

**EARLY ONSET FRONTOTEMPORAL
DEMENTIA AND ALZHEIMERS DISEASE:
DIAGNOSIS, TREATMENT AND CARE**

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This thesis is presented as partial requirement for the degree of Doctor of Psychology at Murdoch University, 2007.

I declare that this thesis is my account of my research and contains as its main content work which has not previously been submitted for a degree at a tertiary education institution.

John Rudge

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Abstract

This research investigated two groups of patients diagnosed with dementia before the age of sixty-five. The patients were diagnosed with Alzheimer's Disease (AD, n = 25) and Frontotemporal Dementia (FTD, n = 37). Patients were assessed for approximately 3 years. The study found that FTD is a valid and useful diagnostic category, and can be reliably differentiated from AD. A combination of behavioural, neurological, and neuropsychological assessments were found to be complementary in the early and accurate diagnosis of early-onset dementia, and the differential diagnosis of FTD from AD. FTD patients were found to have relatively preserved visuo-spatial abilities compared to the AD patients. Problems associated with administering neuropsychological tests to early-onset dementia patients were highlighted. FTD patients were found to deteriorate more rapidly than AD patients, and to have significantly increased behavioural disturbances throughout the course of the illness in comparison with the AD patients. Practical guidelines to assist with care and management of early-onset dementia patients were presented. A strengths-based model of care was outlined. Individualised assessments and care plans were recommended for the development and provision of humane services to early-onset dementia patients. Issues surrounding providing palliative care were discussed.

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“In striking contrast to Alzheimer’s Disease, the majority of dementia of the frontal type patients are brought along to the clinic blissfully unaware of the major changes of personality and behaviour observed by their relatives.”

Gregory & Hodges, 1996, p.111

“The frontal lobes are both massive and neuroanatomically diverse. Their size predicates against generalisations; pathological involvement of different loci within the frontal lobes can be anticipated to produce quite different behavioural alterations. The uniqueness of the human prefrontal lobes removes the ability to use relatively clean animal studies for correlation: only human case material is valid. Thus the type of neuropathology and its relatively focal nature is of paramount importance to investigations of human frontal lobe functions”

Stuss and Benson 1986, p. 39

CHAPTER 1

INTRODUCTION

“Caring for patients with Frontotemporal Dementia necessitates a whole new category of research”.

Passant & Elfgren et al. 2005, p. 17

1.1 OUTLINE OF CURRENT STUDY

1.1.1 Early Onset Dementia

This research investigates conditions affecting people with early-onset dementia. A diagnosis of early-onset dementia is commonly given only if a person develops dementia before the age of sixty-five (Harvey, 1998; McMurtray, & Clark, 2006). In recent years, this group of younger early-onset dementia patients has become of increasing interest to researchers, specialists, and care providers (Harvey, 1998; McMurtray, & Clark, 2006).

Early and accurate diagnosis of specific dementia sub-types has become increasingly important as new behavioural and pharmaceutical interventions become available to assist with the management and treatment of these high care-need patients (Miller & Cummings, 1999; Pasquier, 1999; Rosen & Hartikainen et al. 2002; Pasquier & Richard et al. 2004; van Reekum & Binns et al. 2005; Chapman & Williams et al. 2006). Knibb et al. (2006) make the point that revisions may be necessary to improve the validity and applicability of diagnoses of dementia, and suggest that “Further

research should aim to integrate detailed clinical, radiological, pathological and genetic information". This study has been designed to investigate the relatively new diagnostic category of Frontotemporal Dementia, evaluate current assessment protocols, and most importantly, to provide practical guidelines to assist with care and management of early-onset dementia patients. There have been few systematic studies of the management and treatment of Frontotemporal Dementia (Diehl-Schmid & Pohl et al. 2006; Ishikawa & Shimomura et al. 2006).

This research explores two groups of patients diagnosed with dementia before the age of sixty-five. The groups are patients diagnosed with Alzheimer's Disease (n = 25) and Frontotemporal Dementia (n = 37). The study explores the syndromes associated with Frontotemporal Dementia (FTD), and the differential diagnosis of Frontotemporal Dementia from Alzheimer's Disease (AD).

