
Fruit/Vegetables						
	Mean Total No.	15.1*	14.3*	15.5*	11.8**	20.5
	(SD)	(6.0)	(4.9)	(4.3)	(8.1)	(5.5)

* = p<0.05, ** = p<0.01, *** = p<0.001.

Level 4 Analysis

Using one-way ANOVA, a significant difference was found between the LIFG, Non-LIFG and Control groups in terms of number generated for both semantic categories ($F_{(2,70)}$ = 8.756, p<0.001 and $F_{(2,70)}$ = 15.605, p<0.001, respectively; see Table 34c). Pairwise comparisons found that the LIFG and Non-LIFG groups generated significantly fewer words than Controls for both categories (Living Things: p = 0.002 and p = 0.001, respectively; Fruit/Vegetables: both p<0.001). There was no difference between groups for perseverative errors for either category (See Table 34c and Appendix ref 4.2 and 4.3). However, for both categories, one-way ANOVA's revealed significant differences between groups for inappropriate errors ($F_{(2,70)}$ = 7.067, p = 0.002 and $F_{(2,70)}$ = 3.342, p = 0.041, respectively). As Levene's tests were significant in both cases (Living Things: $F_{(2,70)}$ = 31.905, p<0.001; Fruit/Vegetables: $F_{(2,70)}$ = 20.091, p<0.001), Kruskal-Wallis Tests were used to confirm the significant differences ($\chi^2_{(2)}$ = 14.763, p = 0.001 and $\chi^2_{(2)}$ = 6.276, p = 0.043, respectively). For living things, pairwise Mann-Whitney U comparisons found that the LIFG and Non-LIFG groups made more inappropriate errors than Controls (U = 140.000, p = 0.049

and U = 332.500, p<0.001). For fruit/vegetables only the Non-LIFG group made significantly more inappropriate errors than Controls (U = 420.000, p = 0.011)[15].

Table 34c. *Word Fluency: Semantic Fluency; Mean Number and Standard Deviation (SD) of Total Words Generated, Perseverative Errors and Inappropriate Errors*

Level 4 Analysis		**LIFG N = 9**	**Non-LIFG N = 29**	**Control N = 35**
Living Things	Mean Total No. (SD)	11.44 (6.4)**	14.00 (7.5)**	20.26 (7.1)
	Errors – Perseverative (SD)	.11 (.33)	.31 (.66)	.29 (.67)
	Errors – Inappropriate (SD)	.11 (.33)*	.59 (.98)***	.00 (.00)
Fruit/Vegetables	Mean Total No. (SD)	10.78 (6.4)***	13.69 (6.2)***	20.49 (5.5)
	Errors – Perseverative (SD)	.44 (.88)	.38 (.73)	.34 (1.1)
	Errors – Inappropriate (SD)	.11 (.33)	.17 (.38)*	.00 (.00)

* = p<0.05, ** = p<0.01, *** = p<0.001.

4.6.1.3 Word Fluency Summary and Discussion

In terms of the number of words generated, a severe Frontal deficit was found for both phonemic and semantic fluency. This severe Frontal deficit confirms the sensitivity of the generative aspect of word fluency tests to frontal lesions. However, this deficit was not selective as the Posterior patients were also impaired. A mild Posterior deficit was found for phonemic fluency and a severe Posterior deficit was found for semantic fluency (fruit/vegetables only). Although the Posteriors generated fewer words than Controls for Living Things this failed to reach significance. For phonemic fluency, this finding is not in keeping with numerous studies that reported selective frontal deficits (e.g., Milner, 1964; Perret, 1974); however, the current findings are consistent with studies that report impairments in both frontal and posterior patients (Stuss et al., 1998; Vilkki et al., 1994). Of note, the severity of phonemic fluency deficit differed in that Frontal patients were severely impaired whilst Posterior patients were only mildly impaired. For semantic fluency, the Posterior deficit is consistent with the literature for patients with temporal lesions (e.g., Loring et

[15] Bonferroni correction was applied to this category given the insignificant Level 1 result. This means that the LIFG inappropriate error total is not significant, despite it reaching significance for living things.

al., 1994) and temporal pathology (e.g., Hodges et al., 1992). Why are Posterior patients impaired on word fluency tasks? These tasks are known to be demanding as they involve both generation and word retrieval. Is it possible that mild naming difficulties underpin a word fluency deficit? In terms of nominal ability, the Language Baseline did not reveal a Posterior deficit (4.4.1.3).

On the phonemic task, a selective Left Frontal deficit was evident. Using the fine-grained lesion method, the most severe frontal deficit was found in the Left Lateral group. In addition, moderate Superior and Inferior Medial deficits were documented. On the semantic tasks, there was no left/right lateralisation and all Frontal subgroups showed mild-moderate deficits. The left inferior frontal damage analysis (LIFG vs. Non-LIFG vs. Control) revealed both patients groups were impaired for phonemic and semantic fluency. However, the LIFG patients generated significantly fewer words than Non-LIFG patients <u>only</u> on the phonemic task. Indeed, the LIFG patients generated fewer words than the severely impaired Left Lateral group and approximately half the number generated by the moderately impaired Superior Medial group. This suggests the LIFG is critically involved in phonemic but not semantic fluency and this may be for reasons other than a primary generation deficit. Is it possible that phonemic fluency is reduced because of a failure of selection within a language system? This would mean that phonemic fluency involves more conflict and thus would require selection more than other fluency tasks. In fact, this was suggested by Perret (1974) who specifically argued that phonemic fluency involved conflict between generating words according to initial letter and the automatic use of words according to meaning, whereas this was not the case in semantic fluency.

The selective Left Frontal deficit for phonemic fluency is in keeping with the early studies of Milner (1964) and Benton (1968) that suggested left lateralisation for the phonemic task, although some recent studies have only found a frontal (not lateralised) deficit (e.g., Rogers et al., 1998). The fine-grained findings of severe Left Lateral and moderate Medial (Superior and Inferior) deficits for phonemic fluency corroborate the Left Lateral and Superior Medial phonemic fluency deficits reported by Stuss et al (1998). However, the moderate Inferior Medial deficit also found in this study for phonemic fluency was not evident in the Stuss study. For semantic fluency, the deficit found in all frontal subgroups (i.e., Left Lateral, Right Lateral, Superior Medial, Inferior Medial) is consistent with the fine-grained frontal findings reported by Stuss et al (1998).

PET and fMRI studies have consistently reported increased left dorsolateral prefrontal activation for word generation tasks (Amunts et al., 2004; e.g., Frith et al., 1991b; Klein et al., 1997; Phelps et al., 1997; Warburton et al., 1996). This is consistent with the Left Lateral deficit revealed for both word fluency tasks. The severe semantic fluency impairment found in patients with posterior lesions is consistent with imaging data that associated this task with left inferolateral temporal activation (Mummery et al., 1996). Imaging studies that compare levels of activity fail to reveal less severe deficits, such as the mild Medial and Right Lateral deficits for semantic fluency and the mild posterior deficit for phonemic fluency. The discrepancy between findings highlights the need for lesion studies in identifying all regions involved in a task and not just the region of greatest activity.

For inappropriate errors, a severe Frontal and mild Posterior deficit was found for phonemic and semantic fluency (living things only). All frontal subgroups produced more inappropriate errors on both fluency tasks, except for the Inferior Medials on the phonemic task. This differs from the Stuss findings (1998) that suggested a specific Left Lateral deficit for errors. Perseverative errors were not prevalent in any patient group on either word fluency task. The absence of perseverative errors on word fluency tasks is dissimilar to the performance of the dynamic aphasic KAS (Chapter 3), but similar to the dynamic aphasics CH (Chapter 2) and ANG (Robinson et al., 1998).

4.6.2 Design Fluency

The design fluency tasks were based on Jones-Gotman and Milner (1977). Subjects were asked to generate as many drawings as possible under two conditions: *Free* – 5 minutes to complete drawings that neither represented real objects nor were derived from such objects; and *Fixed* – 4 minutes to do a similar task as in the free condition, except that each drawing had to consist of four lines, straight or curved. The standard instructions were given. Subjects were provided with a pencil and as many A4 sheets of blank paper as was required. The total number of responses generated, excluding errors, was recorded. Errors included perseverative responses (i.e. a repeat or partial repeat of a previous response) and inappropriate responses (i.e. if it clearly broke the rules given). Thus, drawings that could be recognised were scored as errors (e.g., letters or objects in the free condition and roman numerals in the fixed condition).

4.6.2.1 Free Condition

Level 1 Analysis

One-way ANOVA revealed that the Frontal, Posterior and Control groups differed significantly in the number of designs generated ($F_{(2,85)} = 13.481$, $p<0.001$; see Table 35a). Pairwise comparisons found that Frontals generated significantly fewer designs than Controls ($p<0.001$) and Posteriors ($p = 0.008$). The difference between groups for perseverative and inappropriate errors did not reach significance (See Table 35a and Appendix 6 refs 1.5 and 1.6).

Level 2 Analysis

Although Right Frontals generated fewer designs in the free condition than Left Frontals, this just failed to reach significance using univariate ANCOVA ($p = 0.086$). No difference was found for perseverative errors (See Table 35a and Appendix 6 refs 2.9 and 2.10). Univariate ANCOVA, however, revealed that Right Frontals produced more inappropriate errors than Left Frontals ($F_{(1,29)} = 8.326$, $p = 0.007$).

Table 35a. *Design Fluency: Mean Number and Standard Deviation (SD) of Total Drawings Generated, Perseverative Errors and Inappropriate Errors*

Level 1 Analysis		**Frontal N = 38**	**Posterior N = 15**	**Control N = 35**
Free	Mean Total No. (SD)	8.1 (7.2)***	14.8 (10.2)	17.9 (8.3)
	Errors – Perseverative (SD)	1.71 (4.4)	1.60 (3.3)	2.26 (8.6)
	Errors – Inappropriate (SD)	1.37 (2.3)	3.27 (11.3)	1.40 (3.8)
Fixed	Mean Total No. (SD)	11.1 (8.3)*	17.9 (8.8)	21.3 (8.7)
	Errors – Perseverative (SD)	1.63 (3.0)	1.47 (2.1)	1.49 (2.5)
	Errors – Inappropriate (SD)	2.08 (2.5)	2.67 (2.1)	2.40 (2.3)

Level 2 Analysis		**Left Frontal N = 15**	**Right Frontal N = 17**
Free	Mean Total No. (SD)	10.0 (6.9)	5.5 (5.6)
	Errors – Perseverative (SD)	0.93 (2.0)	2.12 (6.0)
	Errors – Inappropriate (SD)	0.47 (1.1)	2.35 (2.8)**
Fixed	Mean Total No. (SD)	16.2 (8.5)	7.4 (5.4)**
	Errors – Perseverative (SD)	2.00 (3.8)	1.47 (2.3)
	Errors – Inappropriate (SD)	1.53 (2.3)	2.94 (2.7)

** = p<0.01.

Level 3 Analysis

One-way ANOVA revealed significant fine-grained frontal effects for the number generated ($F_{(4,56)} = 5.268$, $p = 0.001$; see Table 35b). Pairwise comparisons found that all frontal subgroups, except the Left Laterals, generated significantly fewer designs than Controls (Right Laterals: $p = 0.002$; Superior Medials: $p = 0.003$; Inferior Medials: $p = 0.020$).

Level 4 Analysis

One-way ANOVA revealed a significant difference between the LIFG, Non-LIFG and Control groups for number generated ($F_{(2,69)} = 13.988$, $p<0.001$; see Table 35c). Pairwise comparisons found that LIFG and Non-LIFG frontals generated fewer designs in the free condition than Controls ($p = 0.002$ and $p<0.001$). The difference between groups did not reach significance for perseverative or inappropriate errors (See Table 35c and Appendix 6 refs 4.4 and 4.5).

4.6.2.2 Fixed Condition

Level 1 Analysis

A significant difference in the number of designs generated by the Frontal, Posterior and Control groups was found ($F_{(2,85)} = 13.261$, $p<0.001$; see Table 35a). Pairwise comparisons revealed that Frontals generated significantly fewer designs in the fixed condition than Controls ($p<0.001$) and Posteriors ($p = 0.011$). There was no difference between groups for perseverative or inappropriate errors, using one-way ANOVA (See Table 35a and Appendix 6 refs 1.7 and 1.8).

Level 2 Analysis

Right Frontals generated significantly fewer designs than Left Frontals, as revealed by univariate ANCOVA ($F_{(1,29)} = 8.874$, $p = 0.006$; see Table 35a). For perseverative and inappropriate errors, there was no difference between groups (See Table 35a and Appendix 6 refs 2.11 and 2.12).

Level 3 Analysis

A significant frontal effect was found for the number of designs generated in the fixed condition, using one-way ANOVA ($F_{(4,56)} = 5.326$, $p = 0.001$; see Table 35b). Pairwise comparisons revealed that the Right Laterals and Inferior Medials generated significantly fewer designs than Controls ($p<0.001$ and $p = 0.014$, respectively).

Table 35b. *Design Fluency: Mean Number and Standard Deviation (SD) of Total Drawings Generated, Perseverative Errors and Inappropriate Errors*

Level 3 Analysis		**Left Lateral N = 7**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 5**	**Control N = 35**
Free	Mean Total No.	11.0	6.3**	8.0**	8.6*	17.9
	(SD)	(9.7)	(7.5)	(4.8)	(8.7)	(8.3)
Fixed	Mean Total No.	14.9	6.7***	13.8	10.8*	21.3
	(SD)	(8.5)	(6.5)	(9.4)	(9.2)	(8.7)

* = p<0.05, ** = p<0.01, *** = p<0.001.

Level 4 Analysis

A significant difference in the number of designs generated by the LIFG, Non-LIFG and Control groups was found ($F_{(2,69)}$ = 12.709, p<0.001; see Table 35c). Pairwise comparisons revealed that LIFG and Non-LIFG frontals generated significantly fewer designs than Controls (p = 0.011 and p<0.001). There was no difference between groups for perseverative or inappropriate errors (See Table 35c and Appendix 6 refs 4.6 and 4.7).

Table 35c. *Design Fluency: Mean Number and Standard Deviation (SD) of Total Drawings Generated, Perseverative Errors and Inappropriate Errors*

Level 4 Analysis		**LIFG N = 8**	**Non-LIFG N = 29**	**Control N = 35**
Free	Mean Total No. (SD)	8.13 (7.1)**	8.10 (7.4)***	17.9 (8.3)
	Errors – Perseverative (SD)	1.75 (2.7)	1.76 (4.9)	2.26 (8.6)
	Errors – Inappropriate (SD)	1.13 (1.9)	1.48 (2.5)	1.40 (3.8)
Fixed	Mean Total No. (SD)	12.50 (8.3)*	10.76 (8.5)***	21.3 (8.7)
	Errors – Perseverative (SD)	2.88 (5.2)	1.28 (2.1)	1.49 (2.5)
	Errors – Inappropriate (SD)	0.75 (1.4)	2.52 (2.6)	2.40 (2.3)

* = p<0.05, ** = p<0.01, *** = p<0.001.

4.6.2.3 Design Fluency Summary and Discussion

The findings show a severe and selective Frontal deficit for design fluency. Further, a selective Right Frontal deficit was revealed in the fixed condition and a trend for the same in the free condition. Specifically, moderate-severe Right Lateral and mild Inferior Medial deficits were revealed for number of designs generated in both conditions. An additional moderate Superior Medial deficit was found but only in the free condition. Of note, there was no Left Lateral deficit on any measure, although the number generated is slightly below Controls.

Only the Right Frontal group produced a significant number of inappropriate errors (free condition). Perseverative errors were not prevalent in any patient group on either task. The absence of perseverative errors on design fluency tasks is dissimilar to the performance of the dynamic aphasic KAS (Chapter 3), but similar to the dynamic aphasic CH (Chapter 2).

The right lateralisation for design fluency (number generated and errors) is in keeping with the original Jones-Gotman and Milner (1977) findings and the results reported by Ruff and colleagues (Ruff et al., 1994) based on a slightly different design fluency task. By contrast, this finding is inconsistent with several studies that failed to find a selective right frontal deficit on a range of design fluency tasks (e.g., Baldo et al., 2001; Tucha et al., 1999). There has been one imaging study of design fluency that showed increased bilateral prefrontal activation (Elfgren et al., 1998). This is only consistent with Right Lateral and Medial (Superior and Inferior) deficits and not the absence of a Left Lateral deficit.

4.6.3 Ideational Fluency

This task is based on the Uses of Objects Test (or Alternate Uses Test) and has been reported to assess cognitive flexibility or creativity (Turner, 1999; Lezak et al., 2004). Turner (1999) has argued that ideational fluency taps the ability to generate new and imaginative responses, in addition to the ability to access stored knowledge. Subjects were asked to generate possible uses of two objects (Brick, Table Knife) under 2 conditions: *Conventional Uses* (e.g., build a house, butter bread); and *Unconventional Uses* (e.g., paperweight, open letters). A time limit of 90 seconds was given for each object in each condition. The total number of correct responses generated, perseverative responses (complete or partial) and inappropriate (or incorrect) responses were recorded. For both conditions, the responses from the two objects were analysed together.

4.6.3.1 Conventional Uses

Level 1 Analysis

The number of conventional uses generated by the Frontal, Posterior and Control groups differed significantly ($F_{(2,85)}$ = 12.144, p<0.001; see Table 36a). Pairwise comparisons found that Frontals and Posteriors generated significantly fewer uses than Controls (p =0.000 and p = 0.001, respectively). One-way ANOVA revealed a significance difference between groups for perseverative errors ($F_{(2,85)}$ = 4.861, p = 0.001). Levene's test of homogeneity of error variances was significant ($F_{(2,85)}$ = 20.781, p<0.001), thus, a Kruskal-Wallis Test was used to confirm the significant difference ($\chi^2_{(2)}$ = 10.191, p = 0.006). Pairwise Mann-Whitney U comparisons found that Frontals made more perseverative errors than Controls (U = 472.000, p = 0.001). The difference between groups for inappropriate errors did not reach significance (See Table 36a and Appendix 6 ref 1.9).

Table 36a. *Ideational Fluency: Mean Number and Standard Deviation (SD) of Total Uses Generated, Perseverative Errors and Inappropriate Errors*

Level 1 Analysis		**Frontal N = 38**	**Posterior N = 15**	**Control N = 35**
Conventional Uses	Mean Total No. (SD)	9.37 (4.9)***	9.67 (4.2)**	15.23 (6.3)
	Errors – Perseverative (SD)	.50 (.89)**	.27 (.59)	.03 (.17)
	Errors – Inappropriate (SD)	1.55 (2.3)	2.13 (2.6)	3.34 (4.3)
Unconventional Uses	Mean Total No. (SD)	6.21 (4.3)***	10.67 (6.4)	13.66 (4.8)
	Errors – Perseverative (SD)	.16 (.50)	.27 (.59)	.06 (.24)
	Errors – Inappropriate (SD)	.89 (1.66)	.40 (.51)	.71 (1.55)

Level 2 Analysis		**Left Frontal N = 15**	**Right Frontal N = 17**
Conventional Uses	Mean Total No. (SD)	9.53 (4.4)	10.29 (4.6)
	Errors – Perseverative (SD)	.40 (.83)	.65 (1.06)
	Errors – Inappropriate (SD)	1.33 (1.68)	1.88 (2.96)
Unconventional Uses	Mean Total No. (SD)	6.20 (4.3)	6.47 (3.9)
	Errors – Perseverative (SD)	.07 (.26)	.12 (.49)
	Errors – Inappropriate (SD)	.40 (.63)	1.47 (2.3)

** = p<0.01, *** = p<0.001.

Level 2 Analysis

There was no difference between the Left and Right Frontal groups for number generated, perseverative errors, or inappropriate errors, using univariate ANCOVA (See Table 36a and Appendix 6 refs 2.13 – 2.15).

Level 3 Analysis

One-way ANOVA revealed significant fine-grained frontal effects for number generated ($F_{(4,55)} = 2.816$, $p = 0.034$; see Table 36b). Pairwise comparisons found that Inferior Medials generated significantly fewer conventional uses than Controls ($p = 0.008$). Although a significance difference between groups for perseverative errors was found ($F_{(4,55)} = 6.482$, $p<0.001$), Levene's test was significant ($F_{(4,55)} = 10.424$, $p<0.001$). Subsequent Kruskal-Wallis Test confirmed the difference between groups was significant ($\chi^2_{(4)} = 20.774$, $p<0.001$). Right Laterals and Inferior Medials produced more perseverative errors than Controls, as revealed by pairwise Mann-Whitney U comparisons ($U = 55.000$, $p<0.001$ and $U = 37.000$, $p<0.001$, respectively).

Table 36b. *Ideational Fluency: Mean Number and Standard Deviation (SD) of Total Uses Generated, Perseverative Errors and Inappropriate Errors*

Level 3 Analysis	**Left Lateral N = 6**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 5**	**Control N = 35**
Conventional Uses					
Mean Total No.	13.17	11.17	10.88	7.80**	15.23
(SD)	(4.3)	(5.0)	(3.4)	(4.9)	(6.3)
Errors – Perseverative	.00	.83***	.13	1.00***	.03
(SD)	(.00)	(1.17)	(.35)	(1.23)	(.17)
Unconventional Uses					
Mean Total No.	8.67*	7.17**	6.63***	5.60***	13.66
(SD)	(4.6)	(3.9)	(4.6)	(3.3)	(4.8)

* = p<0.05, ** = p<0.01, *** = p<0.001.