The study assesses the two groups using clinical interviews with the patients, interviews with the patients' primary carers, and behavioural observations over a period of between two years and nine months and three years and three months for each patient. Patients are assessed with a range of standardised neuropsychological measures. Neuropsychological test performance is evaluated qualitatively and quantitatively. Problems associated with administering neuropsychological measures to early-onset Alzheimer's Disease and Frontotemporal Dementia populations are highlighted.

1.1.2 Case Studies

In addition, behavioural and neurological syndromes associated with Frontotemporal Dementia and Alzheimer's Disease are illustrated utilizing case studies. Case studies have been widely used in research into neurological conditions for several reasons. Firstly, researchers have experienced difficulties in obtaining sufficient sample sizes for valid statistical analysis (Stuss & Benson, 1986; Stuss, 1996; Marshall & Hutchinson, 2001). Secondly, many neurological researchers regard case studies as the most appropriate form of investigation due to the heterogeneous nature of many neurological conditions. The diversity of subjects even in established neurological diagnostic categories results in important clinical information being lost in group studies (Stuss & Benson 1986; Miller & Cummings et al. 1991; Marshall & Hutchinson, 2001). Thirdly, case studies have been widely used in the study of patients with acute neurological conditions. Any group of patients with acute neurological conditions characteristically exhibit a wide range of impairments that make standardised neuropsychological assessment difficult or impossible (Johanson & Hagberg, 1989; Smeding & de Koning; 2000).

1.1.3 Qualitative and Quantitative Aspects of this Research

This research adds to the existing literature by providing detailed analysis of the behavioural changes associated with early-onset Frontotemporal Dementia and Alzheimer's Disease. Research in this area is difficult as early-onset dementia is significantly less common than late-onset dementia (i.e. beginning after the age of sixty-five; Snowden & Neary et al. 1996; Stuss, 1996;

Ritchie & Lovestone, 2002). This study provides detailed qualitative and quantitative evaluation of the test variables and behavioural changes in relatively large early-onset dementia subject groups (37 Frontotemporal Dementia and 25 Alzheimer's Disease patients) over a three-year time interval (± 3 months) for each patient. This research also explores the difficulties involved in providing effective clinical services to early-onset dementia patients and their carers, and provides practical guidelines to carers and service-providers to assist with the effective management of this group of relatively young people with disabilities.

1.1.4 Review of Literature

An introductory literature review is presented to outline the diagnostic criteria for the various forms of early-onset dementia, and to show that early-onset dementia diagnostic criteria are still evolving. The introductory literature review sets the scene for the studies that follow.

Several topics are addressed separately in separate chapters in this thesis. The topics include the value of formal psychometric assessment, neuropsychological tests, behavioural observations and neurological investigations in establishing a diagnosis of frontotemporal dementia or early-onset Alzheimer's disease, and in predicting the rate of cognitive deterioration; and making use of this information to formulate care and treatment plans for patients with differing forms of early-onset dementia.

Each of these topics is reviewed in detail before the relevant findings are presented, to help the reader integrate the findings with existing knowledge.

1.2 ORIGINS OF FRONTOTEMPORAL DEMENTIA AS A CATEGORY DISTINCT FROM ALZHEIMER'S DISEASE: DEFINING A NEW FORM OF DEMENTIA

1.2.1 History of Frontotemporal Dementia

A dementing illness with accompanying significant behavioural disturbance was first recorded by Arnold Pick, a professor of psychiatry in Prague (Pick, 1906). Pick described six patients with a dementing illness and behavioural disturbance that occurred in conjunction with bilateral frontal atrophy (Kertez, 1996; Snowden & Neary et al. 1996; Spatt, 2000 & 2003). Pick provided excellent behavioural descriptions of patients with the illness. Pick did not, however, describe the accompanying changes in cells and tissue at the microscopic level, the underlying histological changes associated with Frontotemporal Dementia (Neary & Snowden, 1996; Kertez, 1996; Spatt, 2000 & 2003).