Level 4 Analysis

There was a significant difference in the number of conventional uses generated between the LIFG, Non-LIFG and Control groups, using one-way ANOVA ($F_{(2,69)}$ = 9.844, p<0.001; see Table 36c). Pairwise comparisons found that the LIFG and Non-LIFG groups generated significantly fewer uses than Controls (p = 0.001 and p<0.001). One-way ANOVA revealed a significant difference between groups for perseverative errors ($F_{(2,69)}$ = 5.196, p = 0.008). As Levene's test found the error variances to be unequal ($F_{(2,69)}$ = 19.492, p<0.001), Kruskal-Wallis Test was used to confirm the difference ($\chi^2_{(2)}$ = 11.662, p = 0.003). Pairwise Mann-Whitney U comparisons found that the LIFG and Non-LIFG groups made more perseverative errors than Controls (U = 91.500, p<0.001 and U = 362.500, p = 0.004). There was no difference between groups for inappropriate errors ($F_{(2,69)}$ = 2.373, p = 0.101), although Levene's test found the error variances to be unequal ($F_{(2,70)}$ = 3.631, p = 0.032). A Kruskal-Wallis Test was used to confirm there was no difference (See Table 36c and Appendix 6 ref 4.8).

4.6.3.2 Unconventional Uses

Level 1 Analysis

There was a significant difference between the Frontal, Posterior and Control groups in the number of unconventional uses generated, as revealed by one-way ANOVA ($F_{(2,85)}$ = 21.616, p<0.001; see Table 36a). Pairwise comparisons found that Frontals generated significantly fewer uses than Controls (p<0.001) and Posteriors (p = 0.003). There was no difference between groups for perseverative or inappropriate errors (See Table 36a and Appendix 6 refs 1.10 and 1.11).

Level 2 Analysis

There was no difference between Left and Right Frontal groups for number generated, perseverative errors and inappropriate errors. However, age was a significant covariate for perseverative errors (See Table 36a and Appendix 6 refs 2.16 - 2.18).

Level 3 Analysis

One-way ANOVA revealed a significant fine-grained frontal effect for the number of unconventional uses generated ($F_{(4,55)}$ = 8.042, p<0.001; see Table 36b). Pairwise comparisons found that all Frontal groups generated significantly fewer uses than Controls (Left Laterals: p = 0.016; Right Laterals: p = 0.002; Superior Medials: p<0.001; Inferior Medials: p<0.001).

Level 4 Analysis

One-way ANOVA revealed a significant difference between the LIFG, Non-LIFG and Control groups for unconventional uses generated ($F_{(2,69)} = 24.213$, p<0.001; see Table 36c). Pairwise comparisons found that the LIFG and Non-LIFG groups generated fewer than Controls (p<0.001 for both). There was no difference between groups for perseverative or inappropriate errors (See Table 36c and Appendix 6 ref 4.9 and 4.10).

Table 36c. *Ideational Fluency: Mean Number and Standard Deviation (SD) of Total Uses Generated, Perseverative Errors and Inappropriate Errors*

Level 4 Analysis		**LIFG N = 9**	**Non-LIFG N = 28**	**Control N = 35**
Conventional Uses	Mean Total No. (SD)	8.11 (4.8)**	9.86 (5.0)***	15.23 (6.3)
	Errors – Perseverative (SD)	.67 (1.00)***	.46 (.88)**	.03 (.17)
	Errors – Inappropriate (SD)	1.22 (1.5)	1.71 (2.5)	3.34 (4.3)
Unconventional Uses	Mean Total No. (SD)	5.22 (5.0)***	6.57 (4.1)***	13.66 (4.8)
	Errors – Perseverative (SD)	.11 (.33)	.18 (.55)	.06 (.24)
	Errors – Inappropriate (SD)	.67 (.87)	1.0 (1.87)	.71 (1.55)

** = p<0.01, *** = p<0.001.

4.6.3.3 Ideational Fluency Condition by Level 1 Patient Group Interaction

A two-way mixed model ANOVA with Group (Frontal or Posterior) as the between-subjects factor and Task Type (Conventional or Unconventional) as the within-subjects factor revealed that only a Task x Group interaction was significant ($F_{(1,51)} = 9.626$, p = 0.003; see Figure 4). Thus, the Frontal patients performed significantly worse than the Posterior patients only when required to generate unconventional uses of objects.

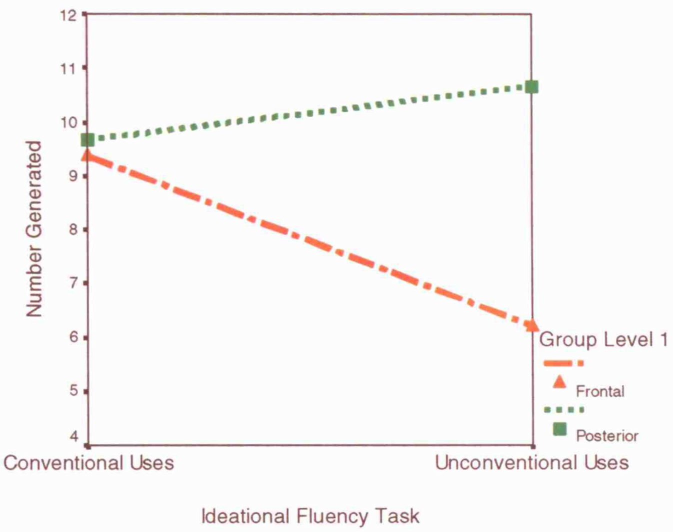

Figure 4. Ideational Fluency: Mean Number of Conventional and Unconventional Uses Generated by Frontal and Posterior Patients

4.6.3.4 Ideational Fluency Summary and Discussion

A severe Frontal and moderate Posterior deficit was found when generating conventional uses of objects. There was a significant interaction between patient group and condition. Thus, both Frontals and Posteriors were impaired for conventional uses but only Frontals were impaired for unconventional uses, the condition with the greater novelty demands (Turner, 1999).

Within the frontal group, only the Inferior Medials were moderately impaired in generating conventional uses of objects. By contrast, when generating unconventional uses of objects, all frontal subgroups were impaired. Specifically, severe Inferior Medial, moderate Superior Medial and Right Lateral, and mild Left Lateral deficits were revealed.

The severe Frontal deficit, without left/right lateralisation, in generating unconventional uses of objects is broadly consistent with previous lesion findings. Eslinger and Gratton (1993) found patients with focal frontal lesions generated fewer unconventional uses of objects, compared to controls and patients with both posterior and basal ganglia lesions. However, this deficit has been documented in one patient with a focal left basal ganglia lesion (Troyer, Black, Armilio, & Moscovitch, 2004). Nevertheless, compared to previous studies, the current study more precisely specifies the frontal regions involved in ideational fluency.

A significant number of perseverative errors were produced by the Right Lateral and Inferior Medial groups only when generating conventional uses. No deficits for inappropriate errors were found. It is noteworthy that Controls and Posteriors produced several inappropriate errors, particularly for conventional uses.

Ideational fluency has been associated with the superior frontal regions in one imaging study, although no distinction was made between conventional and unconventional uses (Carlsson et al., 2000). This does not fit easily with the lesion study that revealed a differential effect for these two tasks in that all Lateral and Medial frontal subgroups, and not just Superior Medial patients, were impaired in generating unconventional uses. Nevertheless, similar to the word fluency imaging data, the convergence between imaging and lesion data is only for the severest lesion deficit.

4.6.4 Gesture Fluency

The gesture fluency tests are based on Jason (1985) who investigated the ability to generate both novel finger positions and meaningful gestures in patients with frontal lesions. Subjects were asked to generate as many movements as possible with the upper limbs in 2 minutes under two conditions: *Meaningless Movements*; and *Meaningful Movements*. The instructions outlined by Jason were used. A video camera recorded responses to aid scoring. The total number of correct responses generated, perseverative responses and inappropriate responses were recorded.

4.6.4.1 Meaningless Movements

Level 1 Analysis

One-way ANOVA revealed a significant difference between the Frontal, Posterior and Control groups for number of meaningless movements generated ($F_{(2,84)} = 7.373$, $p = 0.001$; see Table 37a). Pairwise comparisons found that Frontals generated significantly fewer than Controls ($p<0.001$). There was no difference between the Frontal, Posterior and Control groups for perseverative and inappropriate errors (See Table 37a and Appendix 6 refs 1.12 and 1.13).

Level 2 Analysis

There was no difference between the Left and Right Frontals for number generated, perseverative errors and inappropriate errors (See Table 37a and Appendix 6 refs 2.19 – 2.21).

Table 37a. *Gesture Fluency: Mean Number and Standard Deviation (SD) of Total Gestures Generated, Perseverative Errors and Inappropriate Errors*

Level 1 Analysis		**Frontal N = 37**	**Posterior N = 15**	**Control N = 35**
Meaningless Movements	Mean Total No. (SD)	11.3 (7.2)***	13.3 (5.5)	17.9 (8.2)
	Errors – Perseverative (SD)	1.7 (2.5)	1.7 (1.8)	1.7 (3.1)
	Errors – Inappropriate (SD)	.59 (1.6)	.13 (.35)	.11 (.40)
Meaningful Movements	Mean Total No. (SD)	10.0 (5.1)***	12.5 (4.5)	15.1 (4.7)
	Errors – Perseverative (SD)	.43 (.90)	.40 (.83)	.11 (.32)
	Errors – Inappropriate (SD)	.24 (.64)	.07 (.26)	.03 (.17)

Level 2 Analysis		**Left Frontal N = 15**	**Right Frontal N = 17**
Meaningless Movements	Mean Total No. (SD)	12.5 (7.3)	10.9 (7.2)
	Errors – Perseverative (SD)	2.3 (3.0)	1.2 (1.7)
	Errors – Inappropriate (SD)	.73 (1.6)	.65 (1.8)
Meaningful Movements	Mean Total No. (SD)	10.6 (6.2)	10.6 (3.4)
	Errors – Perseverative (SD)	.20 (.78)	.65 (1.0)*
	Errors – Inappropriate (SD)	.27 (.80)	.18 (.39)

* = p<0.05, *** = p<0.001.

Level 3 Analysis

There was a significant difference between frontal groups in the number generated, using one-way ANOVA ($F_{(4,55)} = 3.244$, p = 0.018; see Table 37b). Pairwise comparisons found that Superior Medials generated fewer meaningless movements than Controls (p = 0.004).

Level 4 Analysis

One-way ANOVA revealed a significant difference between the LIFG, Non-LIFG and Control groups for number generated ($F_{(2,68)} = 6.061$, p = 0.004; see Table 37c). Pairwise comparisons found that LIFG and Non-LIFG frontals generated significantly fewer meaningless movements than Controls (p = 0.047 and p = 0.002). There was no difference between the LIFG, Non-LIFG and Control groups for perseverative and inappropriate errors (See Table 37c and Appendix 6 refs 4.11 and 4.12).

4.6.4.2 Meaningful Movements

Level 1 Analysis

One-way ANOVA revealed a significant difference between the Frontal, Posterior and Control groups for number generated ($F_{(2,84)}$ = 10.146, p<0.001; see Table 37a). The Frontals were shown to generate significantly fewer meaningful movements than Controls using pairwise comparisons (p<0.001). One-way ANOVA's found the difference between groups for perseverative and inappropriate errors did not reach significance (See Table 37a and Appendix 6 refs 1.14 and 1.15).

Level 2 Analysis

The difference between the Left and Right Frontal groups did not reach significance for number generated and inappropriate errors (See Table 37a and Appendix 6 refs 2.22 and 2.23). By contrast, univariate ANCOVA revealed that the Right Frontals made significantly more perseverative errors than the Left Frontals ($F_{(1,29)}$ = 6.482, p = 0.016), with age a significant covariate ($F_{(1,29)}$ = 5.654, p = 0.024).

Level 3 Analysis

One-way ANOVA revealed a significant difference between frontal groups for number of meaningful movements generated ($F_{(4,55)}$ = 3.245, p = 0.018; see Table 37b). Pairwise comparisons found that Superior Medials and Inferior Medials generated fewer meaningful movements than Controls (p = 0.006 and p = 0.021, respectively).

Table 37b. *Gesture Fluency: Mean Number and Standard Deviation (SD) of Total Gestures Generated, Perseverative Errors and Inappropriate Errors*

Level 3 Analysis	**Left Lateral N = 7**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 4**	**Control N = 35**
Meaningless Movements					
Mean Total No. (SD)	12.0 (7.3)	13.7 (8.4)	8.9 (5.1)**	10.5 (4.4)	17.9 (8.2)
Meaningful Movements					
Mean Total No. (SD)	13.0 (7.3)	12.0 (3.2)	9.6 (3.7)**	9.0 (5.6)*	15.1 (4.7)

* = p<0.05, ** = p<0.01.

Level 4 Analysis

One-way ANOVA revealed a significant difference between the LIFG, Non-LIFG and Control groups for number generated ($F_{(2,68)}$ = 9.929, $p<0.001$; see Table 37c). The LIFG and Non-LIFG frontals were shown to generate significantly fewer meaningful movements than Controls (both p = 0.001). There was no difference between groups for perseverative or inappropriate errors (See Table 37c and Appendix 6 refs 4.13 and 4.14).

Table 37c. *Gesture Fluency: Mean Number and Standard Deviation (SD) of Total Gestures Generated, Perseverative Errors and Inappropriate Errors*

Level 4 Analysis	**LIFG N = 8**	**Non-LIFG N = 28**	**Control N = 35**
Meaningless Movements Mean Total No. (SD)	11.75 (8.6)*	11.43 (7.0)**	17.9 (8.2)
Errors – Perseverative (SD)	2.88 (4.1)	1.32 (1.9)	1.7 (3.1)
Errors – Inappropriate (SD)	.63 (.92)	.61 (1.75)	.11 (.40)
Meaningful Movements Mean Total No. (SD)	8.38 (6.4)**	10.64 (4.7)**	15.1 (4.7)
Errors – Perseverative (SD)	.63 (1.19)	.39 (.83)	.11 (.32)
Errors – Inappropriate (SD)	.25 (.71)	.26 (.65)	.03 (.17)

* = p<0.05, ** = p<0.01.

4.6.4.3 Gesture Fluency Summary and Discussion

A severe Frontal deficit without left/right lateralisation was found for both gesture fluency conditions. Specifically, moderate Superior Medial deficits were evident when generating both meaningless and meaningful gestures and a mild Inferior Medial deficit was found only for meaningful gestures. In addition, inappropriate errors in the meaningful movement condition were mildly elevated in the Right Frontals.

With regard to the generative aspect, this finding appears to contradict Jason's (1985) findings of a left frontal deficit for both meaningless and meaningful gesture fleuncy and a right frontal deficit for the meaningful gesture task. However, Jason did specify right frontal lesions as being in the inferior frontal or orbital region. In the current study, orbital lesions fell within the Inferior Medial group. In this respect there is some consistency between the current Inferior Medial deficit and Jason's right frontal deficit for meaningful gestures. However, the Superior Medial deficit is difficult to compare as Jason did not distinguish between medial and lateral lesions. Nevertheless, this study clearly does not implicate Lateral (Left or Right) lesions in gesture fluency. In addition, the dynamic aphasic CH would argue against Left Lateral involvement as he had damage to this region but was intact on this task. For perseverative errors, a selective Right Frontal deficit was found, which is in contrast to the left frontal deficit reported by Jason. Perseverative errors produced by patients with Right Frontal lesions may reflect a monitoring and checking impairment, as recently proposed in patients with Right Lateral lesions (Reverberi et al., 2005b).

Imaging studies have implicated the bilateral dorsolateral prefrontal areas in action generation tasks involving non-verbal material, including tasks that use finger movements (e.g., Frith et al., 1991a). This bilateral dorsolateral activation does not fit with the lesion group study that revealed a selective Superior Medial deficit for gesture fluency and an Inferior Medial deficit for meaningful gesture generation. However, the lesion data are somewhat more in line with a recent fMRI study that associated voluntary action execution with bilateral frontal pole (BA 10) activation, and simultaneous left dorsolateral deactivation (BA 46) (Hunter et al., 2004). This fluency task has been rarely investigated in either lesion or imaging studies and, thus, needs further investigation using comparable tasks.

Table 38. *Fluency Tests: Summary of Deficits for Grouping Levels 1, 2 and 3*

Fluency Task		Deficit for Level of Analysis 1-3		
		1	2	3
Word Fluency				
Phonemic	No. Generated	Frontal Posterior	LF	LL SM IM
	Inappropriate Errors	Frontal Posterior		LL RL SM
Semantic Living Things	No. Generated	Frontal		
	Inappropriate Errors	Frontal Posterior		LL RL SM IM
Fruit/Vegetable	No. Generated	Frontal Posterior		LL RL SM IM
Ideational Fluency				
Conventional	No. Generated	Frontal Posterior		IM
	Perseverative Errors	Frontal		RL IM
Unconventional	No. Generated	Frontal		LL RL SM IM
Design Fluency				
Free	No. Generated	Frontal		RL SM IM
	Inappropriate Errors		RF	
Fixed	No. Generated	Frontal	RF	RL IM
Gesture Fluency				
Meaningless	No. Generated	Frontal		SM
Meaningful	No. Generated	Frontal		SM IM
	Perseverative Errors		RF	

LF = Left Frontal; RF = Right Frontal; LL = Left Lateral; RL = Right Lateral; SM = Superior Medial; IM = Inferior Medial.

4.7 WORD AND SENTENCE LEVEL GENERATION INVESTIGATION

The dynamic aphasia of CH and ANG was accounted for by an inability to select between competing response options, a process thought restricted to the language domain and associated with damage to the LIFG. This battery was designed to investigate the anatomical substrates of the cognitive process involved in generating a single word or sentence. The battery consists of 6 tests: 1- Generation of a Word to Complete a Sentence; 2 - Generation of a Sentence from a Word; 3 - Generation of a Sentence from a Word Pair; 4 - Generation of a Sentence from a Single Picture; 5 - Generation of a Sentence from Pictures Pairs; and 6 - Generation of a Sentence given a Pictorial Scene.

The tests were devised to examine the generation of a single word or sentence when presented with different types of input (verbal: single word, word pair, sentence; pictorial: single picture, picture pair, pictorial scene). In order to investigate the effect of competing response options, stimuli were chosen so that items activated either many response options or a dominant response option. Stimuli that activate many response options include: low constraint sentences (1); high frequency words (2); low inter-word association word pairs (3); pictures of high frequency items (4); and picture pairs of items with low inter-word association (5). By contrast, stimuli that activate a dominant response (or few response options) include: high constraint sentences (1); proper nouns and low frequency words (2); high inter-word association word pairs (3); pictures of proper nouns (4); and picture pairs of items with high inter-word association (5). Of note, Tests 1-3 are based on tests performed by ANG and CH whereas Tests 4 and 5 (i.e., pictorial versions of Tests 2 and 3) have not been performed by dynamic aphasic patients. In addition, this is the first time low frequency words have been used in sentence generation tests.

Number correct and mean response times (RT) for each stimulus type in each test were recorded. RT was defined as the time from the end of stimulus presentation to the time the subject started to generate a response. Mean RT was calculated for correct responses only. Responses were recorded by tape recorder for transcription purposes. Items presented as both verbal and pictorial stimuli were allocated to different testing sessions so that a target stimulus was only presented once within the same session.

4.7.1 Word Generation

4.7.1.1 Generation of a Word to Complete a Sentence

A set of sentence frames with the final word omitted was selected from the Bloom and Fischler (1980) completion norms. The set consisted of: i) 15 high constraint sentences; and ii) 15 low constraint sentences (see Appendix 7). High constraint sentences were chosen to have only 1 or few associated completion words listed, each with a very high probability for being the dominant response produced so that the number of alternative completion words was small (e.g. 'Water and sunshine help plants ...'). By contrast, low constraint sentences were chosen to have many associated alternative completion words that each has a very low probability for being the response produced (e.g. 'There was nothing wrong with the...'). Subjects were presented with the sentence frame and asked to generate an appropriate single word to complete it meaningfully.

4.7.1.1.1 High constraint sentence.

Level 1Analysis

When generating a single word to complete high constraint sentences, there was no difference between the Frontal, Posterior and Control groups (See Table 39a, Figure 5 and Appendix 8 ref 1.1). There was also no difference between groups for RT ($F_{(2,86)}$ = 2.975, p = 0.056), although Levene's test of homogeneity of error variances was significant (F $_{(2,86)}$ = 4.120, p = 0.020). Following logarithm transformation of data, the variances were equal (Levene's Test, p = 0.110). Subsequent one-way ANOVA revealed a significant difference between groups for RT ($F_{(2,86)}$ = 5.159, p = 0.008; see Table 39a). Pairwise comparisons found that Frontals were slower to complete high constraint sentences than Controls (p = 0.002).

Level 2Analysis

Although both Left and Right Frontals performed near ceiling, the difference was significant with Left Frontals completing fewer high constraint sentences, as revealed by univariate ANCOVA ($F_{(1,30)}$ = 5.295, p = 0.029). Age was a significant covariate ($F_{(1,30)}$ = 6.990, p = 0.013; see Table 39a). There was no difference between groups for RT (See Table 39a and Appendix 8 ref 2.1).