Alzheimer first documented the characteristic histological changes accompanying the behavioural disturbances in 1911 (Kertez, 1996; Neary & Snowden et al. 1996).

Alzheimer found that a group of patients with specific behavioural disturbances had “ballooned cells, argentophilic globes, and spongicortical wasting in the frontal and anterior temporal lobes (Snowden & Neary et al. 1996). This presentation of behavioural disturbance with circumscribed atrophy of the

frontal and temporal lobes became known as “Pick’s Disease” (Onari & Spatz, 1926).

1.2.2 Historical Diagnosis of Non-Alzheimer’s Dementia

The groundbreaking early research by Pick, Alzheimer, and other researchers clearly indicated some dementias were not of the Alzheimer’s type (Kertez, 1996; Neary & Snowden, 1996; Spatt, 2000 & 2003). Despite this important early research, dementia, until recently, has been widely viewed as a generalized and undifferentiated impairment of mental functioning, with dementia being seen as synonymous with Alzheimer’s Disease (Miller & Darby et al. 1995; Snowden, Neary, Mann, 1996). A major change in the understanding of the heterogeneity of dementia occurred in the late 1980’s when teams of Swedish and English researchers separately published journal articles that brought to attention the fact that dementing illnesses affecting primarily the frontal and anterior temporal lobes were significantly under diagnosed (Brun, 1987; Neary & Snowden, et al.1988).

1.2.3 Problems with the Diagnosis of Non-Alzheimer’s Disease Dementias

In recent years, researchers have highlighted major shortcomings in the diagnosis, research, and treatment of dementias that affect primarily the frontal and temporal lobes of the brain (Knopman & DeKosky et al. 2001; Derouesne, 2003). Currently accepted diagnostic criteria (see Table 1 p.9) for dementia were put forward by the NINCDS-ADRDA: National Institute of Neurological and Communicative Disorders and Stroke / Alzheimer’s Disease and Related

Disorders Association (McKhann & Drachman et al. 1984; Varma & Snowden et al. 1999; Knopman & DeKosky et al. 2001).

A growing body of research findings has indicated that the NINCDS-ADRDA criteria (see Table 1, p.9), although effective for detecting a wide range of neurological conditions, are overly inclusive (Varma & Snowden et al. 1999; Derouesne, 2003).

The NINCDS-ADRDA criteria include all patients who exhibit disturbances of memory combined with deficits in one or more areas of functioning. The overly inclusive nature of the NINCDS-ADRDA criteria has resulted in the diagnosis of Alzheimer's Disease being given to patients who have later been shown to have unequivocal non-Alzheimer's Disease pathology (Snowden & Neary et al. 1996; Lebert & Pasquier et al. 1998; Varma & Snowden et al. 1999; Graham & Davies et al. 2005).

Table 1: NINCDS-ADRDA diagnostic criteria for dementia.

1) Essential clinical criteria for the diagnosis of possible dementia:
a) Dementia established by a clinical examination and documented by the Mini-Mental State Exam (MMSE, Folstein, Folstein, & McHugh, 1975), and confirmed by neuropsychological tests.
b) Deficits recorded in two or more areas of cognition.
c) Progressive deterioration of memory and other cognitive functions.
d) No disturbance of consciousness.
e) Absence of systemic disorders or other brain diseases that in and of themselves could account for the progressive deficits in memory and cognition.
2) A diagnosis of probable dementia is supported by:
a) Progressive deterioration of specific cognitive functions including language (aphasia), motor skills (apraxia), and perceptions (agnosia).
b) Impaired activities of daily living (ADL's, e.g. Lehfeld, Reisberg, & Finkel, 1997) and altered patterns of behaviour.
c) Family history of dementia, particularly if confirmed neuropathologically.
d) Normal lumbar puncture as evaluated by standard techniques.
e) Normal pattern or non-specific changes in EEG, such as increased slow-wave activity.
f) Evidence of cerebral atrophy on CT with progression documented by serial CT results.
3) Other clinical features consistent with the diagnosis of probable dementia:
a) Plateaus in the course of the progression of the illness.
b) Associated symptoms of depression, insomnia, incontinence, delusions, illusions, hallucinations, catastrophic verbal, emotional, or physical outbursts, sexual disorders, and weight loss.
c) Other neurological abnormalities in some patients, especially with disease that is more advanced and including motor signs such as increased muscle tone, myoclonus, or gait disorder.
d) Seizures in advanced stages of the disease.
4) Features that make the diagnosis of probable dementia uncertain or unlikely:
a) Sudden, apoplectic onset.
b) Focal neurological findings such as paralysis on one side of the body, sensory loss, visual field deficits, and incoordination early in the course of the illness.
c) Seizures or gait disturbances at the onset or very early in the course of the illness.
d) Pseudodementia

1.2.4 The Origins of “Frontotemporal Dementia” as a New Diagnostic Label:

Challenges to the Homogeneity of Dementia

Since the 1970s, a growing body of research has altered the understanding of dementias affecting the frontal and anterior temporal lobes of the brain (e.g. Tissot & Constantinidis et al. 1975; Snowden & Neary et al. 1996; Chow, 2003; Boccardi & Sabattoli et al. 2005; Mariani & Defendi et al. 2006). This research has led to the new classification of Frontotemporal Dementia (FTD). The classification of Frontotemporal Dementia is based on clinical, pathological, and genetic features associated with neuropathological conditions that researchers argue are strikingly different to Alzheimer’s Disease (Gustafson & Risberg, 1974; Brun & Gustafson et al. 1994; Filley & Kleinschmidt-De Masters et al. 1994; Gregory & Hodges, 1996; Snowden & Neary et al. 1996; Knopman & DeKosky et al. 2001; Curcio & Kawarai et al. 2002).

Collaborative research between British and Swedish researchers (Lund and Manchester groups: Gustafson, 1987; Brun & Englund et al. 1994) has resulted in the classification of a dementia affecting primarily the frontal and temporal regions of the brain as “Frontotemporal Dementia” or “FTD” (Gustafson, 1987; Gustafson & Brun et al. 1994). The researchers used the term “Frontotemporal Dementia” to clearly differentiate the disorder from Alzheimer’s Disease (Gustafson & Brun, 1999).

The Lund-Manchester collaboration produced initial clinical criteria for the differential diagnosis of Frontotemporal Dementia from other neurological conditions. The clinical criteria for Frontotemporal Dementia have been further refined by Neary and colleagues (Neary & Snowden & Neary et al. 1998; Faber, 1999) The criteria (see Table 2, p.12) developed by the above researchers have been found to significantly improve the differential diagnosis of Frontotemporal Dementia from other dementing conditions, especially Alzheimer's disease (Duara & Barker et al. 2002; Mariani & Defendi et al. 2006).

Table 2: Diagnostic criteria for probable Frontotemporal Dementia (FTD).

1) Essential diagnostic features
a) Insidious onset and gradual progression of the disease process.
b) Decline in social interpersonal conduct early in the course of the illness.
c) Impairment in regulation of personal conduct early in the course of the illness.
d) Early emotional blunting.
e) Early loss of insight.
2) Supportive diagnostic features
a) Behavioural disorder.
i. Decline in personal hygiene and grooming.
ii. Mental rigidity and inflexibility.
iii. Distractibility and impersistence.
iv. Hyperorality and dietary changes.
v. Perseverative and stereotyped behaviour.
vi. Utilization behaviour.
b) Speech and Language
i. Altered speech output.
ii. Aspontaneity and economy of speech.
iii. Stereotypy of speech.
iv. Echolalia.
v. Perseveration.
vi. Mutism.

Table 2 continued: Diagnostic criteria for Frontotemporal Dementia (FTD).

c) Physical signs
i. Early primitive reflexes.
ii. Early incontinence.
iii. Akinesia, rigidity, and tremor.
iv. Low and labile blood pressure.
d) Investigations
i. Neuropsychological examination.
ii. Electroencephalography: normal on conventional EEG despite clinically evident dementia.
iii. Brain imaging (structural and/or functional): predominant frontal and/or anterior temporal abnormality.
e) Supportive Features
i. Onset before 65: positive family history of similar disorder in first-degree relative.
ii. Bulbar palsy, muscular weakness and wasting, fasciculations (associated motor neuron disease present in a minority of patients).