Level 3Analysis

One-way ANOVA did not reveal a significant difference between frontal subgroups for number correct ($F_{(4,56)}$ = 2.329, p = 0.067; see Table 39b). However, Levene's test was significant ($F_{(4,56)}$ = 9.843, $p<0.001$). Subsequent Kruskal-Wallis

Test did not find a significant difference between groups and no frontal effects were found for RT (See Appendix 8 ref 3.1 and 3.2).

Table 39a. *Generation of a word to complete a sentence: Mean Number Correct (Max = 15), Response Time (RT) and Standard Deviation (SD)*

Level 1 Analysis		**Frontal N = 39**	**Posterior N = 15**	**Control N = 35**
High Constraint	Mean No. Correct (SD)	14.74 (0.7)	14.73 (0.5)	14.91 (0.3)
	Mean RT (SD)	1.43 (1.9)**	0.79 (0.55)	0.71 (0.4)
Low Constraint	Mean No. Correct (SD)	12.90 (2.7)***	14.07 (1.2)	14.60 (0.9)
	Mean RT (SD)	3.99 (3.2)**	2.22 (0.9)	2.32 (1.3)
Level 2 Analysis		**Left Frontal N = 16**	**Right Frontal N = 17**	
High Constraint	Mean No. Correct (SD)	14.69 (0.8)*	14.88 (0.3)	
	Mean RT (SD)	1.06 (0.8)	1.09 (0.6)	
Low Constraint	Mean No. Correct (SD)	12.50 (1.9)**	14.12 (1.7)	
	Mean RT (SD)	3.72 (3.2)	3.86 (2.3)	

* = p<0.05, ** = p<0.01, *** = p<0.001

Level 4 Analysis

For the number of sentences completed, there was no difference between the LIFG, Non-LIFG and Control groups (See Table 39c, Figure 6 and Appendix 8 ref 4.1). No difference was found between groups for RT ($F_{(2,70)}$ = 2.458, p = 0.093), however, Levene's test showed unequal error variances ($F_{(2,70)}$ = 3.376, p = 0.040). Following logarithm transformation of data, Levene's Test was not significant (p = 0.384). Subsequent one-way ANOVA revealed a significant difference between groups for RT ($F_{(2,70)}$ = 4.712, p = 0.012) with pairwise comparisons showing that the Non-LIFG Frontals were slower to complete high constraint sentences than Controls (p = 0.004).

4.7.1.1.2 Low constraint sentence.

Level 1Analysis

For the number of low constraint sentences completed, one-way ANOVA revealed a significant difference between Frontal, Posterior and Control groups ($F_{(2,86)}$

= 7.386, p = 0.001; see Table 39a). As Levene's test found the error variances were unequal ($F_{(2,86)}$ = 12.958, p<0.001), a Kruskal-Wallis Test was used to confirm the significant difference ($\chi^2_{(2)}$ = 13.186, p = 0.001). Pairwise Mann-Whitney U comparisons found that Frontals completed fewer sentences than Controls (U = 390.500, p<0.001) (See Figure 5). A significant difference was also found between groups for RT ($F_{(2,86)}$ = 6.011, p = 0.004), although Levene's test was significant ($F_{(2,86)}$ = 9.238, p<0.001). Following logarithm transformation of data, Levene's Test was not significant (p = 0.136). Subsequent one-way ANOVA confirmed a significant difference between groups for RT ($F_{(2,86)}$ = 5.656, p = 0.005; see Table 39a). Pairwise comparisons found Frontals were slower than Controls (p = 0.003). Although Frontals were also slower than Posteriors, this failed to reach significance after Bonferroni adjustment (p = 0.019).

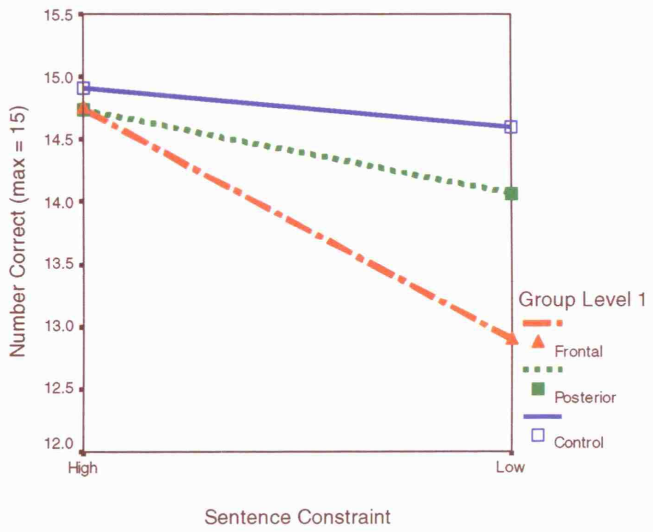

Figure 5. Mean Number of Single Words Generated to Complete High and Low Constraint Sentences by Group (Level 1)

Level 2Analysis

Left Frontals completed fewer low constraint sentences than Right Frontals, as revealed by univariate ANCOVA ($F_{(1,30)}$ = 8.027, p = 0.008; see Table 39a). No difference was found for RT (See Appendix 8 ref 2.2).

Level 3 Analysis

One-way ANOVA revealed a significant difference between frontal subgroups for number correct ($F_{(4,56)} = 4.415$, p = 0.004; see Table 39b), although Levene's test showed unequal error variances ($F_{(4,56)} = 7.381$, p<0.001). Subsequent Kruskal-Wallis Test confirmed the significant difference ($\chi^2_{(4)} = 12.976$, p = 0.011), with pairwise Mann-Whitney U comparisons showing specific Left Lateral and Superior Medial deficits, compared to Controls (U = 50.000, p = 0.003 and U = 70.500, p = 0.008, respectively). No further frontal effects were found for RT (See Appendix 8 ref 3.3).

Table 39b. *Generation of a word to complete a sentence: Mean Number Correct (Max = 15), Response Time (RT) and Standard Deviation (SD)*

Level 3 Analysis	**Left Lateral N = 7**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 5**	**Control N = 35**
High Constraint					
Mean No. Correct (SD)	14.4 (1.1)	15.0 (0.0)	15.0 (0.0)	15.0 (0.0)	14.9 (0.3)
Low Constraint					
Mean No. Correct (SD)	12.7 (1.9)**	14.7 (0.5)	12.6 (2.5)**	12.8 (3.9)	14.6 (0.9)

** = p<0.01

Level 4 Analysis

There was a significant difference between the LIFG, Non-LIFG and Controls groups for the number of low constraint sentences completed ($F_{(2,70)} = 7.055$, p = 0.002; see Table 39c). As Levene's test of homogeneity of error variances was significant ($F_{(2,70)} = 10.787$, p<0.001), a Kruskal-Wallis Test was used to confirm the difference was significant ($\chi^2_{(2)} = 13.577$, p = 0.001). Pairwise Mann-Whitney U comparisons found that LIFG and Non-LIFG Frontals completed fewer sentences than Controls (U = 57.000, p = 0.001 and U = 333.500, p = 0.006, respectively) (See Figure 6). A significant difference between groups was found for RT ($F_{(2,70)} = 4.024$, p = 0.022). Although Levene's test was significant ($F_{(2,70)} = 5.382$, p = 0.007), logarithm transformation of the data equalled the variances (p = 0.232). Subsequent one-way ANOVA confirmed a significant difference between groups for RT ($F_{(2,70)} = 4.861$, p =

0.011; see Table 39c). Pairwise comparisons found that the Non-LIFG Frontals were slower to complete sentences than Controls (p = 0.003).

Table 39c. *Generation of a word to complete a sentence: Mean Number Correct (Max = 15), Response Time (RT) and Standard Deviation (SD)*

Level 4 Analysis		**LIFG N = 9**	**Non-LIFG N = 29**	**Control N = 35**
High constraint	Mean No. Correct (SD)	14.89 (0.3)	14.69 (0.8)	14.91 (0.3)
	Mean RT (SD)	1.26 (1.1)	1.51 (2.2)**	0.71 (0.4)
Low constraint	Mean No. Correct (SD)	12.11 (3.4)**	13.24 (2.4)**	14.60 (0.9)
	Mean RT (SD)	3.45 (3.8)	4.08 (3.0)**	2.32 (1.3)

** = p<0.01.

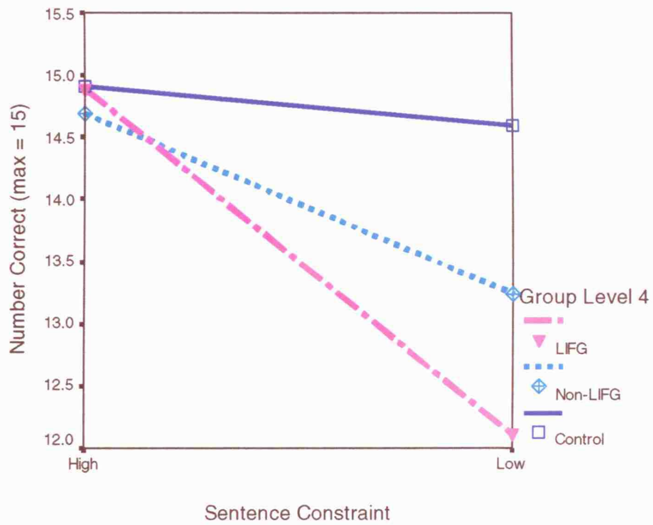

Figure 6. Mean Number of Single Words Generated to Complete High and Low Constraint Sentences by Group (Level 4)

4.7.1.2 Word Generation Interim Summary

When generating a single word to complete a sentence with many alternative completion words (i.e., low constraint), there was a severe and selective Frontal deficit that was left lateralised. No Posterior deficit was evident. More specifically, Left

Lateral and Superior Medial frontal deficits were revealed. The LIFG group was impaired compared to Controls, as was the Non-LIFG group. By contrast, for high constraint sentences with few completion words there was no Frontal deficit or fine-grained frontal effect. Although the Left Frontals were impaired compared to Controls for high constraint sentences, this is likely to reflect the ceiling effect in all subjects, including Left Frontals, and the relatively small standard deviations. For response time, the Frontals were slower to complete all sentences in comparison to Posteriors and Controls, with no specific frontal effects.

4.7.2 Sentence Generation from Verbal Input

4.7.2.1 Generation of a Sentence from a Word

The stimuli consisted of: 15 single proper nouns (e.g., Hitler); 15 high frequency words (e.g., table); and 15 low frequency words (e.g., kite; see Appendix 7). High frequency words have multiple referents and should activate many verbal response options. Low frequency words have less referents than high frequency words and should also activate few or a dominant response. In contrast, proper nouns have a singular or few referents and should strongly activate a single prepotent response. Subjects were randomly presented with the stimuli and asked to produce a meaningful sentence that incorporated the target word.

4.7.2.1.1 Proper noun - word.

Level 1Analysis

For the Proper Nouns, there was no difference between Frontal, Posterior and Control groups for number correctly generated ($F_{(2,86)}$ = 2.396, p = 0.097; see Table 40a and Figure 7). However, Levene's test found the error variances were unequal ($F_{(2,86)}$ = 8.941, p<0.001). Although a Kruskal-Wallis Test did reveal a significant difference between groups ($\chi^2_{(2)}$ = 6.987, p = 0.030), pairwise Mann-Whitney U comparisons found no further effects. There was no difference between groups for RT (See Table 40a and Appendix 8 ref 1.2).

Level 2 Analysis

There was no difference between the Left and Right Frontal groups for Proper Nouns for both number correct and RT (See Table 40a and Appendix 8 refs 2.3 - 2.4).

Level 3Analysis

One-way ANOVA did not reveal further frontal effects for the number correctly generated for Proper Nouns (See Appendix 8 refs 3.4).

Table 40a. *Generation of a sentence from a single word: Mean Number Correct (Max = 15), Response Time (RT) and Standard Deviation (SD)*

Level 1 Analysis		**Frontal N = 39**	**Posterior N = 15**	**Control N = 35**
Proper Nouns	Mean No. Correct (SD)*	14.44 (1.7)	15.00 (.0)	14.97 (0.2)
	Mean RT (SD)	3.77 (5.5)	1.88 (0.9)	2.39 (1.7)
High Frequency	Mean No. Correct (SD)	13.56 (3.5)**	15.00 (.0)	14.94 (.2)
	Mean RT (SD)	4.55 (8.1)	2.59 (1.4)	2.61 (1.6)
Low Frequency	Mean No. Correct (SD)	13.85 (2.7)	15.00 (.00)	14.49 (1.1)
	Mean RT (SD)	4.30 (8.2)	1.87 (0.8)	2.33 (1.5)
Level 2 Analysis		**Left Frontal N = 16**	**Right Frontal N = 17**	
Proper Nouns	Mean No. Correct (SD)	14.81 (0.5)	14.76 (0.6)	
	Mean RT (SD)	3.57 (5.1)	2.49 (1.3)	
High Frequency	Mean No. Correct (SD)	13.81 (2.8)	14.65 (1.0)	
	Mean RT (SD)	3.36 (3.1)	3.56 (2.5)	
Low Frequency	Mean No. Correct (SD)	14.19 (1.5)	14.59 (0.9)	
	Mean RT (SD)	3. 57 (5.6)	2.39 (1.1)	

* = p<0.05, ** = p<0.01.

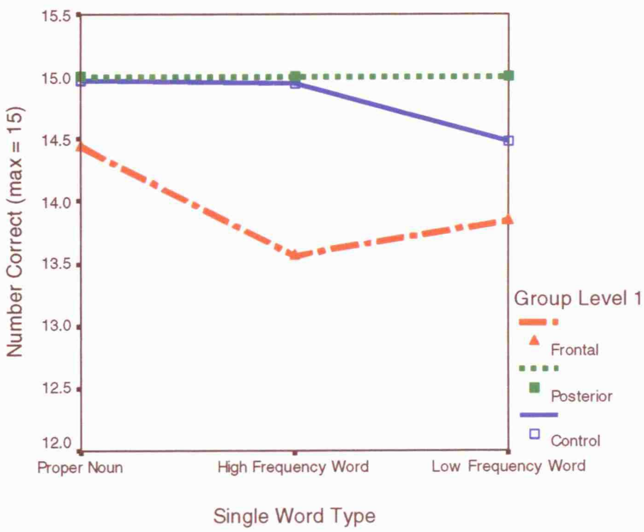

Figure 7. Mean Number of Sentences Generated for Proper Nouns, High Frequency Words and Low Frequency Words by Group (Level 1)

Level 4 Analysis

The LIFG, Non-LIFG and Control groups did not differ significantly for either number correct or RT (See Table 40b, Figure 8 and Appendix 8 refs 4.2 and 4.3).

4.7.2.1.2 High frequency - word.

Level 1Analysis

Although a significant difference was found between Frontal, Posterior and Control groups for number correct ($F_{(2.86)}$ = 3.930, p = 0.023), Levene's test of homogeneity was significant ($F_{(2.86)}$ = 14.183, p<0.001). Subsequent Kruskal-Wallis Test confirmed the significant difference between groups ($\chi^2_{(2)}$ = 10.938, p = 0.004; see Table 40a). Pairwise Mann-Whitney U comparisons found that Frontals generated fewer sentences to High Frequency words than Controls (U = 522.000, p = 0.009), with the lower score than the Posteriors just failing to reach significance after Bonferroni adjustment (p = 0.023) (See Figure 7). There was no difference between groups for RT (See Table 40a and Appendix 8 ref 1.3).

Level 2 Analysis

The difference between Left and Right Frontals for High Frequency words, for number correct and RT, did not reach significance (See Table 40a and Appendix 8 refs 2.5 and 2.6).

Level 3Analysis

One-way ANOVA did not reveal further frontal effects for number correct for High Frequency Words (See Appendix 8 ref 3.5).

Level 4 Analysis

For high frequency words, one-way ANOVA revealed a significant difference between the LIFG, Non-LIFG and Control groups for number of sentences generated ($F_{(2.70)}$ = 3.606, p = 0.032; see Table 40b). As Levene's test found the error variances to be unequal ($F_{(2.70)}$ = 8.836, p<0.001), a Kruskal-Wallis Test was used to confirm the significant difference ($\chi^2_{(2)}$ = 13.370, p = 0.001). Pairwise Mann-Whitney U comparisons found that only the LIFG Frontals generated fewer sentences for High Frequency words than Controls (U = 75.000, p<0.001). The LIFG Frontals also generated fewer sentences than the Non-LIFG Frontals (U = 82.000, p = 0.031) (See Figure 8). There was no difference between groups for RT (See Table 40b and Appendix 8 ref 4.4).

Table 40b. *Generation of a sentence from a single word: Mean Number Correct (Max = 15) Response Time (RT) and Standard Deviation (SD)*

Level 4 Analysis		**LIFG N = 9**	**Non-LIFG N = 29**	**Control N = 35**
Proper Nouns	Mean No. Correct (SD)	14.67 (0.7)	14.34 (2.0)	14.97 (0.2)
	Mean RT (SD)	4.69 (6.7)	3.55 (5.3)	2.39 (1.7)
High Frequency	Mean No. Correct (SD)	12.56 (3.6)***~	13.86 (3.5)	14.94 (.2)
	Mean RT (SD)	3.99 (4.0)	4.81 (9.2)	2.61 (1.6)
Low Frequency	Mean No. Correct (SD)	13.44 (1.8)	13.93 (3.0)	14.49 (1.1)
	Mean RT (SD)	4.61 (7.4)	4.28 (8.6)	2.33 (1.5)

*** = p<0.001 , ~ = compared to both Non-LIFG and Control groups.

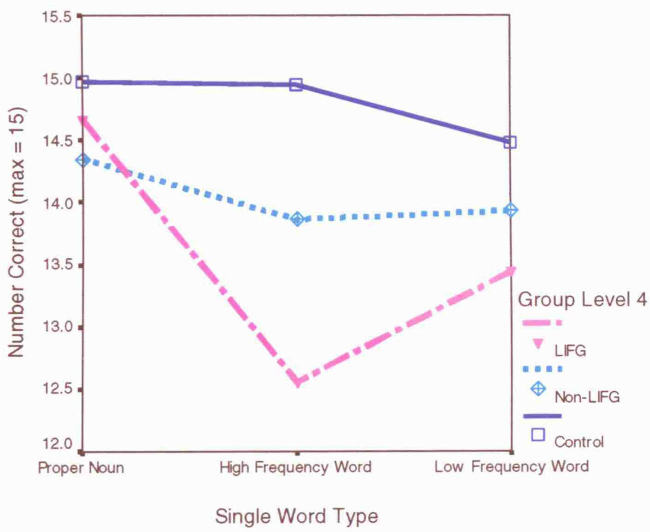

Figure 8. Mean Number of Sentences Generated for Proper Nouns, High Frequency Words and Low Frequency Words by Group (Level 4)

4.7.2.1.3 Low frequency - word.

Level 1Analysis

The Frontal, Posterior and Control groups did not differ for number correct and RT (See Table 40a, Figure 7 and Appendix 8 refs 1.4 and 1.5).

Level 2 Analysis

There was no difference between Left and Right Frontals for Low Frequency Words, for both number correct and RT (See Table 40a and Appendix 8 refs 2.7-2.8).

Level 4 Analysis

The difference between the LIFG, Non-LIFG and Control groups for number correct and RT did not reach significance (See Table 40b, Figure 8 and Appendix 8 refs 4.5-4.6).

4.7.2.2 Generation of a Sentence from a Word Pair

The stimuli were: i) 15 word pairs high in association (e.g., butter-bread); and ii) 15 word pairs low in association (e.g., butter-finger; see Appendix 7). Classifying word pairs as either High or Low in association was based on the Free Associative Norms (Riegal, 1965). Word pairs with high inter-word associations should strongly activate a dominant response in addition to weakly activating other response options. Word pairs with low inter-word associations should activate many competing verbal response options. Subjects were presented with the stimuli in a random order and asked to produce a meaningful sentence that incorporated both targets from the word pair.

4.7.2.2.1 High association word pair.

Level 1Analysis

For the number of sentences generated for word pairs high in association, or the time taken to do this (RT), no difference between Frontal, Posterior and Control groups was found using one-way ANOVA tests (See Table 41a, Figure 9 and Appendix 8 refs 1.6-1.7).

Level 2Analysis

Left and Right Frontal groups did not differ in number correct or RT, although age was a significant covariate for RT (See Table 41a, Figure 10 and Appendix 8 refs 2.9-2.10).

Level 4Analysis

The difference between the LIFG, Non-LIFG and Control groups for number correct and RT did not reach significance using one-way ANOVA tests (See Table 41c and Appendix 8 refs 4.7-4.8).