1.2.5 Labels for Frontotemporal Lobar Atrophy

The understanding of disease processes involving primarily Frontotemporal lobar atrophy continues to improve with new research findings (Stuss, 1993; Brun & Passant, 1996; Gustafson & Brun, 1999; Neary & Snowden et al. 1998; Knopman & DeKosky et al. 2001; Gee & Ding et al. 2003; Pasquier & Richard et al. 2004; Harciarek & Jozio, 2005; Roberson & Hesse et al. 2005). A variety of terms have been used for this condition (See Appendix 2, p.235, Hodges, 2001; Tanabe, 2000; Rossor, 2001; Wahlund, Andersen, & Östberg, 2002; Pasquier & Richard et al. 2004; Pasquier, 2005). For the purposes of this research, in line with recent consensus criteria “Frontotemporal Dementia” or “FTD” refers specifically to neurological disorders that cause damage primarily to the frontal and anterior temporal lobes of the brain (Levy & Miller et al. 1996; Neary & Snowden, 1996; Neary & Snowden et al. 1998; Tanabe, 2000). The term “Frontotemporal Dementia” is now used in preference to “Pick’s Disease” (Hodges, 2001).

1.2.6 Heterogeneity of Frontotemporal Dementia

It is important to note that the term “Frontotemporal Dementia” is a heterogeneous term. Frontotemporal Dementia refers to a clinical and pathological cluster of disorders. The pathological cluster includes Motor Neurone Disease with associated dementia (MND/FTD), Pick’s Disease, frontal lobar degeneration (FLD). Progressive aphasia is a clinical cluster for anterior-type dementia (Snowden & Neary et al. 1996; Boone & Miller et al. 1999; Gustafson & Brun, 1999; Kertesz, Martinez-Lage et al. 2000). In line with the

heterogeneity of Frontotemporal Dementia, research indicates that there is no single specific cause, as the frontal and temporal regions of the brain can be damaged by a wide range of disease processes (Bird, 1998; Gustafson & Brun, 1998; Snowden & Neary et al. 2004).

1.2.7 Heterogeneity of Alzheimer's Disease

Galton and colleagues (Galton & Patterson et al. 2000) described the widely differing clinical presentations of patients diagnosed with Alzheimer's Disease. The researchers found that in a group of thirteen Alzheimer's Disease patients four presented with a typical Alzheimer's Disease amnesic syndrome, one exhibited progressive visual dysfunction, two progressive biparietal syndrome, and six progressive aphasia. Imaging studies of the patients indicated significantly different patterns of neurodegeneration.

The heterogeneity of both Alzheimer's Disease and Frontotemporal Dementia groups provides challenges for researchers attempting to accurately diagnose each group, and to accurately diagnose the variations in the disease taking place in each patient.

1.2.8 The Underdiagnosis of Frontotemporal Dementia

Despite the significant recent advances in the understanding and diagnosis of different forms of dementia, it is believed that Frontotemporal Dementia is frequently misdiagnosed as Alzheimer's Disease, or under-diagnosed (Gregory & Hodges, 1996; Neary & Snowden et al. 1998; Pasquier & Lebert et al. 1998; Ratnavalli & Brayne et al. 2002; Pasquier & Richard et al. 2004; Passant &

Elfgren et al. 2005). A U.K. study has indicated that Alzheimer's Disease may account for only fifty per cent of dementia cases if patients are diagnosed in line with the latest clinical diagnostic criteria (Harvey, 1998).

One study found that approximately 85 percent of patients eventually diagnosed with Frontotemporal Dementia had previously been given a diagnosis of Alzheimer's Disease (Miller & Ikonte et al. 1997). Passant and colleagues (2005) in a study of 19 Frontotemporal Dementia patients found that only 1 had been initially diagnosed correctly. Patients were diagnosed initially with psychiatric disorders and other neurological conditions. Dementias affecting primarily the frontal and temporal lobes are believed to affect between eight and twenty percent of dementia patients (Gustafson, 1987, 1993; Neary & Snowden et al. 1987; Harvey, 1998; Lebert & Pasquier et al. 1998; Ikeda & Ishikawa et al. 2004). Recent studies have found Frontoemporal Dementia to be more common in men, and to be a significant cause of early onset dementia (Ratnavalli & Brayne et al. 2002).

1.2.9 Current Criteria for the Diagnosis of Frontotemporal Dementia

The clinical diagnosis of Frontotemporal Dementia is based on the occurrence of profound personality change and alterations in social conduct accompanying frontal and anterior temporal lobe deterioration (Snowden & Neary et al. 1996;

Kertesz & Davidson et al. 1997; Snowden & Neary et al. 2002). The diagnosis of Frontotemporal Dementia always requires a complex assessment, as the diagnostic criteria do not fit precisely with known neuropathological phenotypes. In contrast to Frontotemporal Dementia, a condition such as Creutzfeldt–Jakob disease (CJD) has a precise match between diagnostic criteria and neuropathology (Knopman & DeKosky et al. 2001). Diagnosis of Frontotemporal Dementia consists of a complete family and medical history, behavioural assessment, neuropsychological assessment, neurological examination, MRI, SPECT, and CT imaging studies of the brain (Snowden & Neary et al. 1996; Neary & Snowden et al. 1998; Duara & Barker et al. 1999; Charpentier & Lavenue et al. 2000; Sjogren & Gustafson et al. 2000).

Obtaining a correct diagnosis is important for patients, their families, and carers, as the diagnosis has major implications for prognosis, possible treatments, and the provision of appropriate supports. Due to the genetic link in many families, diagnosis can have serious long-term implications for other family members. Patients diagnosed with early onset dementia often require costly and specialized institutional care (Harvey, 1998; Cucio & Kawarai et al. 2002; Chapman & Williams et al. 2006). Understanding the specific care needs of relatively young dementia patients is important if health services are to provide appropriate ongoing care (Harvey, 1998).

1.2.10 Age of Onset & Length of Illness

The age of onset for Frontotemporal Dementia is generally between the 45 and 60 years (Snowden & Neary et al. 1996; Diehl & Kurz, 2002). Equal incidences for men and women have been reported. The length of the illness varies from 2 to 20 years, with a median duration of illness of approximately 8 years before the patient dies (Pasquier & Lebert et al. 1999; Pasquier & Richard et al. 2004; Kertesz & McMonagle et al. 2005).

1.3 SUMMARY

This research explores and evaluates two groups of patients (Alzheimer's Disease and Frontotemporal Dementia) diagnosed with early-onset dementia. The evaluation uses behavioural, neurological, and neuropsychological assessment. Case studies are also utilised to illustrate differing neurological conditions. A major objective of the research is to provide practical information to those involved in the care and treatment of patients with early-onset dementia.

A review of the literature supporting Frontotemporal Dementia as a distinct category from Alzheimer's Disease was provided. Current diagnostic criteria for Frontotemporal Dementia and Alzheimer's Disease were given. Problems associated with the overly inclusive Alzheimer's Disease diagnostic criteria were explored. Methodology is presented in Chapter 2.

1.4 MAJOR OBJECTIVES OF CURRENT STUDY

The major objectives of this study are to:

- Further evaluate the validity and utility of the relatively new diagnostic category of Frontotemporal Dementia.
- Evaluate the importance of behavioural, neurological, and neuropsychological assessment in the early and accurate diagnosis of dementia.
- Provide practical information to care providers regarding the needs of people who receive a diagnosis of early onset dementia.