Table 41a. *Generation of a sentence from a word pair: Mean Number Correct (Max = 15), Response Time (RT) and Standard Deviation (SD)*

Level 1 Analysis		**Frontal N = 39**	**Posterior N = 15**	**Control N = 35**
High Association	Mean No. Correct (SD)	13.41 (4.2)	14.93 (0.3)	14.94 (0.2)
	Mean RT (SD)	3.13 (2.1)	2.15 (1.0)	2.63 (1.8)
Low Association	Mean No. Correct (SD)	12.21 (4.6)***	14.93 (0.3)	14.89 (0.3)
	Mean RT (SD)	5.10 (3.3)	3.20 (1.4)	3.97 (2.7)
Level 2 Analysis		**Left Frontal N = 16**	**Right Frontal N = 17**	
High Association	Mean No. Correct (SD)	13.50 (4.2)	14.59 (0.9)	
	Mean RT (SD)	2.95 (2.1)	3.45 (2.0)	
Low Association	Mean No. Correct (SD)	12.44 (4.7)	13.41 (2.9)	
	Mean RT (SD)	5.26 (4.1)	4.82 (2.1)	

*** = p<0.001

4.7.2.2.2 Low association word pair.

Level 1 Analysis

One-way ANOVA revealed a significant difference between the Frontal, Posterior and Control groups for number correct ($F_{(2,86)}$ = 7.8.357, p<0.001; see Table 41a), although Levene's test showed unequal error variances ($F_{(2,86)}$ = 32.958, p<0.001). A subsequent Kruskal-Wallis Test confirmed the significant difference ($\chi^2_{(2)}$ = 17.242, p<0.001). Pairwise Mann-Whitney U comparisons found that Frontals generated significantly fewer sentences from word pairs low in association than both Controls (U = 419.500, p<0.001) and Posteriors (U = 170.500, p = 0.006) (See Figure 6). The difference between groups for RT just failed to reach significance using one-way ANOVA (See Table 41a, Figure 9 and Appendix 8 ref 1.8).

Level 2 Analysis

There was no difference between the Left and Right Frontal groups for number correct or RT (See Table 41a and Appendix 8 refs 2.11 and 2.12).

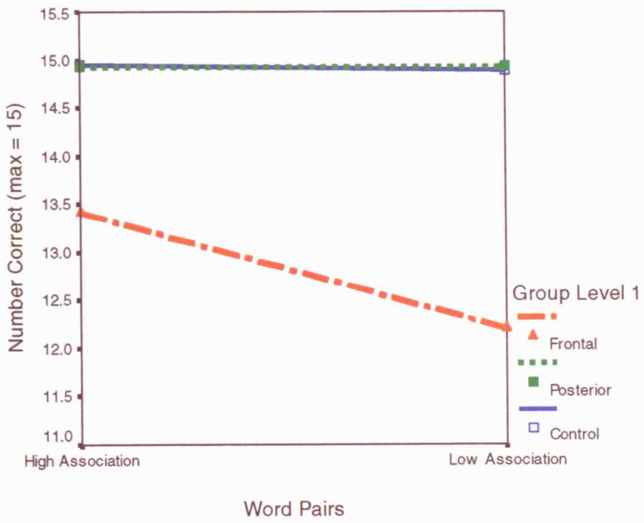

Figure 9. Mean Number of Sentences Generated for Word Pairs High and Low in Association by Group (Level 1)

Level 3Analysis

A significant difference was found between frontal subgroups for number correct ($F_{(4,56)}$ = 3.381, p = 0.015). However, as Levene's test was significant ($F_{(4,56)}$ = 14.868, p<0.001), a Kruskal-Wallis Test was used to confirm the significant difference ($\chi^2_{(2)}$ = 10.467, p = 0.033; see Table 41b). Pairwise Mann-Whitney U comparisons found that the Left Lateral and Superior Medial groups generated fewer sentences than Controls (U = 80.000, p = 0.027 and U = 78.000, p = 0.004, respectively). The difference between the Inferior Medials and Controls did not reach significance (p = 0.075) (See Figure 6).

Table 41b. *Generation of a sentence from a word pair: Mean Number Correct (Max = 15), Response Time (RT) and Standard Deviation (SD)*

Level 3 Analysis	**Left Lateral N = 7**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 5**	**Control N = 35**
High Association Mean No. Correct	13.71	15.00	14.38	12.00	14.94
(SD)	(4.4)	(0.0)	(1.2)	(6.7)	(0.2)
Low Association Mean No. Correct	12.71*	14.83	12.13**	11.80	14.89
(SD)	(4.4)	(0.4)	(3.8)	(6.6)	(0.3)

* = p<0.05, ** = p<0.01.

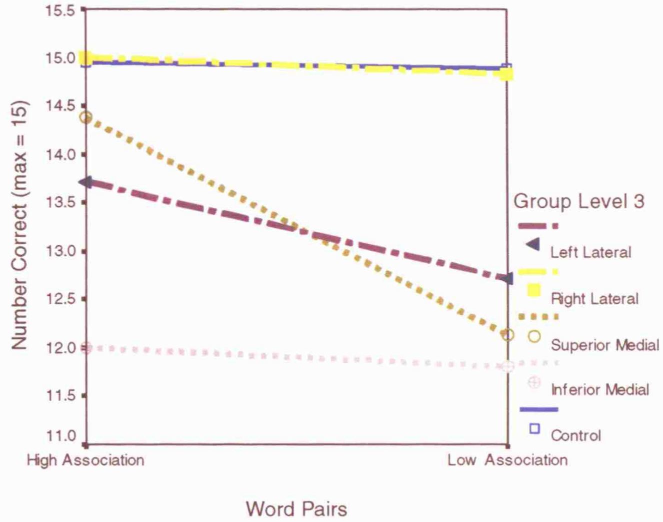

Figure 10. Mean Number of Sentences Generated for Word Pairs High and Low in Association by Group (Level 3)

Level 4Analysis

One-way ANOVA revealed a significant difference between groups for number correct ($F_{(2,70)} = 5.291$, p = 0.007). As Levene's test showed unequal error variances ($F_{(2,70)} = 21.117$, p<0.001), a Kruskal-Wallis Test was used to confirm the significant difference ($\chi^2_{(2)} = 11.548$, p = 0.003; see Table 23c). Pairwise Mann-Whitney U comparisons found that LIFG and Non-LIFG Frontals generated significantly fewer sentences than Controls (U = 101.500, p = 0.015 and U = 318.000, p = 0.001, respectively). The difference between groups for RT just failed to reach significance using one-way ANOVA (See Table 41c and Appendix 8 refs 4.9).

Table 41c. *Generation of a sentence from a word pair: Mean Number Correct (Max = 15), Response Time (RT) and Standard Deviation (SD)*

Level 4 Analysis		**LIFG N = 9**	**Non-LIFG N = 29**	**Control N = 35**
High Association	Mean No. Correct (SD)	13.22 (5.0)	13.41 (4.1)	14.94 (0.2)
	Mean RT (SD)	3.41 (2.6)	3.11 (2.1)	2.63 (1.8)
Low Association	Mean No. Correct (SD)	12.11 (5.4)*	12.38 (4.5)**	14.89 (0.3)
	Mean RT (SD)	6.58 (5.7)	4.80 (2.3)	3.97 (2.7)

* = p<0.05, ** = p<0.01.

4.7.2.3 Sentence Generation Interim Summary (Verbal Input)

When generating a sentence from a single word, the Frontal group as a whole were moderately impaired for high frequency words compared to both Posterior patients and Controls. More specifically, only patients with LIFG damage were severely impaired. Moreover, the LIFG patients group were impaired compared to both Controls and patients without LIFG damage (i.e., Non-LIFG). Thus, for stimuli that activate many response options (i.e., high frequency words) a selective and severe LIFG impairment was found. By contrast, Frontal patients were intact when generating a sentence from stimuli that activates a dominant response option (i.e., Proper Nouns, low frequency words).

For word pairs, a selective Frontal impairment was found when generating a sentence only for word pairs that activate many response options (i.e., low association). Specific Left Lateral and Superior Medial deficits were revealed with Inferior Medials performing poorly although not significantly so. By contrast, no frontal impairments were found when generating a sentence from word pairs that activate a dominant response option (i.e., high association).

4.7.3 Sentence Generation from Pictorial Input

4.7.3.1 Generation of a Sentence from a Single Picture

The stimuli were a subset of those used in 4.7.2.1 and consisted of: 8 pictures of a single proper noun; and 8 pictures of a high frequency word (see Appendix 7). Subjects were randomly presented with each picture and asked to produce a meaningful sentence that included the target picture.

4.7.3.1.1 Proper noun- picture.

Level 1 Analysis

The difference between Frontal, Posterior and Control groups for number of sentences generated did not reach significance using one-way ANOVA ($F_{(2,85)} = 2.824$, $p = 0.065$; see Table 42a). As Levene's test of homogeneity of error variances was significant ($F_{(2,85)} = 7.967$, $p = 0.001$), a Kruskal-Wallis Test revealed a significant difference between groups ($\chi^2_{(2)} = 6.704$, $p = 0.035$). Pairwise Mann-Whitney U comparisons found a trend for Frontals to generate fewer sentences than Controls although this failed to reach significance after Bonferroni adjustment ($U = 526.000$, $p = 0.025$). Analysis of the RT differences did not reveal significant effects (See Table 42a and Appendix 8 ref 1.9).

Level 2 Analysis

There was no difference between the Left and Right Frontal groups for number correct or RT (See Table 42a and Appendix 8 refs 2.13 - 2.14).

Level 3Analysis

For number correct, no difference was found between frontal subgroups using one-way ANOVA ($F_{(4,56)} = 1.209$, $p = 0.317$). As Levene's test showed unequal error variances ($F_{(4,56)} = 4.970$, $p = 0.002$), a Kruskal-Wallis Test was used and confirmed there was no difference (See Appendix 8 ref 3.6).

Level 4 Analysis

For Proper Nouns, the difference between the number of sentences generated by the LIFG, Non-LIFG and Control groups just failed to reach significance using one-way ANOVA ($F_{(2,69)} = 2.557$, $p = 0.085$; see Table 42b). Levene's test was significant ($F_{(2,69)} = 7.053$, $p = 0.002$) and subsequent Kruskal-Wallis Test just failed to reach significance (See Appendix 8 ref 4.10). The RT differences did not reach significance (See Table 42b and Appendix 8 ref 4.11).

Table 42a. *Generation of a sentence from a single picture: Mean Number Correct (Max = 8), Response Time (RT) and Standard Deviation (SD)*

Level 1 Analysis		**Frontal N = 38**	**Posterior N = 15**	**Control N = 35**
Proper Nouns	Mean No. Correct (SD)*	7.32 (1.6)	7.87 (0.5)	7.89 (0.4)
	Mean RT (SD)	3.99 (2.3)	2.75 (1.3)	4.52 (4.4)
High Frequency Words	Mean No. Correct (SD)	7.16 (1.8)**	7.80 (0.6)	7.91 (0.4)
	Mean RT (SD)	4.65 (2.6)	2.89 (0.9)	4.50 (3.0)
Level 2 Analysis		**Left Frontal N = 16**	**Right Frontal N = 16**	
Proper Nouns	Mean No. Correct (SD)	7.63 (1.3)	7.63 (0.7)	
	Mean RT (SD)	3.77 (1.8)	4.15 (2.2)	
High Frequency Words	Mean No. Correct (SD)	7.44 (1.1)	7.94 (0.3)	
	Mean RT (SD)	3.82 (1.9)	4.50 (2.1)	

* = p<0.05; ** = p<0.01.

4.7.3.1.2 High frequency - picture.

Level 1 Analysis

There was a significant difference between Frontal, Posterior and Control groups for number correct, as revealed by one-way ANOVA ($F_{(2,85)} = 3.720$, $p = 0.028$; see Table 42a), although Levene's test was significant ($F_{(2,85)} = 12.260$, $p<0.001$). A Kruskal-Wallis Test confirmed a significant difference ($\chi^2_{(2)} = 7.351$, $p = 0.025$). Pairwise Mann-Whitney U comparisons found that Frontals generated fewer sentences than Controls ($U = 507.500$, $p = 0.009$). Analysis of the RT differences between groups did not reveal significant effects (See Table 42a and Appendix 8 ref 1.10).

Level 2 Analysis

The Left and Right Frontal groups did not differ in the number correct, using univariate ANCOVA ($F_{(1,29)} = 20.045$, $p = 0.163$; see Table 42a). As Levene's test was significant ($F_{(1,30)} = 11.557$, $p = 0.002$), a Mann-Whitney U test was used and found the difference just failed to reach significance ($p = 0.067$; see Appendix 8 ref 2.15). The difference in RT did not reach significance (See Table 42a and Appendix 8 ref 2.16).

Level 3Analysis

One-way ANOVA revealed a significant difference between frontal subgroups for number correct ($F_{(4,56)} = 4.248$, $p = 0.005$). As Levene's test showed unequal error variances ($F_{(4,56)} = 17.331$, $p<0.001$), a Kruskal-Wallis Test was used and failed to find a difference between groups for high frequency pictures (See Appendix 8 ref 3.7).

Level 4 Analysis

There was a significant difference between the LIFG, Non-LIFG and Control groups for number of sentences generated from pictures of high frequency items, as revealed by one-way ANOVA ($F_{(2,69)} = 3.473$, $p = 0.037$; see Table 42b). As Levene's test was significant ($F_{(2,69)} = 9.798$, $p<0.001$), a Kruskal-Wallis Test was used and confirmed the difference ($\chi^2_{(2)} = 9.036$, $p = 0.011$). Pairwise Mann-Whitney U comparisons found that the LIFG and Non-LIFG groups generated fewer sentences than Controls ($U = 94.500$, $p = 0.002$ and $U = 394.500$, $p = 0.030$). The difference in RT did not reach significance using one-way ANOVA test (See Table 42b and Appendix 8 ref 4.12).

Table 42b. *Generation of a sentence from a single picture: Mean Number Correct (Max = 8), Response Time (RT) and Standard Deviation (SD)*

Level 4 Analysis		**LIFG** N = 9	**Non-LIFG** N = 28	**Control** N = 35
Proper Nouns	Mean No. Correct (SD)	7.00 (1.8)	7.39 (1.6)	7.89 (0.4)
	Mean RT (SD)	4.24 (2.2)	3.94 (2.4)	4.52 (4.4)
High Frequency Words	Mean No. Correct (SD)	6.78 (1.7)**	7.25 (1.9)*	7.91 (0.4)
	Mean RT (SD)	4.84 (3.0)	4.68 (2.5)	4.50 (3.0)

* = p<0.05, ** = p<0.01.

4.7.3.2 Generation of a Sentence from Two Pictures

This task was a pictorial version of 4.7.2.3. Thus, the stimuli consisted of: 15 picture pairs high in association; and 15 picture pairs low in association (see Appendix 7). Subjects were presented with picture pairs in a random order and asked to produce a meaningful sentence that included both of the target pictures. Responses were scored as correct if both concepts were included in the sentence. Semantic naming errors (e.g., seat for chair) were allowed as long as a meaningful sentence was generated.

4.7.3.2.1 High association picture pair.

Level 1 Analysis

When generating a sentence to picture pairs high in association, a significant difference between Frontal, Posterior and Control groups was found for number correct ($F_{(2,84)} = 6.971$, $p = 0.002$). As Levene's test of homogeneity of error variances was significant ($F_{(2,84)} = 16.652$, $p<0.001$), a Kruskal-Wallis Test was used to confirm the significant difference ($\chi^2_{(2)} = 23.208$, $p<0.001$; see Table 43a). Pairwise Mann-Whitney U comparisons found that Frontals generated fewer sentences than Posteriors ($U = 147.500$, $p = 0.003$) and Controls ($U = 349.500$, $p<0.001$). There was for no difference between groups for RT (See Table 43a, Figure 11 and Appendix 8 ref 1.11).

Level 2 Analysis

There was no difference in the performance of the Left and Right Frontal groups in terms of number correct or RT (See Table 43a and Appendix 8 ref 2.17 and 2.18).

Table 43a. *Generation of a sentence from two pictures: Mean Number Correct (Max = 15), Response Time (RT) and Standard Deviation (SD)*

Level 1 Analysis		**Frontal N = 37**	**Posterior N = 15**	**Control N = 35**
High Association	Mean No. Correct (SD)	12.89 (3.7)***	14.93 (0.3)	14.86 (0.7)
	Mean RT (SD)	5.12 (5.4)	3.18 (1.5)	3.89 (2.9)
Low Association	Mean No. Correct (SD)	11.95 (4.60)***	14.73 (0.5)	14.77 (0.5)
	Mean RT (SD)	6.21 (4.7)	5.03 (2.7)	5.97 (4.14)

Level 2 Analysis		**Left Frontal N = 15**	**Right Frontal N = 16**
High Association	Mean No. Correct (SD)	13.67 (3.2)	13.56 (1.7)
	Mean RT (SD)	3.88 (4.0)	5. 45 (3.2)
Low Association	Mean No. Correct (SD)	12.93 (3.3)	13.06 (3.0)
	Mean RT (SD)	6.17 (5.0)	7.62 (4.3)

*** = p<0.001.

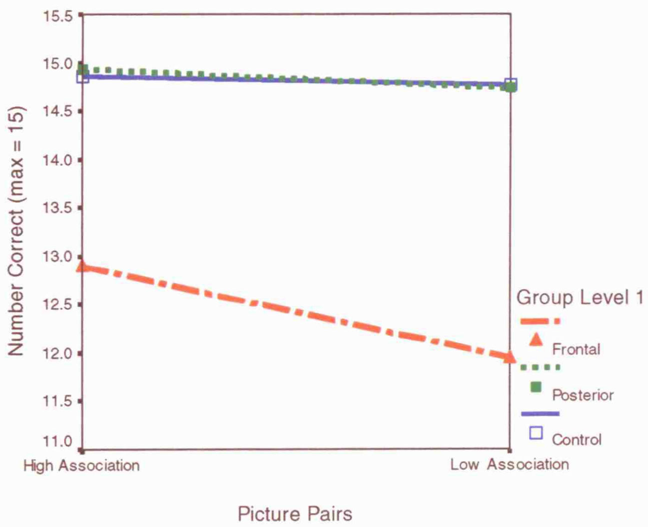

Figure 11. Mean Number of Sentences Generated for Picture Pairs High and Low in Association by Group (Level 1)

Level 3 Analysis

One-way ANOVA revealed a significant difference between frontal subgroups for number correct ($F_{(4,55)}$ = 3.219, p = 0.019). As Levene's test was significant ($F_{(4,55)}$ = 11.277, p<0.001), a Kruskal-Wallis Test was used to confirm the significant difference ($\chi^2_{(4)}$ = 28.141, p<0.001; see Table 43b and Figure 12). Pairwise Mann-Whitney U comparisons identified that the Right Lateral and Inferior Medial groups generated fewer sentences than Controls (U = 5.500, p<0.001 and U = 57.000, p = 0.017, respectively).

Level 4 Analysis

A significant difference was found between groups for number correct using one-way ANOVA found ($F_{(2,68)}$ = 4.535, p = 0.014; see Table 43c) although Levene's test was significant ($F_{(2,68)}$ = 10.968, p<0.001). Kruskal-Wallis Test confirmed the difference was significant ($\chi^2_{(2)}$ = 16.672, p<0.001). Pairwise Mann-Whitney U comparisons found that the LIFG and Non-LIFG Frontals generated fewer sentences from picture pairs high in association than Controls (U = 95.000, p = 0.002 and U = 254.000, p<0.001, respectively). There was no difference between groups for RT (See Table 43c and Appendix 8 ref 4.13).

4.7.3.2.2 Low association picture pair.

Level 1 Analysis

A significant difference was found between Frontal, Posterior and Control groups for number correct ($F_{(2,84)}$ = 9.127, p<0.001), however, Levene's test found the error variances were unequal ($F_{(2,84)}$ = 31.570, p<0.001). Subsequent Kruskal-Wallis Test confirmed a significant difference between groups ($\chi^2_{(2)}$ = 16.379, p<0.001; see Table 43a). Pairwise Mann-Whitney U comparisons found that the Frontals generated significantly fewer sentences than Posteriors (U = 166.000, p = 0.015) and Controls (U = 359.000, p<0.001) (See Figure 11). There was no difference between groups for RT (See Table 43a and Appendix 8 ref 1.12).

Level 2 Analysis

For number correct and RT, the Left and Right Frontal groups did not differ (See Table 43a and Appendix 8 ref 2.19 and 2.20).

Level 3 Analysis

A significant difference was found between frontal subgroups for number correct ($F_{(4,55)}$ = 3.510, p = 0.013), although Levene's test was significant ($F_{(4,55)}$ = 10.029, p<0.001). Subsequent Kruskal-Wallis Test confirmed the significant difference

($\chi^2_{(4)} = 12.089$, $p = 0.017$; see Table 43b) with pairwise Mann-Whitney U comparisons revealing that all frontal subgroups generated significantly fewer sentences than Controls (Left laterals: U = 66.500, p = 0.049; Right Laterals: U = 49.000, p = 0.006; Superior Medials: U = 87.000, p = 0.025; Inferior Medials: U = 45.000, p = 0.017) (See Figure 12).

Table 43b. *Generation of a sentence from two pictures: Mean Number Correct (Max = 15), Response Time (RT) and Standard Deviation (SD)*

Level 3 Analysis	**Left Lateral N = 6**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 5**	**Control N = 35**
High Association Mean No. Correct	13.00	12.33***	14.75	12.40*	14.86
(SD)	(4.9)	(2.0)	(0.7)	(5.3)	(0.7)
Low Association Mean No. Correct	13.00*	12.50**	13.00*	11.00*	14.77
(SD)	(3.5)	(3.5)	(3.0)	(6.4)	(0.5)

* = p<0.05, ** = p<0.01, *** = p<0.001.

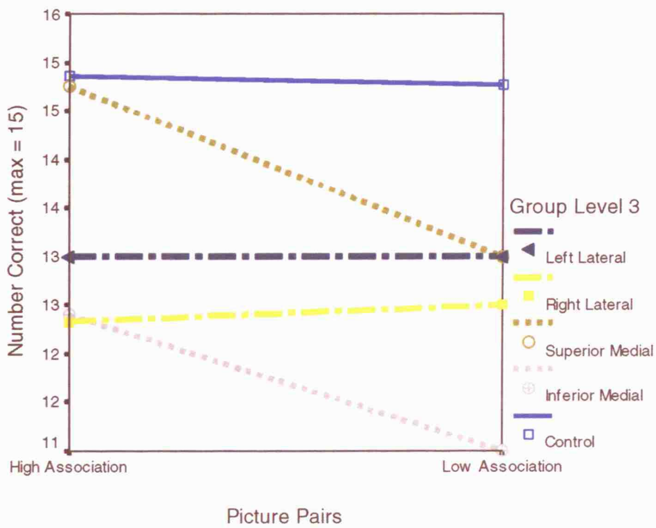

Figure 12. Mean Number of Sentences Generated for Picture Pairs High and Low in Association by Group (Level 3)

Level 4 Analysis

A significant difference was found between the LIFG, Non-LIFG and Control groups for number correct ($F_{(2,68)} = 6.459$, $p = 0.003$; see Table 25c). As Levene's test was significant ($F_{(2,68)} = 23.050$, $p<0.001$), a Kruskal-Wallis Test was used to confirm the significant difference ($\chi^2_{(2)} = 13.123$, $p = 0.001$). Pairwise Mann-Whitney U comparisons found that compared to Controls, fewer sentences were generated by the LIFG and Non-LIFG Frontals (U = 90.000, p = 0.01 and U = 269.000, p = 0.001, respectively). There was no difference between groups for RT (See Table 43c and Appendix 8 ref 4.14).

Table 43c. *Generation of a sentence from two pictures: Mean Number Correct (Max = 15), Response Time (RT) and Standard Deviation (SD)*

Level 4 Analysis		**LIFG N = 9**	**Non-LIFG N = 27**	**Control N = 35**
High Association	Mean No. Correct (SD)	12.56 (4.1)**	13.07 (3.7)***	14.86 (0.7)
	Mean RT (SD)	4.66 (5.0)	5.28 (5.6)	3.89 (2.9)
Low Association	Mean No. Correct (SD)	11.11 (5.6)*	12.37 (4.3)**	14.77 (0.5)
	Mean RT (SD)	6.34 (6.8)	6.13 (4.1)	5.97 (4.14)

* = p<0.05, ** = p<0.01, *** = p<0.001.

4.7.3.3 Generation of a Sentence given a Pictorial Scene

The stimuli consisted of 10 pictorial scenes (See Appendix 7). Subjects were randomly presented with each scene and asked to produce a whole sentence to describe it. Although this test was not devised to investigate stimulus type, describing a scene is a constrained task that is thought to activate a dominant response option. This is in comparison to the task given to the dynamic aphasics ANG and CH requiring them to generate 'What might happen next in this scene?' that activates many response options (Chapter 2.3 Test 4).

Level 1 Analysis

When subjects were asked to generate a sentence to describe a simple pictorial scene, no difference was found between Frontal, Posterior and Controls groups for number correct or RT, using one-way ANOVA tests (See Table 44a and Appendix 8 refs 1.13 and 1.14). Of note, 4 Frontals scored below ceiling compared to only 1 Control.

Level 2 Analysis

The Left and Right Frontal groups did not differ significantly for number correct or RT (See Table 44a and Appendix 8 refs 2.21-2.22).

Table 44a. *Generation of a sentence given a pictorial scene: Mean Number Correct (Max = 10), Response Time (RT) and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 34**	**Posterior N = 15**	**Control N = 35**
Mean No. Correct (SD)	9.74 (0.9)	10.00 (0.0)	9.97 (0.2)
Mean RT (SD)	5.45 (10.6)	2.53 (1.3)	3.78 (3.0)
Level 2 Analysis	**Left Frontal N = 14**	**Right Frontal N = 16**	
Mean No. Correct (SD)	9.93 (0.27)	9.81 (0.54)	
Mean RT (SD)	4.30 (7.2)	3.55 (1.6)	

Level 4 Analysis

There was no difference between LIFG, Non-LIFG and Controls groups for number correct or RT (See Table 44b and Appendix 8 refs 4.15-4.16).

Table 44b.*Generation of a sentence given a pictorial scene: Mean Number Correct (Max = 10), Response Time (RT) and Standard Deviation (SD)*

Level 4 Analysis	**LIFG N = 7**	**Non-LIFG N = 26**	**Control N = 35**
Mean No. Correct (SD)	9.86 (0.4)	9.33 (2.1)	9.97 (0.2)
Mean RT (SD)	5.78 (10.3)	5.47 (11.0)	3.78 (3.0)

4.7.3.4 Sentence Generation Interim Summary (Pictorial Input)

For the generation of a sentence from a picture of a single item, a selective Frontal deficit was found only for high frequency items that activate many response options. Although moderate LIFG and mild Non-LIFG deficits were revealed, no further frontal effects were found.

A selective Frontal deficit was found when generating sentences from picture pairs that activate both many and few response options (i.e., high and low association). Specific Left Lateral and Superior Medial deficits were found only for picture pairs that activate many response options (i.e., low association). These frontal groups were unimpaired, compared to Controls, for picture pairs that activate few response options. In contrast, Right Lateral and Inferior Medial deficits were found for picture pairs that activate both many and few response options.

All subjects performed virtually at ceiling when generating a sentence to simply describe pictorial scenes, a task dynamic aphasic patients, including ANG, CH and KAS, are reported to pass. If anything, the LIFG patients performed slightly better than frontal patients without this damage.

Table 45. *Word and Sentence Generation Tests: Summary of Deficits for Grouping Levels 1-4.*

Generation Task		Deficit for Level of Analysis 1-4			
		1	2	3	4
Word Generation to complete:					
High Constraint Sentences	No. Correct		LF		
	RT	Frontal			Non-LIFG
Low Constraint Sentences	No. Correct	Frontal	LF	LL SM	LIFG Non-LIFG
	RT	Frontal			Non-LIFG
Sentence Generation from:					
High Frequency Words	No. Correct	Frontal			LIFG
Low Association Word Pairs	No. Correct	Frontal		LL SM	LIFG Non-LIFG
High Frequency Pictures	No. Correct	Frontal			LIFG Non-LIFG
High Association Picture Pairs	No. Correct	Frontal		RL IM	LIFG Non-LIFG
Low Association Picture Pairs	No. Correct	Frontal		LL RL SM IM	LIFG Non-LIFG

LF = Left Frontal; RF = Right Frontal; LL = Left Lateral; RL = Right Lateral; SM = Superior Medial; IM = Inferior Medial; LIFG = Left Inferior Frontal Gyrus; RT = response time.

4.7.4 Word and Sentence Generation Investigation Discussion

A selective and severe LIFG deficit was only found for sentence generation that involved many competing response options (high frequency words). No deficit was observed for the LIFG patients, or any frontal patient, when generating sentences from Proper Nouns and low frequency words that activate few or a dominant response option. This finding of a selective LIFG deficit when a stimulus activates many (vs. one or a few) verbal response options is consistent with the findings in dynamic aphasic patients ANG and CH. They were only impaired on sentence generation tasks involving stimuli that activate many response options (i.e., common words). By contrast, they were unimpaired when stimuli activated a dominant response option (i.e., Proper nouns). The most compelling neuroimaging evidence for a LIFG role in selection comes from Thompson-Schill and colleagues (Thompson-Schill et al., 1997; Thompson-Schill et al., 1998; Thompson-Schill et al., 1999; Thompson-Schill et al., 2002). This group has found LIFG activation when selection demands are high, that is when tasks involve selection of semantic knowledge from among competing information. This LIFG activity was further clarified to be modulated by competition and not repetition demands (Thompson-Schill et al., 1999). The neuroimaging data suggesting a role of the LIFG in selection of semantic information is entirely consistent with the group lesion study findings.

The group study also revealed a LIFG deficit on the sentence completion and sentence generation from a word pair tests in the fine-grained frontal analysis. In this analysis, patients with LIFG lesions were encompassed in the Left Lateral group. Moderate Left Lateral and Superior Medial deficits were revealed only for stimuli that activated many response options. These deficits were not present for stimuli that activate a dominant response option. These findings are consistent with the findings for the dynamic aphasic patients ANG (both tasks) and CH (sentence completion task). These findings are also consistent with neuroimaging data that implicates the left posterior LIFG in sentence production (e.g., Indefrey et al., 2001) or propositional language (Blank et al., 2002). Blank and colleagues revealed a left lateralised network (anterior left temporal cortex, left operculum, left superior frontal gyrus) and inferred that disconnection between these areas would be associated with impaired propositional speech. This would fit with the group data finding of a Superior Medial deficit for some word and sentence generation tasks. These group study findings are also consistent with imaging studies of word and sentence completion tasks involving many (vs. few) verbal response options. In particular, two studies have shown increased left dorsolateral prefrontal cortex (BA 46/9/10) activation that has been interpreted as reflecting selection requirements (Desmond et al., 1998; Nathaniel-James et al., 2002).

This selective left frontal involvement is only evident in terms of the number generated. For response time, a general Frontal deficit was found but only for the sentence completion task (both high and low constraint). Thus, Frontal patients were no slower than Controls to generate a sentence, which argues against an alternative explanation for the sentence generation findings related to processing time.

A firm conclusion cannot be drawn about the role of the left posterior frontal lobe on the basis of sentence generation tasks involving pictorial stimuli. Although it was predicted that sentence generation from verbal and pictorial stimuli should mirror one another, methodological difficulties with the tasks need to be addressed. First, the absence of selective frontal deficits on the sentence generation task involving single pictures may be due to a lack of power. This is in terms of both small patient groups and small number of stimuli in each condition. Second, the unexpected finding of Right Lateral and Inferior Medial deficits when generating a sentence from picture pairs (i.e., many and few response options) raises the possibility that this task may engage other cognitive processes. For instance, prior to the generation of a meaningful sentence, this task involves the identification of 2 pictures and the formation of an association or connection between them. Another consideration is that words and pictures initially elicit different associations, as revealed by a recent study (Saffran, Coslett, & Keener, 2003). This suggests a fundamental difference between picture and word pair stimuli. This requires further investigation as the association ratings used in this study were based on word stimuli. It is also possible that the association process is mediated by visual imagery ability such that good and poor imagers perform the task differently.

Overall, for word and sentence generation from verbal input, there is strong convergence between the lesion group study findings, the dynamic aphasic patients ANG and CH, and neuroimaging data. This convergence across methodologies provides strong evidence for a role of the LIFG in a highly specialised cognitive mechanism involved in the selection of verbal responses from amongst competitors.

4.8 DISCOURSE GENERATION INVESTIGATION

The dynamic aphasic KAS (Chapter 3) was severely impaired on tasks requiring the generation of multiple connected sentences (i.e., discourse). For KAS, who exemplifies the 2^{nd} subtype of dynamic aphasia, this deficit contrasted with intact single word and sentence level generation. Story retelling, picture description and story generation from memory and pictures are tasks previously used to investigate a range of language abilities in both normal children and children with language difficulties or closed head injuries (Merritt & Liles, 1987; Merritt & Liles, 1989; Morris-Friehe & Sanger, 1992; Hemphill et al., 1994).

This battery was designed to investigate the generation of a fluent sequence of novel thought from verbal and pictorial input. The discourse level generation battery consisted of four tests: (1) Retell "Cinderella"; (2) Generate "What might happen in the next year to Cinderella"; (3) Describe the "Cookie Theft" complex scene; and (4) Generate "What might happen next in the Cookie Theft scene". The four tests were devised to elicit a sample of discourse level speech that could form the basis for in-depth quantitative analysis. All four tests involve the generation of multiple connected sentences and are relatively unconstrained in that each task activates many possible options. However, these tasks differ in the degree of novelty required. Tasks 1 and 3 involve familiar (i.e., Cinderella story) or visible (i.e., Cookie Theft complex scene) material and thus require little novelty. By contrast, the two generate tasks (2 and 4) have a greater novelty component as they require the generation of new stories.

The tests were administered in order from 1 - 4 so that the generate conditions (2 and 4) always followed the retell (1) and describe (3) tasks. For each test a maximum of 2 minutes was allowed. Responses were recorded on audiotape and then later transcribed. The method of scoring included five QPA measures (Berndt et al., 2000) and two novelty measures that were introduced in Chapter 3. The QPA measures used were: total words uttered, number of nouns, number of verbs, proportion of verbs (i.e., verbs + nouns/verbs) and number of sentences (i.e., a group of words containing a subject-verb combination). The novelty measures used were: novel words and novel sentences. A novel sentence was a group of words containing a subject-verb combination <u>and</u> expressing a new conceptual idea not previously given. The number of novel sentences was expressed as a percentage of the total number of sentences (i.e., novel/total). A word was considered novel if it was not present in the immediately preceding sentence, and if it was not a neologism, a non-linguistic filler (e.g., *um*) or a false start. The number of novel words was expressed as a percentage of the total words uttered (i.e., novel/total).

4.8.1. Retell "Cinderella"

In this test subjects were asked to tell the story of Cinderella as best as possible from memory. Subjects were told that it was not important to get every detail exactly right, but to try and remember the story as best as possible.

Level 1 Analysis

There was a significant difference between the Frontal, Posterior and Control groups for all QPA and novelty measures, as revealed by one-way ANOVA tests (See Table 46a). For total words uttered, pairwise comparisons found that Frontals produced significantly fewer total words than Controls ($p<0.001$) and Posteriors ($p = 0.011$). Pairwise comparisons found that Frontals produced fewer nouns and verbs than Controls ($p<0.001$ and $p<0.001$, respectively), as well as a significantly higher proportion of verbs than Controls ($p = 0.001$). For the number of sentences, pairwise comparisons found that Frontals produced fewer than Controls ($p<0.001$) and Posteriors ($p = 0.001$). On the novelty measures pairwise comparisons did not reveal Frontal or Posterior deficits in comparison to Controls; however, Posteriors produced fewer novel words and sentences than Frontals ($p = 0.001$ and $p = 0.010$, respectively).

Level 2 Analysis

There were no significant effects between the Left and Right Frontal groups on any measure (See Table 46a).

Level 3 Analysis

Using one-way ANOVA, there was no difference between frontal subgroups on any measure, except for number of sentences. One-way ANOVA revealed a significant difference between groups for the number of sentences produced (see Table 46b). Pairwise comparisons found that Left Laterals and Right Laterals produced significantly fewer sentences than Controls ($p = 0.008$ and $p = 0.008$, respectively).

Table 46a. *Discourse Generation: Retell Cinderella Mean Number and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 38**	**Posterior N = 15**	**Control N = 35**	**ANOVA/ Kruskal-Wallis**
Total Words Uttered (SD)	135.8 (95.6)***	205.9 (90.6)	226.5 (78.2)	$F_{(2,85)} = 10.190$ $p<0.001$
Nouns (SD)	22.5 (17.2)***	32.8 (17.2)	39.7 (16.2)	$F_{(2,85)} = 9.680$ $p<0.001$
Verbs (SD)	21.8 (14.8)***	29.3 (12.1)	34.2 (14.3)	$F_{(2,85)} = 6.986$ $p = 0.002$
Proportion of Verbs (SD)	0.51 (0.07)**	0.49 (.07)	0.46 (0.07)	$F_{(2,84)} = 5.823$ $p = 0.004$
Sentences (SD)	14.11 (11.6)***	26.13 (11.8)	26.34 (11.0)	$F_{(2,85)} = 12.334$ $p<0.001$
% Novel Words (SD)	96.7 (5.0)	91.3 (5.8)**~	93.9 (4.7)	$F_{(2,84)} = 6.800$ $p = 0.002$
% Novel Sentences (SD)	97.9 (4.8)	93.7 (6.5)*~	97.2 (5.0)	$F_{(2,85)} = 3.811$ $p = 0.026$

Level 2 Analysis	**Left Frontal N = 16**	**Right Frontal N = 16**	**ANCOVA/ Mann-Whitney U**
Total Words Uttered (SD)	136.88 (85.0)	150.31 (105.5)	$F_{(1,29)} = 0.723$ $p = 0.402$
Nouns (SD)	22.63 (17.3)	24.81 (17.6)	$F_{(1,29)} = 0.650$ $p = 0.427$
Verbs (SD)	22.31 (13.1)	23.81 (16.1)	$F_{(1,29)} = 0.468$ $p = 0.499$
Proportion of Verbs (SD)	0.52 (0.06)	0.51 (0.07)	$F_{(1,29)} = 0.972$ $p = 0.332$
Sentences (SD)	13.00 (7.8)	17.69 (14.7)	$F_{(1,29)} = 1.119$ $p = 0.299$
% Novel Words (SD)	95.3 (6.3)	98.1 (2.2)	$U = 98.000$ $p = 0.248$
% Novel Sentences (SD)	96.9 (6.4)	98.3(3.2)	$F_{(1,29)} = 0.029$ $p = 0.866$

* = p<0.05, ** = p<0.01, *** = p<0.001; ~ = lower than Frontals only

Table 46b. *Discourse Generation: Retell Cinderella Mean Number and Standard Deviation (SD)*

Level 3 Analysis	**Left Lateral N = 7**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 5**	**Control N = 35**	**ANOVA/ Kruskal-Wallis**
Total Words Uttered (SD)	151.4 (108.2)	148.3 (95.7)	169.3 (90.7)	153.8 (127.0)	226.5 (78.2)	$F_{(4,56)} = 2.342$ p = 0.066
Nouns (SD)	26.9 (23.4)	23.5 (15.1)	29.0 (16.9)	23.6 (19.6)	39.7 (16.2)	$F_{(4,56)} = 2.397$ p = 0.061
Verbs (SD)	24.4 (16.4)	22.3 (12.0)	26.9 (14.7)	24.2 (21.0)	34.2 (14.3)	$F_{(4,56)} = 1.591$ p = 0.189
Proportion of Verbs (SD)	0.51 (0.08)	0.51 (.05)	0.49 (0.07)	0.53 (0.10)	0.46 (0.07)	$F_{(4,56)} = 1.905$ p = 0.122
Sentences (SD)	12.9** (9.5)	12.2** (6.4)	22.0 (14.0)	16.6 (19.3)	26.3 (11.0)	$F_{(4,56)} = 3.573$ p = 0.012
% Novel Words (SD)	97.2 (4.3)	98.7 (2.1)	93.7 (7.8)	96.2 (6.1)	93.9 (4.7)	$F_{(4,56)} = 1.744$ p = 0.153
% Novel Sentences (SD)	100.0 (0.0)	99.2 (1.9)	95.3 (5.4)	98.8 (2.7)	97.2 (5.0)	$\chi^2_{(4)} = 6.052$ p = 0.195

** = p<0.01.

4.8.2 Generate "What might happen in the next year to Cinderella"

Subjects were asked to generate a novel story, based on a familiar story and, thus, were asked "What might happen in the next year to Cinderella"?

Level 1 Analysis

Using one-way ANOVA, there was no difference between Frontal, Posterior and Control groups for: total words uttered, nouns, verbs, proportion of verbs, and percentage of novel words, although there was a trend for the Frontals to produce fewer nouns (See Table 47a). By contrast, one-way ANOVA revealed a significant difference between groups for the number of sentences produced. Pairwise comparisons found that Frontals produced fewer sentences than Posteriors (p = 0.009) with the lower score than Controls just failing to reach significance after Bonferroni correction (p = 0.039). A significant difference between groups was also found for percentage of novel sentences ($F_{(2,81)} = 3.228$ p = 0.045), however, Levene's test found unequal error variances ($F_{(2,81)} = 6.852$, p = 0.002). Subsequent Kruskal-Wallis Test confirmed the significant difference (See Table 47a). Pairwise Mann-Whitney U comparisons found that Posteriors produced fewer novel sentences than Controls (U = 171.500, p = 0.010).

Table 47a. *Discourse Generation: Generate Cinderella Mean Number and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 38**	**Posterior N = 15**	**Control N = 35**	**ANOVA/ Kruskal-Wallis**
Total Words Uttered (SD)	80.79 (91.4)	126.67 (68.8)	114.46 (83.0)	$F_{(2,85)} = 2.207$ $p = 0.116$
Nouns (SD)	11.34 (13.2)	19.33 (12.1)	17.91 (14.2)	$F_{(2,85)} = 2.978$ $p = 0.056$
Verbs (SD)	12.47 (13.8)	18.87 (10.5)	15.97 (11.5)	$F_{(2,85)} = 1.619$ $p = 0.204$
Proportion of Verbs (SD)	0.56 (0.18)	0.54 (0.15)	0.49 (0.09)	$F_{(2,82)} = 2.114$ $p = 0.127$
Sentences (SD)	8.16 (9.0)**~	15.87 (9.7)	12.77 (9.7)	$F_{(2,85)} = 4.323$ $p = 0.016$
% Novel Words (SD)	94.1 (17.0)	89.6 (11.0)	93.6 (7.1)	$F_{(2,83)} = 0.681$ $p = 0.509$
% Novel Sentences (SD)	97.0 (7.6)	93.5 (8.8)*	98.6 (3.5)	$\chi^2_{(2)} = 6.854$ $p = 0.032$

Level 2 Analysis	**Left Frontal N = 16**	**Right Frontal N = 16**	**ANCOVA/ Mann-Whitney U**
Total Words Uttered (SD)	86.50 (103.3)	90.00 (90.5)	$F_{(1,29)} = 0.591$ $p = 0.448$
Nouns (SD)	11.50 (14.3)	12.50 (13.5)	$F_{(1,29)} = 0.957$ $p = 0.336$
Verbs (SD)	13.63 (15.3)	14.12 (14.0)	$F_{(1,29)} = 0.457$ $p = 0.505$
Proportion of Verbs (SD)	0.57 (0.20)	0.58 (0.17)	$F_{(1,29)} = 0.307$ $p = 0.584$
Sentences (SD)	7.19 (6.2)	10.81 (11.7)	$F_{(1,29)} = 1.874$ $p = 0.182$
% Novel Words (SD)	95.2 (6.8)	97.9 (3.4)	$F_{(1,29)} = 0.938$ $p = 0.341$
% Novel Sentences (SD)	100 (0.0)	93.5 (10.1)**	U = 67.500 p = 0.005

* = p<0.05, ** = p<0.01; ~ lower than Posteriors only.

Level 2 Analysis

There were no significant differences between the Left and Right Frontal groups on any measure except for the lower percentage of novel sentences produced by the Right Frontals (See Table 47a).

Level 3 Analysis

There was no difference between frontal groups for the measures of number of sentences and percentage of novel sentences (See Table 47b).

Table 47b. *Discourse Generation: Generate Cinderella Mean Number and Standard Deviation (SD)*

Level 3 Analysis	Left Lateral N = 7	Right Lateral N = 6	Superior Medial N = 8	Inferior Medial N = 5	Control N = 35	ANOVA/ Kruskal-Wallis
Sentences (SD)	8.43 (8.1)	8.33 (3.8)	10.88 (7.0)	14.60 (19.6)	12.77 (9.7)	$F_{(2,56)} = 0.583$ $p = 0.676$
% Novel Sentences (SD)	100.0 (0.0)	96.3 (5.7)	97.7 (4.5)	92.7 (12.0)	98.6 (3.5)	$\chi^2_{(4)} = 5.838$ $p = 0.212$

4.8.3 Describe the "Cookie Theft" complex scene

In this test subjects were presented with the "Cookie Theft" complex scene (Goodglass et al., 1983) and asked to describe the contents.

Level 1 Analysis

Using one-way ANOVA, a significant difference between the Frontal, Posterior and Control groups was found for the following measures: total words uttered; nouns; verbs; sentences; and percentage of novel words (See Table 48a). Pairwise comparisons found that Frontals produced a lower number of total words, nouns, verbs and sentences than Controls ($p = 0.003$, $p = 0.002$, $p = 0.004$ and $p<0.001$, respectively), and fewer sentences than Posteriors ($p = 0.001$). Although there was no Frontal or Posterior deficit, compared to Controls, for percentage of novel words, pairwise comparisons showed that Posteriors produced fewer novel words than Frontals ($p = 0.017$). By contrast, no difference was found between groups for proportion of verbs or percentage of novel sentences, using one-way ANOVA (See Table 48a).

Table 48a. *Discourse Generation: Describe Complex Scene Mean Number and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 38**	**Posterior N = 15**	**Control N = 35**	**ANOVA/ Kruskal-Wallis**
Total Words Uttered (SD)	105.2 (82.4)**	146.7 (65.0)	159.9 (75.3)	$F_{(2,85)} = 4.842$ $p = 0.010$
Nouns (SD)	18.8 (15.1)**	23.1 (8.6)	28.8 (13.9)	$F_{(2,85)} = 4.891$ $p = 0.010$
Verbs (SD)	15.3 (10.2)**	20.9 (9.7)	22.4 (10.3)	$F_{(2,85)} = 4.770$ $p = 0.011$
Proportion of Verbs (SD)	0.48 (0.11)	0.46 (0.06)	0.44 (0.07)	$F_{(2,85)} = 1.295$ $p = 0.279$
Sentences (SD)	10.5 (6.8)***	17.8 (8.4)	17.2 (7.3)	$F_{(2,85)} = 9.815$ $p<0.001$
% Novel Words (SD)	97.4 (5.3)	94.2 (3.8)**~	95.7 (3.0)	$F_{(2,85)} = 3.286$ $p = 0.042$
% Novel Sentences (SD)	97.1 (6.7)	95.6 (6.7)	97.5 (4.8)	$F_{(2,85)} = 0.599$ $p = 0.552$

Level 2 Analysis	**Left Frontal N = 16**	**Right Frontal N = 16**	**ANCOVA/ Mann-Whitney U**
Total Words Uttered (SD)	107.25 (75.4)	107.88 (77.5)	$F_{(1,29)} = 0.054$ $p = 0.818$
Nouns (SD)	19.06 (14.3)	19.63 (13.6)	$F_{(1,29)} = 0.196$ $p = 0.661$
Verbs (SD)	15.63 (10.0)	15.75 (9.5)	$F_{(1,29)} = 0.024$ $p = 0.878$
Proportion of Verbs (SD)	0.46 (0.07)	0.45 (0.06)	$F_{(1,29)} = 0.944$ $p = 0.339$
Sentences (SD)	10.50 (5.5)	11.56 (8.0)	$F_{(1,29)} = 0.000$ $p = 0.990$
% Novel Words (SD)	96.0 (6.1)	99.0 (1.5)	$U = 83.000$ $p = 0.073$
% Novel Sentences (SD)	96.1 (6.7)	97.1 (6.8)	$F_{(1,29)} = 2.136$ $p = 0.155$

** = p<0.01, *** = p<0.001; ~ = lower than Frontals only

Level 2Analysis

There was no the difference between Left and Right Frontals on any measure (See Table 48a).

Level 3 Analysis

Frontal effects were not found for the measures of total words uttered, nouns or verbs. By contrast, there was a significant difference between frontal groups for the number of sentences and percentage of novel words (See Table 48b). Pairwise comparisons found that Left Laterals, Right Laterals and Superior Medials produced fewer sentences than Controls (p = 0.033, p = 0.011 and p = 0.012, respectively). Inferior Medials also produced fewer sentences than Controls, however, this failed to reach significance (p = 0.062). A higher percentage of novel words was produced by Right Laterals than Controls (U = 26.000, p =.004), as revealed by pairwise comparisons.

Table 48b. *Discourse Generation: Describe Complex Scene Mean Number and Standard Deviation (SD)*

Level 3 Analysis	**Left Lateral N = 7**	**Right Lateral N = 6**	**Superior Medial N = 8**	**Inferior Medial N = 5**	**Control N = 35**	**ANOVA/ Kruskal-Wallis**
Total Words Uttered (SD)	124.4 (110.1)	98.3 (75.2)	94.0 (34.3)	132.6 (108.7)	159.9 (75.3)	$F_{(2,56)} = 1.726$ p = 0.157
Nouns (SD)	20.9 (21.5)	17.8 (12.5)	19.0 (6.8)	24.4 (20.4)	28.8 (13.9)	$F_{(2,56)} = 1.414$ p = 0.241
Verbs (SD)	18.0 (14.8)	14.7 (8.5)	13.5 (4.3)	19.6 (13.3)	22.4 (10.3)	$F_{(2,56)} = 1.726$ p = 0.157
Sentences (SD)	11.3* (7.8)	8.7 * (2.8)	11.0* (4.2)	12.8 (13.2)	17.2 (7.3)	$F_{(2,56)} = 3.017$ p = 0.025
% Novel Words (SD)	95.7 (7.6)	99.3** (1.6)	97.1 (4.3)	95.3 (9.2)	95.7 (3.0)	$\chi^2_{(4)} = 11.532$ p = 0.021

* = p<0.05, ** = p<0.01.

4.8.4 Generate "What might happen next in the Cookie Theft scene"

Subjects were asked to generate a novel story based on the "Cookie Theft" complex scene: "What might happen next in the Cookie Theft scene?"

Level 1 Analysis

Using one-way ANOVA, there was no difference between the Frontal, Posterior and Control groups for the QPA measures of total words uttered, nouns, verbs or proportion of verbs, of for the novelty measure of percentage of novel words. By contrast, one-way ANOVA did reveal a significant difference between groups for number of sentences (See Table 49a). Pairwise comparisons found that Frontals produced fewer sentences than Posteriors ($p = 0.008$) and Controls ($p = 0.015$). There was also a significant difference for percentage of novel sentences ($F_{(2,85)} = 5.197$ $p = 0.007$), however, Levene's test was significant ($F_{(2,85)} = 6.254$, $p = 0.003$). Subsequent Kruskal-Wallis Test confirmed the significant difference, with pairwise Mann-Whitney U comparisons showing that Posteriors produced fewer novel sentences than Controls ($U = 171.500$, $p = 0.010$).

Level 2 Analysis

Left and Right Frontals did not differ on any measure (See Table 49a).

Table 49a. *Discourse Generation: Generate Complex Scene Mean Number and Standard Deviation (SD)*

Level 1 Analysis	**Frontal N = 38**	**Posterior N = 15**	**Control N = 35**	**ANOVA/ Kruskal-Wallis**
Total Words Uttered (SD)	91.0 (70.8)	98.9 (34.9)	114.9 (79.5)	$\chi^2_{(2)} = 2.352$ $p = 0.308$
Nouns (SD)	13.5 (9.3)	14.8 (7.1)	17.1 (13.0)	$\chi^2_{(2)} = 1.272$ $p = 0.529$
Verbs (SD)	14.2 (11.0)	16.4 (6.3)	18.4 (13.2)	$F_{(2,85)} = 1.286$ $p = 0.282$
Proportion of Verbs (SD)	0.50 (0.12)	0.53 (0.09)	0.53 (0.08)	$F_{(2,85)} = 0.762$ $p = 0.470$
Sentences (SD)	8.5 (6.6)*	13.9 (5.7)	12.3 (6.9)	$F_{(2,85)} = 4.991$ $p = 0.009$
% Novel Words (SD)	97.0 (5.6)	96.9 (3.6)	95.8 (3.9)	$F_{(2,85)} = 0.704$ $p = 0.498$
% Novel Sentences (SD)	98.1 (5.5)	93.6 (7.3)*	98.5 (3.5)	$\chi^2_{(2)} = 11.038$ $p = 0.004$

Level 2 Analysis	Left Frontal N = 16	Right Frontal N = 16	ANCOVA/ Mann-Whitney U
Total Words Uttered (SD)	95.69 (87.4)	91.00 (54.6)	$F_{(1,29)} = 0.217$ $p = 0.645$
Nouns (SD)	12.56 (9.8)	15.0 (9.1)	$F_{(1,29)} = 2.385$ $p = 0.133$
Verbs (SD)	14.69 (13.0)	14.81 (9.0)	$F_{(1,29)} = 0.830$ $p = 0.370$
Proportion of Verbs (SD)	0.54 (0.10)	0.50 (0.06)	U = 97.000 $p = 0.240$
Sentences (SD)	8.50 (5.7)	9.50 (8.1)	$F_{(1,29)} = 0.462$ $p = 0.502$
% Novel Words (SD)	96.3 (5.9)	99.0 (1.5)	U = 99.000 $p = 0.228$
% Novel Sentences (SD)	97.3 (6.5)	100.0 (0.0)	U = 104.000 $p = 0.074$

* = $p<0.05$

Level 3 Analysis

No frontal effects were found for sentences or novel sentences (See Table 49b).

Table 49b. *Discourse Generation: Generate Complex Scene Mean Number and Standard Deviation (SD)*

Level 3 Analysis	Left Lateral N = 7	Right Lateral N = 6	Superior Medial N = 8	Inferior Medial N = 5	Control N = 35	ANOVA/ Kruskal-Wallis
Sentences (SD)	9.3 (7.3)	7.5 (6.1)	10.3 (7.9)	9.2 (9.8)	12.3 (6.9)	$F_{(2,56)} = 0.809$ $p = 0.525$
% Novel Sentences (SD)	98.4 (4.2)	100.0 (0.0)	98.9 (3.1)	100.0 (0.0)	98.5 (3.5)	$\chi^2_{(4)} = 2.100$ $p = 0.717$

Table 50. *Discourse Generation Tests: Summary of Deficits for Levels of Analysis 1-3*

Discourse Task	Deficit for Level of Analysis 1-3		
	1	2	3
Cinderella Retell			
Total Words Uttered	Frontal		
Nouns	Frontal		
Verbs	Frontal		
Proportion of Verbs	Frontal		
Sentences	Frontal		LL RL
% Novel Words	*Posterior(only worse than Frontals)*		
% Novel Sentences	*Posterior(only worse than Frontals)*		
Cinderella Generate			
Sentences	Frontal		
% Novel Sentences	Posterior	RF	
Cookie Describe			
Total Words Uttered	Frontal		
Nouns	Frontal		
Verbs	Frontal		
Sentences	Frontal		LL RL SM
% Novel Words	*Posterior(only worse than Frontals)*		*RL (better than Controls)*
Cookie Generate			
Sentences	Frontal		
% Novel Sentences	Posterior		

RF = Right Frontal; LL = Left Lateral; RL = Right Lateral; SM = Superior Medial.

4.8.5 Discourse Generation Summary and Discussion

For the QPA measures, in comparison to both Controls and Posterior patients, a Frontal deficit was revealed for the production of words (including nouns and verbs) and sentences for the familiar and visible tasks that place less demand on novelty (i.e., *Retell* Cinderella and *Describe* Complex Scene). More specifically within the Frontal group, the Left and Right Laterals produced fewer sentences on both tasks, as did the Superior Medials for the complex scene description. Thus, a general reduction in the quantity produced (i.e., words and sentences) was evident for the Frontal group. For the tasks with greater novelty demands requiring subjects to *generate* new stories (i.e., What might happen next?), a Frontal deficit was found for the QPA measure of sentences. Similar to the less novel tasks, this suggests a general reduction in the quantity produced by the Frontals. For the novelty measures, neither the Frontal or Posterior groups showed a deficit compared to Controls on the less novel tasks (Retell Cinderella and Describe Complex Scene). The only exception was that the Right Frontals, in comparison to Left Frontals, produced fewer novel sentences on one generate task (Cinderella). The reduced propositional language generated by Frontal patients is consistent with the performance of dynamic aphasic patient KAS (Chapter 3). However, the absence of a novelty deficit is not consistent with KAS who had a paucity of novel concepts in her propositional language.

The Posterior patients were found to have a mild novelty deficit compared to Frontal patients on the two less novel tasks. That is, Posteriors produced fewer novel words and sentences than Frontals. For the two generate tasks, the Posterior group had a deficit for novel sentences in comparison to Controls. One may speculate that a novelty deficit only becomes apparent with either a larger quantity of words and sentences (Posteriors produced a much larger sample of propositional language than Frontals) or a more severe deficit than that demonstrated in the Frontal group. However, the first speculation was not the case for the dynamic aphasic KAS as her lack of novelty was present in the context of a severe reduction in quantity. Thus, it seems more likely that a novelty deficit would appear in the context of a more severe propositional language deficit. The Cognitive Baseline (4.3.3) showed the Frontal patients were relatively intact globally. Mild visual memory impairment was evident in the Right Frontal and Posterior groups (4.3.2.2). This may have contributed to the novelty deficits. As the Posterior groups' novelty deficit was for both a verbal story and a complex pictorial scene, a mild visual memory deficit seems an unlikely explanation. For this to account for the novelty deficit one would have to propose that recall of the Cinderella story involves a high loading on visual memory.

How does the imaging data fit with the lesion study findings? A bilateral anterior and posterior network was highlighted in the few imaging studies that have involved the generation of multiple connected sentences. Braun and colleagues (2001) suggested that anterior and posterior areas have distinct roles in early and late stages of language production. This was suggested to be a progression from bilateral posterior to left-lateralised anterior activation for the discourse generation. The left-lateralisation for discourse generation does not easily fit with the bilateral frontal involvement revealed by the group study. Bilateral frontal activation was revealed in two fMRI studies of connected speech when describing pictorial stimuli (Rorschach inkblot plates) (Kircher et al., 2004; Kircher et al., 2000). Specifically, articulation during continuous speech involved bilateral frontal (BA 44/45, BA 8, BA 24), temporal (BA 21/22) and cerebellar areas. The bilateral frontal activation is in keeping with the general frontal deficit identified here.

4.9 GROUP STUDY CONCLUSIONS

The Frontal group as a whole performed almost normally on baseline cognitive tests. This suggests that the Frontal group presented with relatively mild global deficits. On baseline language tests reduced spontaneous speech was more prevalent in Frontal patients, compared to Posterior patients and Controls. Left Frontals produced more dysphasic errors than Right Frontals and only Left Lateral and Superior Medial patients presented with nonfluent spontaneous speech and sentence repetition errors. Nominal, comprehension and reading ability of the Frontal patients was within normal limits.

The executive function assessment confirmed a role of the frontal lobes on standard clinical measures. In addition, an abstraction deficit was only found for Superior and Inferior Medial patients. On the Hayling, Lateral deficits (Left and Right) were revealed for response suppression and there was a strong trend for a Left Frontal deficit for response initiation. In addition, Right Lateral and Inferior Medial deficits were found for response time in the response suppression condition.

The verbal and non-verbal fluency investigation revealed a role of the frontal lobes in the generation of all items. This was selective to Frontal patients for designs, gestures and novel uses of objects. The group study found some support for left/right lateralisation along material specific lines. In particular, the Left Lateral region was implicated in phonemic word fluency and the Right Lateral region was implicated in design fluency (plus Medial involvement in both). The data also revealed a selective Medial deficit for gesture fluency.

The word and sentence level generation investigation revealed a selective LIFG deficit for sentence generation only when stimuli activated many competing verbal response options. This, in conjunction with evidence from dynamic aphasia patients (ANG and CH) and neuroimaging studies, strongly supports a role of this region in the selection of verbal responses.

The discourse level generation investigation revealed a selective Frontal deficit in the generation of multiple connected sentences. This replicated the findings of dynamic aphasic KAS. The group study did not reveal a novelty of content deficit that was present in KAS's propositional language. Thus, the lesion study provided support for a bilateral frontal role in the generative of a fluent sequence of novel thought specifically in terms of quantity of new thoughts rather than the novelty of the thoughts.

Finally, the method of lesion analysis adopted in this study is concluded to be useful in precisely localising deficits and in testing hypotheses pertaining to specific lesions (e.g., LIFG).

CHAPTER FIVE: GENERAL CONCLUSIONS

This thesis investigated both single case studies of patients with propositional language generation impairment and a group of patients with focal frontal and non-frontal lesions and healthy controls. The results of these investigations start to elucidate some of the cognitive mechanisms involved in voluntary generation processes, particularly propositional language generation, and the anatomical substrates that support these. The combination of single case and group study methodologies allowed several questions to be addressed: namely, what are the cognitive mechanisms involved in generating propositional language?; are these cognitive mechanisms specific to language?; what are the neuroanatomical substrates that support these cognitive mechanisms?; and what is the role of the frontal lobes in the generation of novel verbal and non-verbal responses?

5.1 CLINICAL CHARACTERISATION OF DYNAMIC APHASIA

Propositional language generation has rarely been investigated and, thus far, it has been little understood. The hallmark impairment in *frontal dynamic aphasia* (Luria, 1966; 1970; 1973; Luria et al., 1968) is severely reduced propositional language generation. Thus, dynamic aphasia allows for the investigation of impaired propositional language although there have only been a handful of investigations. As a result dynamic aphasia remains poorly characterised. The current investigation of patients with dynamic aphasia and review of this literature has allowed for an improved characterisation of dynamic aphasia in two respects. One characterisation is regarding the presenting language profile and the second characterisation pertains to the pattern of language generation performance.

The first characterisation is based on the presenting language profile of dynamic aphasia patients. As detailed in Chapter 2, the language profiles of reported dynamic aphasic patients fall within two forms: *pure* and *mixed*. In the *pure* form, the propositional language impairment occurs without any other language deficits such as articulatory or grammatical difficulties. The language profiles of the dynamic aphasic patients KAS (Chapter 3), ANG (Robinson et al., 1998), ROH (Costello et al., 1989), CO (Gold et al., 1997) and some of Luria's cases (Luria, 1970) are of this *pure* form. In the *mixed* form, the core propositional language impairment occurs in the presence of additional language impairments. This may be additional articulatory or grammatical difficulties like the dynamic patient CH (Chapter 2), the 3 Progressive Supranuclear Palsy (PSP) patients (Esmonde et al., 1996), KC (Snowden et al., 1996) or some of Luria's cases (Luria, 1970). In some instances, dynamic aphasia presents with additional nominal or comprehension difficulties (Luria, 1970; Warren et al., 2003).

The second characterisation of dynamic aphasia is derived from the pattern of performance on specific language generation tasks. If one examines dynamic aphasia patients' performance on word, phrase and sentence generation tests, two different patterns emerge. These two patterns are classed as *1st subtype* and *2nd subtype* dynamic aphasia. As detailed in Chapter 3, the majority of dynamic aphasic patients have significant difficulty on tasks requiring the generation of a single word or sentence (e.g., generate a meaningful sentence that includes *glass*, generate a word to meaningfully complete the sentence *Water and sunshine help plants...)*. Dynamic aphasia patients who fail these tasks are classed as having the *1st subtype* and include CH (Chapter 2), ANG (Robinson et al., 1998), ROH (Costello et al., 1989), ADY (Warren et al., 2003) and MP (Raymer et al., 2002). By contrast, a few dynamic aphasic patients appear to be unimpaired and perform well on word and sentence level generation tests. These patients are classed as *2nd subtype* dynamic aphasics and include KAS (Chapter 3), the 3 PSP patients (Esmonde et al., 1996) and KC (Snowden et al., 1996).

5.2 COGNITIVE MECHANISMS INVOLVED IN PROPOSITIONAL LANGUAGE GENERATION

What are the cognitive mechanisms involved in generating propositional language? The single case studies suggest evidence for at least two cognitive mechanisms involved in propositional language generation. The first set of cognitive mechanisms is involved in the *selection of verbal response options* from amongst competitors. Evidence for this set of mechanisms comes from the dynamic patient CH reported in Chapter 2 and the previously reported patient ANG (Robinson et al., 1998). CH and ANG were impaired in generating phrases and sentences when more than a simple description was required. Specifically, the investigation of CH demonstrated that he was only impaired on phrase and sentence generation tasks when stimuli activated many competing response options (e.g., generate a meaningful sentence that includes *table*). In stark contrast, CH was unimpaired on phrase and sentence generation tasks when stimuli strongly activated a dominant response (e.g., generate a meaningful sentence that includes *London*). This replicated the findings of the pure dynamic aphasic ANG and was extended to the single word level. Thus, CH's ability to generate a single word on sentence completion tasks was unimpaired for high constraint sentences that are strongly associated with a dominant response. By contrast, his ability to generate a single word was impaired for low constraint sentences that are associated with many alternative completion words with no dominant response. Thus, it was concluded that CH and ANG have damage to the cognitive mechanism responsible for the selection of a verbal response option from amongst competitors.

The second set of cognitive mechanisms involved in propositional language generation is responsible for generating a *fluent sequence of novel thought*. Evidence for this set of mechanisms comes from the dynamic patient KAS reported in Chapter 3. Despite severely reduced propositional language skills, KAS's performance on word and sentence generation tasks was intact. KAS was, however, impaired on discourse generation tasks involving multiple connected sentences. In particular, KAS produced a reduced quantity of propositional language that also had a paucity of novelty in the content. Notably, external support only marginally increased the quantity but not novelty of the content. Thus, it was concluded that KAS has a deficit in the set of cognitive mechanisms involved in generating *multiple* connected sentences, that is, an impairment in *generating a fluent sequence of novel thought.*

5.2.1 Are these Cognitive Mechanisms Within the Language Domain?

Are these two cognitive mechanisms specific to language or do they encompass the generation of both verbal and non-verbal responses? The first cognitive mechanism involved in the *selection of verbal response options* appears to be within the language domain. Evidence for this comes from the performance of the dynamic aphasic CH (Chapter 2). CH was intact on a series of non-verbal generation tasks including design fluency, gesture fluency and motor movement generation. This well preserved performance is in sharp contrast to his impaired performance on word and sentence generation tasks involving many competing response options. This clearly demonstrated that his propositional language impairment was specific to the production of language. Thus, the set of cognitive mechanisms involved in the selection of verbal responses that underpins CH's dynamic aphasia was concluded to be within the language domain.

The second cognitive mechanism involved in *generating a fluent sequence of novel thought* is not specific to language production. Evidence for this comes from the performance of the dynamic aphasic KAS (Chapter 3). KAS's impairment in generating multiple connected sentences was documented in the context of impaired word and design fluency performances. Her ability to generate multiple nonverbal items (i.e., designs) was severely impaired. Thus, her generation impairment was not confined to language output. The set of cognitive mechanisms involved in generating a fluent sequence of novel thought encompasses novel verbal and nonverbal generation.

5.3 THE ANATOMICAL SUBSTRATES OF PROPOSITIONAL LANGUAGE GENERATION

What are the neuroanatomical substrates that support these cognitive mechanisms? The two distinct sets of cognitive mechanisms involved in propositional language generation are supported by different anatomical substrates. The first set of mechanisms responsible for the selection of verbal response options is associated with the *left inferior frontal region* (LIFG). Evidence for this comes from both single cases of patients with dynamic aphasia and the group study lesion. Two dynamic aphasic patients (CH, Chapter 2, and ANG, Robinson et al., 1998) were demonstrated to have a failure in the first set of cognitive mechanisms. This was characterised by an inability to select between competing verbal response options. CH and ANG had lesions specifically involving the LIFG. CH had focal atrophy in the left frontal and temporal lobes, particularly involving BA 44 maximally and BA 45 to a lesser extent. ANG had a frontal meningioma in the LIFG particularly affecting BA 45 and BA 44 to a lesser extent. The group study confirmed an association between the LIFG and selection of verbal responses. Specifically, frontal patients with damage to the LIFG had a severe and selective deficit when generating a sentence only from a single word that activated many response options (e.g., high frequency word - *table*). In contrast, patients with LIFG damage were unimpaired when generating a sentence from a single word that activated few or a dominant response (e.g., Proper Noun - *London*, low frequency word - *sundial*). Moreover, frontal patients without LIFG damage (and Posterior patients and Controls) were unimpaired on this sentence generation task regardless of the number of possible response options (i.e., many or a dominant). The two single cases of dynamic aphasia suggested a role for the LIFG in a high level process responsible for the selection between competing verbal responses. The data from the group study confirmed this LIFG role in the selection of verbal responses. There is convergence between this lesion and imaging data. The series of imaging studies conducted by Thompson-Schill and colleagues implicate LIFG in the selection of semantic knowledge from among competing information (Thompson-Schill et al., 1997; Thompson-Schill et al., 1998; Thompson-Schill et al., 1999; Thompson-Schill et al., 2002). In addition, imaging studies using sentence completion tasks have associated the LIFG in the generation of single words (response initiation) (Collette et al., 2001; Nathaniel-James et al., 1997). Moreover, left dorsolateral prefrontal activation has been shown when stimuli activate many (vs. few) response options (Nathaniel-James et al., 2002).

The second cognitive mechanism involved in generating a fluent sequence of novel thought is associated with the *bilateral frontal and possibly subcortical* region. Evidence for this comes from the dynamic aphasia patient KAS (Chapter 3) and the group study lesion. The case study demonstrated that KAS had a deficit in the second cognitive mechanism. This is characterised as an impairment of fluent novel thought generation that manifests within language as an impairment in generating multiple connected sentences. Specifically, KAS produced a reduced quantity of speech (i.e., word and sentences) that was also lacking in the novelty of content. KAS had widespread damage including the frontal lobes bilaterally and subcortical structures such as the basal ganglia. The group study confirmed that patients with frontal lesions had a deficit on discourse generation tasks (e.g., Retell Cinderella). In particular, frontal patients produced a significantly lower quantity of speech than posterior patients and healthy controls. The frontal deficit does not appear to have a clear localisation or lateralisation within the frontal region. Thus, the dynamic aphasic patient KAS suggested a role for the bilateral frontal and possibly subcortical regions in the generation of a fluent sequence of novel thought. The group study supported a role of the bilateral frontal lobes for this specifically in terms of the quantity of novel thoughts generated. The group study failed to replicate the single case finding of a lack of novelty in the content of the speech produced. This raises the possibility that novelty of content may be underpinned by a larger or more widespread lesion (c.f. focal frontal). This warrants further investigation in both single case and group studies of patients with larger and more widespread lesions, particularly subcortical lesions. A bilateral anterior and posterior network has been highlighted in the few imaging studies involving multiple connected sentences In particular, Kircher and colleagues (2004; 2000) implicated bilateral frontal (BA 44/45, BA 8, BA 24), temporal (BA 21/22) and cerebellar areas during the articulation of continuous speech.

5.4 THE ROLE OF THE FRONTAL LOBES IN VERBAL AND NON-VERBAL FLUENCY TASKS

What is the role of the frontal lobes in the voluntary generation of verbal and non-verbal responses? In the process of investigating propositional language, there was opportunity to explore the performance of Frontal and Posterior patients on verbal and non-verbal fluency tasks. The group study included a fine-grained method of lesion analysis developed by Stuss and colleagues (2002). This revealed more specific Frontal deficits and a somewhat different overall pattern for Medial and Lateral patients. Medial patients were impaired on almost every fluency task. In contrast, Lateral patients showed a more selective pattern for verbal and non-verbal items. Specifically, only the Left Lateral group had a phonemic fluency deficit and only the Right Lateral group had a design fluency deficit, although Medial deficits were evident on both. This provides some support for the idea of material-specific lateralisation within the frontal lobes. However, this is not the complete picture as a semantic fluency deficit was present in all frontal subgroups. In comparison to Controls, Frontal patients were impaired on all fluency tasks. This Frontal deficit was only selective (i.e., no Posterior deficit) for the generation of designs, gestures and novel uses of objects.

The lesion and imaging data partially converge for fluency tasks. As discussed in Chapter 4, overlap occurs in the left dorsolateral region for phonemic and semantic fluency and in the left posterior region for semantic fluency (e.g., Frith et al., 1991b; Klein et al., 1997; Mummery et al., 1996; Phelps et al., 1997; Warburton et al., 1996). However, imaging studies fail to reveal the less severe deficits found in the group study (e.g., Superior Medial, Inferior Medial and Right Lateral deficits for semantic fluency, Posterior deficit for phonemic fluency). The discrepancy between findings highlights the importance of fine-grained lesion studies in identifying all regions involved in a task and not just the region of greatest involvement. The data for design, ideational and gesture fluency tasks less clearly support specific frontal regions. Further fine-grained lesion and imaging studies are needed to explore the voluntary generation of novel responses, particularly in the non-verbal domain (e.g., gesture and design fluency).

5.5 CONCLUSIONS

These data strongly suggest that propositional language generation involves at least two distinct cognitive mechanisms that are supported by different anatomical substrates. One cognitive mechanism is responsible for *high-level selection among competing verbal response options.* This mechanism is specific to the language domain and is implemented by the left inferior frontal region. The second cognitive mechanism is responsible for *generating a fluent sequence of novel thought.* It encompasses the generation of novel verbal and non-verbal responses and is supported by the bilateral frontal region. This second mechanism is not specific to language, but within language the domain is discourse generation. These data also confirm a role of the frontal lobes in the primary voluntary generation of novel verbal and non-verbal responses. In broad terms, the data speaks to a distinction between the processes of language and thought.

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APPENDICES

APPENDIX 1: Item Analysis for Meaningful Sentence Completion: Number of occasions CH generated a correct response for each sentence across three trials.

	Number Correct			
Level of Constraint	3/3 trials	2/3 trials	1/3 trials	0/3 trials
Very High Constraint (VHC) = 0.93	27	3	0	2
Medium-High Constraint (MHC) = 0.73	19	8	4	1
Low Constraint (LC) = 0.53	15	9	4	4
Very Low Constraint (VLC)= 0.20	9	8	8	7

APPENDIX 2: Case Reports for the Patient Controls of Dynamic Aphasic KAS

Progressive Supranuclear Palsy (PSP) Patient Control

This 74-year-old, right-handed, female retired actress first noted a change in walking at the age of 68. From the age of 70, speech was noted to have slowed but to have remained clearly intelligible. The inpatient admission concurrent with the present investigation was to review status. On neurological examination, she was found to have a severe vertical supranuclear gaze palsy, mild limitation of horizontal eye movements and dysarthric speech. Mini-Mental State Examination was 29/30. MRI revealed generalised cerebral volume loss, with no particular midbrain or hippocampal volume loss.

Cognitive Function Baseline

The PSP patient control was assessed on the shortened version of the WAIS-R and obtained average Verbal and Performance IQ's (see Table 11). On Recognition Memory Tests (Warrington, 1984; 1996), she obtained a high average score for words. Although her performance was impaired for faces, she obtained an average score for topography. Visual perceptual skills, as assessed by the Object Decision test (Warrington et al., 1991), were entirely within normal limits.

Frontal Executive Function

Mild impairment was noted in her performance on tests sensitive to executive dysfunction (See Table 11). Although she obtained 6/6 categories on the Modified Card Sorting Test (Nelson, 1976), several perseverative errors were made. Proverb interpretations were mildly concrete. Performance on the Stroop Test (Stroop, 1935) was impaired. Verbal fluency was in the average range for a phonemic task and in the low average range for a semantic task (animals = 12 names; Spreen et al., 1998).

Language Function Baseline

Spontaneous speech was very slow and somewhat dysprosodic but well articulated and fluent, with normal syntax. There was no evidence of nominal difficulties as an average score was obtained on the Graded Naming Test (McKenna et al., 1980; see Table 13). Reading ability on the NART was within the high average range (Nelson et al., 1991).

Summary

The PSP patient presented with a mild to moderate intellectual decline and frontal executive difficulties. By contrast, memory and visuoperceptual functions were satisfactory. Although spontaneous speech was slow, there was no evidence of aphasia, and specifically dynamic aphasia.

Left Frontal Lesion (LF) Patient Control

This 40-year-old, right-handed, female teacher suffered a left frontal bleed two years previously. Following the bleed, she experienced epilepsy that was subsequently controlled by phenytoin. Examination was normal. MRI at the time of the bleed revealed a large left frontal haemorrhage involving the inferior and middle frontal gyri, with some surrounding oedema.

Cognitive Function Baseline

The LF control patient obtained a superior score on an un-timed, nonverbal test of general intelligence (Advanced Progressive Matrices, Set 1, Raven, 1976a; see Table 11). This is in keeping with the estimated high average premorbid level of optimal function. On the Recognition Memory Test (Warrington, 1984), she obtained an average score for words and a high average score for faces. Visual perceptual skills, as assessed by the Incomplete Letters test (Warrington et al., 1991), were entirely within normal limits.

Frontal Executive Function

Performance on some tests sensitive to executive dysfunction was mildly impaired (see Table 11). Performance was mildly impaired and in the lower end of the average range on the Trail Making Test (Army Individual Test Battery, 1944) and Hayling Sentence Completion Test (Burgess et al., 1996b). Further, Proverb interpretations were mildly concrete and verbal fluency was mildly reduced although within the average range (Spreen et al., 1998). By contrast, the Stroop (1935) and Cognitive Estimates Tests (Shallice et al., 1978) were both passed.

Language Function Baseline

Spontaneous speech was well articulated and fluent, with normal prosody and syntax. Repetition of sentences was flawless (see Table 13). There was no evidence of nominal difficulties as a superior score was obtained on the Graded Naming Test (McKenna et al., 1980). Word comprehension skills were intact and in the high average range (Synonyms Test, Warrington et al., 1998). Reading ability on the NART was in the high average range (Nelson et al., 1991).

Summary

The LF patient presented with mild executive difficulties. This was in the context of intact intellectual, memory, visuoperceptual and language functions. In particular, spontaneous speech was fluent and there was no evidence for any aphasia including dynamic aphasia.

Severe Frontal Executive Dysfunction (TBI) Patient Control

This 42-year-old, right-handed, male engineer suffered a traumatic brain injury two years previously. Following the accident, a bi-frontal decompressive craniotomy was performed due to severe oedema. MRI revealed bi-frontal and right temporal lobe contusions. Neurological examination was normal apart from the cognitive impairments described below.

Cognitive Function Baseline

The TBI patient control obtained a low average score on the Verbal scale and an impaired score on the Performance scale of the WAIS-R (see Table 11). Performance was borderline impaired on an un-timed, nonverbal test of general intelligence (Advanced Progressive Matrices, Set 1, Raven, 1976a). These scores reflect severe intellectual decline from the estimated high average/superior premorbid level of optimal function. On the short and easy version of the Recognition Memory Test (Clegg et al., 1994), performance was impaired for verbal and visual material. Visual perceptual skills, as assessed by the Incomplete Letters Test (Warrington et al., 1991), were normal.

Frontal Executive Function

Performance on tests sensitive to executive dysfunction was severely impaired (see Table 11). All tests were failed including a simple version of the Stroop Test (1935), the Weigl Test (1941), the Trail Making Test (Army Individual Test Battery, 1944), the Cognitive Estimates Test (Shallice et al., 1978), the Modified Card Sorting Test (Nelson, 1976), the Hayling Sentence Completion Test (Burgess et al., 1996b), and the Brixton Test (Burgess et al., 1996a). In addition, all Proverb interpretations were concrete.

Language Function Baseline

Spontaneous speech was well articulated and fluent, with normal prosody and syntax. Repetition of sentences was flawless (see Table 13). There was a mild nominal dysphasia as an average score was obtained on the Graded Naming Test (McKenna et al., 1980). Word comprehension skills were intact and in the high average range (Synonyms Test, Warrington et al., 1998). Reading ability on the NART was in the high average range (Nelson et al., 1991).

Summary

The TBI patient presented with marked frontal executive dysfunction and severe intellectual and global memory impairments. This was in the context of intact visuoperceptual and relatively well preserved language functions. In particular, spontaneous speech was fluent and there was no evidence for dynamic aphasia.

APPENDIX 3: Lesion Analysis Coding Form

Subject ID:	**Left**	**Right**
Frontal		
Lateral		
Inferior frontal gyrus - anterior		
Inferior frontal gyrus - posterior		
Middle frontal gyrus - anterior		
Middle frontal gyrus - posterior		
Medial		
Superior frontal gyrus – anterior		
Superior frontal gyrus - posterior		
Cingulate cortex - anterior		
Cingulate cortex - posterior		
Orbital Frontal		
Basal Ganglia (Striatum)		
Caudate nucleus		
Putamen		
Globus pallidus		
Nonfrontal		
Temporal		
Parietal		
Occipital		

Provide a numerical rating scale for severity of damage in each of the areas of interest:
None = 0, mild = 1, moderate = 2, severe = 3, very severe = 4

Other Comments:

APPENDIX 4: Lesion Location* and Group for Level 2, 3 and 4 Analyses for Frontal Patients

Patient Number	Lesion Location*	Group for Level 2 Analysis	Group for Level 3 Analysis	Group for Level 4 Analysis
1	LLat (+CN, Put)	LF	LLat	Non-LIFG
3	LLat, SMIM(+CN, Put)	LF	-	LIFG
7	LLat, SM (+CN)	LF	-	LIFG
9	LLat	LF	LLat	LIFG
10	LLat, SM	LF	LLat	LIFG
11	IM (L only)	LF	IM	Non-LIFG
12	SM	LF	SM	Non-LIFG
13	LLat, SM	LF	LLat	LIFG
14	LLat	LF	LLat	Non-LIFG
15	SMIM, LLat (+CN)	LF	SM	Non-LIFG
16	LLat, SMIM (L only)	LF	-	LIFG
17	SMIM, LLat (+CN)	LF	SM	Non-LIFG
18	LLat, SMIM	LF	LLat	Non-LIFG
59	SM, LLat	LF	SM	LIFG
60	LLat (+CN, Put, Parietal)	LF	LLat	Non-LIFG
61	*Scan unavailable for detailed analysis*	LF	-	-
19	RLat	RF	RLat	Non-LIFG
20	RLat, SMIM (+CN, Put)	-	-	Non-LIFG
22	RLat, IM	RF	-	Non-LIFG
24	RLat (+parietal)	RF	RLat	Non-LIFG
25	RLat	RF	RLat	Non-LIFG
26	RLat, SM	RF	RLat	Non-LIFG
27	SM, RLat	RF	SM	Non-LIFG
28	RLat, SMIM, (+CN)	RF	-	Non-LIFG
30	RLat, SMIM	RF	-	Non-LIFG
34	RLat. (+CN)	RF	RLat	Non-LIFG
53	RLat, (+CN, +parietal)	RF	RLat	Non-LIFG
54	RLat, IM (+CN)	RF	-	Non-LIFG
58	SM	RF	SM	Non-LIFG
51	*Scan unavailable for detailed analysis*	RF	-	Non-LIFG
63	SM (R only)	RF	SM	Non-LIFG
55	SMIM (R only)	RF	SM	Non-LIFG
21	IM (R only)	RF	IM	Non-LIFG
29	IM (R only)	RF	IM	Non-LIFG
32	RLat, LLat	-	-	LIFG
62	LLat RLat	-	-	LIFG
5	SMIM, LLat, RLat	-	-	Non-LIFG
6	IM (+CN, Put) (bilaterally)	-	IM	Non-LIFG
8	IM (+CN) (bilaterally)	-	IM	Non-LIFG

Note: * = lesion location detailed in Table 2; LF = Left Frontal; RF = Right Frontal; LLat = left lateral; RLat = right lateral; SM = superior medial; SMIM = superior and inferior medial; IM = inferior medial; CN = caudate nucleaus; Put = putamen; - = not included in analysis.

APPENDIX 5: Baseline Cognitive, Language and Frontal/Executive Tests: Insignificant Analyses

Level 1 Analysis

Ref	Test	ANOVA/ t-test/ Kruskal-Wallis Result
1.1	Advanced Progressive Matrices Mean Score	$F_{(2,77)} = 1.741, p = 0.182$
1.2	Mean Recognition Memory Test Score: Words	$t_{(42)} = -.559, p = 0.579$
	Faces	$t_{(42)} = -0.558, p = 0.580$
1.3	Synonym Test Score	$F_{(2,80)} = 3.006, p = 0.055$
1.4	Cognitive Estimates Error Score	$\chi^2_{(2)} = 4.654, p = 0.098$
1.5	Trail Making A time	$F_{(2,65)} = 3.011, p = 0.056$
1.6	Stroop Colour Ink Naming Error Score	$\chi^2_{(2)} = 2.483, p = 0.289$

Level 2 Analysis

Ref	Test	ANCOVA/Mann-Whitney U Result
2.1	Advanced Progressive Matrices Mean Score	$F_{(2,33)} = 1.684, p = 0.201$
	Covariate of Age	$F_{(1,33)} = 5.491, p = 0.025$
2.2	Mean Recognition Memory Test Score: Words	$F_{(1,27)} = 2.154, p = 0.154$
2.3	Mean Incomplete Letters Test Score	$F_{(1,30)} = 1.139, p = 0.294$
2.4	Complex Scene Description: Fluency	$\chi^2_{(1)} = 3.566, p = 0.059$
	Quantity Produced	$\chi^2_{(1)} = 0.010, p = 0.922$
2.5	Sentence Repetition Score	$U = 100.500, p = 0.057$
2.6	Graded Naming Test Score	$F_{(1,30)} = 0.016, p = 0.901$
2.7	Synonym Test Score	$F_{(1,29)} = 0.604, p = 0.443$
2.8	Cognitive Estimates: Error Score	$F_{(1,27)} = 0.033, p = 0.857$
	Pass/Fail	$\chi^2_{(2)} = 0.271, p = 0.602$
2.9	Trail Making A time	$F_{(1,28)} = 0.113\ p = 0.739$
2.10	Trail Making B time	$F_{(1,28)} = 0.106\ p = 0.748$
	Covariate Age	$F_{(1,28)} = 7.400\ p = 0.011$
2.11	Stroop colour word reading score	$F_{(1,28)} = 0.766\ p = 0.389$
2.12	Stroop colour ink naming measure	$U = 91.000, p = 0.569$
2.13	Stroop colour ink naming error measure	$F_{(1,26)} = .258, p = 0.615$
2.14	Mean Proverb Test Score	$F_{(1,29)} = 1.041, p = 0.316$
2.15	Hayling Overall Score	$F_{(1,29)} = 0.422, p = 0.521$
	Covariate Age	$F_{(1,29} = 11.418, p = 0.002$
2.16	Hayling Initiation condition RT	$F_{(1,29)} = 3.975, p = 0.056$
2.17	Hayling Suppression condition RT	$F_{(2,31)} = 0.055, p = 0.946$
2.18	Hayling Suppression Condition Errors	$F_{(1,29)} = 0.001, p = 0.981$
	Covariate Age	$F_{(1,29)} = 7.588, p = 0.010$

Level 3 Analysis

Ref	Test	Left Lateral	Right Lateral	Superior Medial	Inferior Medial	Control	ANOVA/ Kruskal-Wallis Result
3.1	Graded Naming Test Score (SD)	20.00 (5.8)	19.83 (5.7)	19.38 (3.1)	18.40 (2.1)	22.27 (4.9)	$F_{(4,54)} = 1.384$, $p = 0.252$
3.2	Cognitive Estimates Test Pass (0-6)	4	5	5	4	26	$\chi^2_{(2)} = 5.690$,
	Fail (7+)	1	1	3	0	2	$p = 0.224$
3.3	Trail Making B time (SD)	104.33 (55.2)	149.33 (104.5)	97.75 (49.0)	167.00 (131.2)	76.10 (30.3)	$\chi^2_{(4)} = 6.094$, $p = 0.192$
3.4	Stroop Colour Word Reading Score (SD)	201.67 (83.3)	184.17 (43.5)	177.38 (55.4)	195.25 (32.1)	229.25 (67.8)	$F_{(4,51)} = 1.540$, $p = 0.205$
3.5	Stroop Colour Ink Naming Score (SD)	92.20 (44.5)	89.50 (33.9)	96.25 (19.6)	81.75 (26.9)	106.19 (21.5)	$\chi^2_{(4)} = 3.912$, $p = 0.418$
3.6	Stroop Colour Ink Naming Error Score (SD)	1.00 (1.7)	4.67 (6.9)	0.88 (1.5)	0.75 (0.5)	1.38 (1.8)	$\chi^2_{(4)} = 2.330$, $p = 0.666$
3.7	Hayling Initiation Condition RT (SD)	4.57 (1.5)	5.50 (0.5)	4.63 (1.8)	4.75 (1.5)	5.72 (1.1)	$F_{(4,52)} = 2.384$, $p = 0.063$

APPENDIX 6: Fluency Experimental Tests: Insignificant Analyses

Level 1 Analysis

Ref	Test	ANOVA/Kruskal-Wallis Result
1.1	Phonemic Fluency: perseverative errors	$\chi^2_{(2)} = 1.646$, p = 0.439
1.2	Semantic Fluency – Living Things: perseverative errors	$\chi^2_{(2)} = 1.676$, p = 0.433
1.3	Semantic Fluency – Fruit/Vegetables: perseverative errors	$F_{(2,86)} = 0.106$, p = 0.900
1.4	Semantic Fluency – Fruit/Vegetables: inappropriate errors	$\chi^2_{(2)} = 5.655$, p = 0.059
1.5	Design Fluency – Free: perseverative errors	$F_{(2,85)} = 0.090$, p = 0.914
1.6	Design Fluency – Free: inappropriate errors	$\chi^2_{(2)} = 0.467$, p = 0.792
1.7	Design Fluency – Fixed: perseverative errors	$F_{(2,85)} = 0.036$, p = 0.965
1.8	Design Fluency – Fixed: inappropriate errors	$F_{(2,85)} = 0.375$, p = 0.689
1.9	Ideational Fluency – Conventional Uses: inappropriate errors	$\chi^2_{(2)} = 3.725$, p = 0.155
1.10	Ideational Fluency – Unconventional Uses: perseverative errors	$\chi^2_{(2)} = 2.381$, p = 0.304
1.11	Ideational Fluency – Unconventional Uses: inappropriate errors	$F_{(2,85)} = 0.608$, p = 0.547
1.12	Gesture Fluency – Meaningless: perseverative errors	$F_{(2,84)} = 0.006$, p = 0.994
1.13	Gesture Fluency – Meaningless: inappropriate errors	$\chi^2_{(2)} = 1.995$, p = 0.369
1.14	Gesture Fluency – Meaningful: perseverative errors	$\chi^2_{(2)} = 2.446$, p = 0.294
1.15	Gesture Fluency – Meaningful: inappropriate errors	$\chi^2_{(2)} = 4.056$, p = 0.132

Level 2 Analysis

Ref	Test	ANOVA/ Mann-Whitney U Result
2.1	Phonemic Fluency- perseverative errors	U = 104.500, p = 0.170
2.2	Phonemic Fluency- inappropriate errors	$F_{(1,30)} = 0.527$, p = 0.473
2.3	Semantic Fluency – Living Things: number generated	$F_{(1,30)} = 1.599$, p = 0.216
2.4	Semantic Fluency – Living Things: perseverative errors	$F_{(1,30)} = 1.494$, p = 0.231
2.5	Semantic Fluency – Living Things: inappropriate errors	U = 106.000, p = 0.195
2.6	Semantic Fluency – Fruit/Vegetables: number generated	$F_{(1,30)} = 0.569$, p = 0.456
2.7	Semantic Fluency – Fruit/Vegetables: perseverative errors	U = 113.000, p = 0.289
2.8	Semantic Fluency – Fruit/Vegetables: inappropriate errors	$F_{(1,30)} = 0.091$, p = 0.765
2.9	Design Fluency – Free: number generated	$F_{(1,29)} = 3.154$, p = 0.086
2.10	Design Fluency – Free: perseverative errors	$F_{(1,29)} = 0.282$, p = 0.600
2.11	Design Fluency – Fixed: perseverative errors	$F_{(1,29)} = 0.079$, p = 0.781
2.12	Design Fluency – Fixed: inappropriate errors	$F_{(1,29)} = 3.469$, p = 0.073
2.13	Ideational Fluency – Conventional Uses: number generated	$F_{(1,29)} = 0.503$, p = 0.484

2.14	Ideational Fluency – Conventional Uses: perseverative errors	$F_{(1,29)} = 0.260, p = 0.614$
2.15	Ideational Fluency – Conventional Uses: inappropriate errors	$F_{(1,29)} = 2.344, p = 0.137$
2.16	Ideational Fluency – Unconventional Uses: number generated	$F_{(1,29)} = 1.236, p = 0.275$
2.17	Ideational Fluency – Unconventional Uses: perseverative errors Covariate Age	$F_{(1,29)} = 2.688, p = 0.112$ $F_{(1,29)} = 5.079, p = 0.032$
2.18	Ideational Fluency – Unconventional Uses: inappropriate errors	$U = 88.500, p = 0.102$
2.19	Gesture Fluency – Meaningless: number generated	$F_{(1,29)} = 0.026, p = 0.874$
2.20	Gesture Fluency – Meaningless: perseverative errors	$F_{(1,29)} = 0.233, p = 0.633$
2.21	Gesture Fluency – Meaningless: inappropriate errors	$F_{(1,29)} = 0.130, p = 0.721$
2.22	Gesture Fluency – Meaningful: number generated	$U = 119.000, p = 0.747$
2.23	Gesture Fluency – Meaningful: inappropriate errors	$F_{(1,29)} = 0.474, p = 0.497$

Level 4 Analysis

Ref	Test	ANOVA/ Mann-Whitney U Result
4.1	Phonemic Fluency- perseverative errors	$\chi^2_{(2)} = 1.811, p = 0.404$
4.2	Semantic Fluency – Living Things: perseverative errors	$F_{(2,70)} =.349, p = 0.706$
4.3	Semantic Fluency – Fruit/Vegetables: perseverative errors	$F_{(2,70)} = 0.046, p = 0.955$
4.4	Design Fluency – Free: perseverative errors	$F_{(2,69)} = 0.048, p = 0.953$
4.5	Design Fluency – Free: inappropriate errors	$F_{(2,69)} = 0.040, p = 0.960$
4.6	Design Fluency – Fixed: perseverative errors	$\chi^2_{(2)} = 440\ p = 0.802$
4.7	Design Fluency – Fixed: inappropriate errors	$\chi^2_{(2)} = 4.486\ p = 0.106$
4.8	Ideational Fluency – Conventional Uses: inappropriate errors	$\chi^2_{(2)} = 3.338, p = 0.188$
4.9	Ideational Fluency – Unconventional Uses: perseverative errors	$\chi^2_{(2)} = 0.678, p = 0.713$
4.10	Ideational Fluency – Unconventional Uses: inappropriate errors	$F_{(2,69)} =.288, p = 0.751$
4.11	Gesture Fluency – Meaningless: perseverative errors	$F_{(2,68)} =.937, p = 0.397$
4.12	Gesture Fluency – Meaningless: inappropriate errors	$\chi^2_{(2)} = 4.349, p = 0.114$
4.13	Gesture Fluency – Meaningful perseverative errors	$\chi^2_{(2)} = 2.122, p = 0.346$
4.14	Gesture Fluency – Meaningful: inappropriate errors	$\chi^2_{(2)} = 3.975, p = 0.137$

APPENDIX 7: Word and Sentence Generation Stimuli

Generation of a sentence from a word

* stimuli used in the picture version

Proper Nouns	*High Frequency words*	*Low Frequency words*
Hitler*	table*	thimble
Eiffel Tower*	plant*	bagpipe
Italy*	children*	claw
Mona Lisa *	wall*	helmet
Gandhi*	man*	hockey
South America*	water*	kite
Napoleon*	face *	tutu
George W Bush*	picture*	leotard
Twin Towers	time	pagoda
London	history	monocle
Tony Blair	family	sporran
Afghanistan	room	sundial
Beatles	law	chopsticks
David Beckham	mother	trampoline
Ireland	moment	shuttlecock
(n = 15)	*(n=15)*	*(n=15)*

Generation of a sentence from a word (or picture) pair

NB: all stimuli used in the word and picture version

High Association word pairs		*Low Association word pairs*	
butter	bread	butter	finger
doctor	nurse	doctor	church
road	car	road	tree
shoe	foot	foot	rat
baby	child	baby	shoes
bath	water	bath	basketball
door	knob	door	wood
chair	table	chair	wheel
giraffe	neck	cat	neck
hammer	nail	hammer	sock
spider	web	spider	dog
green	grass	green	milk
hand	ring	hand	heel
needle	thread	needle	nose
river	fish	river	tile
	(n=15)		*(n=15)*

Sentence completion from a sentence

Very Constrained

Bill jumped in the lake and made a big ...
Joan fed her baby some warm...
He loosened the tie around his ...
Water and sunshine help plants ...
To keep the dogs out of the yard he put up a..
Father carved the turkey with a ...
His job was to keep the sidewalk...
To pay for the car Al simply wrote a...
The children went outside to...
The movie was so jammed they couldn't find a single...
She went to the salon to colour her...
They sat together without speaking a single...
The lecture should last about one...
I could not remember his...
The paint turned out to be the wrong...

(n=15)

Very Low Constrained

Seth couldn't imagine anyone less...
There's something grand about the...
There was nothing wrong with the...
The sun went down before we could...
The Smiths had never visited that...
The kind old man asked us to...
They went to see the famous...
Even infants can be taught to...
His ability to work was...
The police had never seen a man so...
He was soothed by the gentle...
You could count on Dale for being late for ...
Sometimes success is simply a matter of ...
He wondered if the storm would be ...
The difficult concept was beyond his ...

(n=15)

Generation of a sentence given a pictorial scene

dentist
mountain climber
chef
beggar
football
barber
broken window
library
skater
watching tv

(n = 10)

APPENDIX 8: Word and Sentence Generation Experimental Tests: Insignificant Analyses

Level 1 Analysis

Ref	Test	ANOVA/Kruskal-Wallis Result
1.1	Sentence Completion: High Constraint Score	$\chi^2_{(2)}$ = 2.672, p = 0.263
1.2	Sentence Generation: Proper Noun (word) RT	$F_{(2,86)}$ = 1.849, p = 0.164
1.3	Sentence Generation: High Frequency Word (word) RT	$F_{(2,86)}$ = 1.364, p = 0.261
1.4	Sentence Generation: Low Frequency Word (word) Score	$\chi^2_{(2)}$ = 5.867, p = 0.053
1.5	Sentence Generation: Low Frequency Word (word) RT	$F_{(2,86)}$ = 2.659, p = 0.076
1.6	Sentence Generation: High Association Word Pair Score	$\chi^2_{(2)}$ = 4.842, p = 0.089
1.7	Sentence Generation: High Association Word Pair RT	$\chi^2_{(2)}$ = 2.137, p = 0.343
1.8	Sentence Generation: Low Association Word Pair RT	$\chi^2_{(2)}$ = 4.861, p = 0.088
1.9	Sentence Generation: Proper Noun (picture) RT	$\chi^2_{(2)}$ = 2.970, p = 0.226
1.10	Sentence Generation: High Frequency (picture) RT	$\chi^2_{(2)}$ = 5.557, p = 0.062
1.11	Sentence Generation: High Association Picture Pair RT	$F_{(2,84)}$ = 1.538, p = 0.221
1.12	Sentence Generation: Low Association Picture Pair RT	$F_{(2,84)}$ = 0.418, p = 0.659
1.13	Sentence Generation: Pictorial Scene Score	$\chi^2_{(2)}$ = 3.629, p = 0.163
1.14	Sentence Generation: Pictorial Scene RT	$F_{(2,81)}$ = 1.017, p = 0.366

Level 2 Analysis

Ref	Test	ANCOVA/ Mann-Whitney U Result
2.1	Sentence Completion: High Constraint RT	$F_{(1,30)}$ = 0.531, p = 0.472
2.2	Sentence Completion: Low Constraint RT	$F_{(1,30)}$ = 0.436, p = 0.514
2.3	Sentence Generation: Proper Noun (word) Score	$F_{(1,30)}$ = 0.250, p = 0.621
2.4	Sentence Generation: Proper Noun (word) RT	$F_{(1,30)}$ = 1.023, p = 0.320
2.5	Sentence Generation: High Frequency Word (word) Score	$F_{(1,30)}$ = 1.356, p = 0.253
2.6	Sentence Generation: High Frequency Word (word) RT	$F_{(1,30)}$ = 0.005, p = 0.943
2.7	Sentence Generation: Low Frequency Word (word) Score	$F_{(1,30)}$ = 0.863, p = 0.360
2.8	Sentence Generation: Low Frequency Word (word) RT	$F_{(1,30)}$ = 1.065, p = 0.310
2.9	Sentence Generation: High Association Word Pair Score	U = 132.000, p = 0.817
2.10	Sentence Generation: High Association Word Pair RT Covariate Age	$F_{(1,29)}$ = 0.335, p = 0.567 $F_{(1,29)}$ = 5.029, p = 0.033
2.11	Sentence Generation: Low Association Word Pair Score	$F_{(1,30)}$ = 2.647, p = 0.114
2.12	Sentence Generation: Low Association Word Pair RT	U = 117.000, p = 0.692
2.13	Sentence Generation: Proper Noun (picture) Score	$F_{(1,29)}$ = 0.127, p = 0.724

2.14	Sentence Generation: Proper Noun (picture) RT	$F_{(1,29)} = 0.000$, $p = 0.988$
2.15	Sentence Generation: High Frequency (picture) Score	$U = 95.000$, $p = 0.067$
2.16	Sentence Generation: High Frequency (picture) RT	$F_{(1,29)} = 0.023$, $p = 0.879$
2.17	Sentence Generation: High Association Picture Pair Score	$F_{(1,28)} = 0.150$, $p = 0.701$
2.18	Sentence Generation: High Association Picture Pair RT	$F_{(1,28)} = 0.001$, $p = 0.977$
2.19	Sentence Generation: Low Association Picture Pair Score	$F_{(1,28)} = 0.934$, $p = 0.342$
2.20	Sentence Generation: Low Association Picture Pair RT	$F_{(1,28)} = 0.031$, $p = 0.862$
2.21	Sentence Generation: Pictorial Scene Score	$F_{(1,27)} = 0.078$, $p = 0.782$
2.22	Sentence Generation: Pictorial Scene RT	$F_{(1,27)} = 0.581$, $p = 0.453$

Level 3 Analysis

Ref	Test	Left Lateral	Right Lateral	Superior Medial	Inferior Medial	Control	ANOVA/ Kruskal-Wallis Result
3.1	Sentence Completion: High Constraint Score (SD)	14.4 (1.1)	15.0 (0.0)	15.0 (0.0)	15.0 (0.0)	14.9 (0.3)	$\chi^2_{(4)} = 5.729$ $p = 0.220$
3.2	Sentence Completion: High Constraint RT (SD)	1.21 (1.0)	1.29 (0.9)	0.78 (0.3)	1.72 (1.9)	0.71 (0.4)	$F_{(4,56)} = 2.187$ $p = 0.082$
3.3	Sentence Completion: Low Constraint RT (SD)	3.96 (4.3)	3.87 (2.4)	3.50 (1.9)	3.86 (2.4)	2.32 (1.3)	$F_{(4,56)} = 2.115$ $p = 0.091$
3.4	Sentence Generation: Proper Noun (word) Score (SD)	14.86 (0.4)	15.00 (.0)	14.75 (0.5)	13.80 (2.7)	14.97 (0.2)	$\chi^2_{(4)} = 6.095$ $p = 0.192$
3.5	Sentence Generation: High Frequency Word Score (SD)	13.43 (4.2)	14.67 (0.5)	14.38 (1.4)	12.00 (6.7)	14.94 (0.2)	$\chi^2_{(4)} = 4.919$ $p = 0.296$
3.6	Sentence Generation: Proper Noun Picture Score (SD)	7.29 (1.9)	7.83 (0.4)	7.75 (0.7)	7.40 (0.5)	7.89 (0.4)	$\chi^2_{(4)} = 8.036$ $p = 0.090$
3.7	Sentence Generation: High Frequency Picture Score (SD)	7.29 (1.5)	7.83 (0.4)	7.88 (0.4)	6.00 (3.1)	7.91 (0.4)	$\chi^2_{(4)} = 7.137$ $p = 0.129$

Level 4 Analysis

Ref	Test	ANOVA/Kruskal-Wallis Result
4.1	Sentence Completion: High Constraint Score	$\chi^2_{(2)}$ = 1.265, p = 0.531
4.2	Sentence Generation: Proper Noun Word Score	$\chi^2_{(2)}$ = 4.751, p = 0.093
4.3	Sentence Generation: Proper Noun Word RT	$F_{(2,70)}$ = 1.300, p = 0.279
4.4	Sentence Generation: High Frequency Word RT	$F_{(2,70)}$ = 1.052, p = 0.355
4.5	Sentence Generation: Low Frequency Word Score	$F_{(2,70)}$ = 1.063, p = 0.351
4.6	Sentence Generation: Low Frequency Word RT	$F_{(2,70)}$ = 1.021, p = 0.365
4.7	Sentence Generation: High Association Word Pair Score	$\chi^2_{(2)}$ = 4.060, p = 0.131
4.8	Sentence Generation: High Association Word Pair RT	$F_{(2,69)}$ = 0.720, p = 0.490
4.9	Sentence Generation: Low Association Word Pair RT	$\chi^2_{(2)}$ = 3.033, p = 0.220
4.10	Sentence Generation: Proper Noun (picture) Score	$\chi^2_{(2)}$ = 5.489, p = 0.064
4.11	Sentence Generation: Proper Noun (picture) RT	$F_{(2,69)}$ =.208, p = 0.813
4.12	Sentence Generation: High Frequency (picture) RT	$F_{(2,69)}$ =.065, p = 0.937
4.13	Sentence Generation: High Association Picture Pair RT	$F_{(2,68)}$ = 0.761, p = 0.471
4.14	Sentence Generation: Low Association Picture Pair RT	$F_{(2,68)}$ = 0.026, p = 0.975
4.15	Sentence Generation: Pictorial Scene Score	$\chi^2_{(2)}$ = 3.142, p = 0.208
4.16	Sentence Generation: Pictorial Scene RT	$F_{(2,65)}$ = 0.430 p = 0.652