1.5 HYPOTHESES

1. The clinical criteria developed by Neary & Snowden et al. (1998) will be able to differentially diagnose early-onset Frontotemporal Dementia patients from early-onset Alzheimer's Disease patients.
2. The analysis of this group of patients will provide information that may assist in the formulation of care and treatment plans for patients with differing forms of early-onset dementia.
3. The Frontotemporal Dementia patient group will have significantly increased behavioural disturbances throughout the course of the illness in comparison with Alzheimer's Disease patient group. Evaluation of

4. behavioural profiles will assist with the differential diagnosis of Frontotemporal Dementia patients from Alzheimer's Disease patients. Previous research has indicated that the evaluation of behavioural profiles can assist in differentially diagnosing Frontotemporal Dementia from Alzheimer's Disease (Levy & Miller et al. 1996; Duara & Barker et al. 1999; Pasquier 1999; Tanabe & Ikeda et al. 1999; Bozeat & Gregory et al. 2000; Cummings & McPherson, 2001; Ikeda & Brown et al. 2002; Shingenobu & Ikeda, 2002; Kertesz & Davidson et al. 2003; Mourik & Rosso et al. 2004; Srikanth & Nagaraja et al. 2005; Engelborghs & Maertens et al. 2005; Thompson & Stopford et al. 2005).

5. Frontotemporal Dementia and Alzheimer's Disease patients will show significant differences on neuropsychological tests, with Frontotemporal Dementia patients having relatively preserved visuo-spatial functioning. This pattern of impaired visuo-spatial abilities in Alzheimer's Disease and relatively preserved visuo-spatial abilities in Frontotemporal Dementia has been a consistent result of neuropsychological investigations of these two groups (Elfgren & Passant et al. 1993; Stuss, 1993; Gregory & Orrell et al. 1997; Duara & Barker et al. 1999; Pasquier, 1999; Ikeda & Tanabe, 2000; Storey & Slavin et al. 2002; Kramer & Jurik et al. 2003; Harciarek Jodzio, 2005).

6. The course of the illnesses will differ significantly between the early-onset Frontotemporal Dementia and Alzheimer's Disease groups. Frontotemporal Dementia patients are expected to have rapid progression of disease symptoms, with Alzheimer's Disease patients showing a more gradual deterioration. Early-onset Frontotemporal Dementia patients have consistently been found to deteriorate more rapidly than early-onset Alzheimer's Disease patients (Barber, Snowden & Caufurd, 1995; Pasquier & Richard et al. 2004; Kertesz & McMonagle et al. 2005; Roberson & Hesse et al. 2005; Pasquier & Lebert et al. 2005).

CHAPTER 2

METHOD

2.1 SUBJECTS AND PROCEDURE

Subjects in the study were sixty-two Health Department of Western Australia outpatients diagnosed with dementia. The author was involved in the assessment and management of the patients over a five-year period. He provided behavioural management training and support to families and staff in the home and in hospitals or nursing homes.

Patients in the study were referred to a unit specialising in early-onset (onset before 65 years of age) neurodegenerative disorders. Referrers were families, self-referrals, general practitioners, psychiatrists, and neurologists. Data were collected from the sixty-two patients aged between 35 and 65 (mean age = 58.8 years, Table 3 below). The average number of years of education for the subjects was 10.9 years. Thirty-four of the subjects were female, and twenty-eight of the subjects were male. There was no significant difference between the two groups for age, sex, or education (Tables 3 & 4 below).

Family members were asked to estimate the age when changes in behaviour and/or memory were first noticed (Table 3 below). Average estimated age of onset was 54.1 years for the Frontotemporal Dementia group and 55.9 years for the Alzheimer's Disease group. There was no significant difference between the two groups.

Table 3: Age first assessed for current study, estimated age of onset, and years of education of Frontotemporal Dementia and Alzheimer’s Disease patients at first assessment.

	FTD			AD			Levene’s Test For	
	N	Mean	Std. Dev	N	Mean	Std. Dev	Equality of Variance	t(df)*
Age	37	58.8	7.1	25	60.1	4.8	0.96	.81(60)
Est. Age of Onset	27	54.1	7.5	18	55.9	5.4	0.55	.87(43)
Education	37	10.9	2.4	24	10	1.8	3.80	1.74(59)

* = none of the differences between groups were statistically significant

Table 4: Sex of Frontotemporal Dementia and Alzheimer’s Disease patients.

SEX	FTD	AD	Total	Chi Square
Male	17	11	28	0.02 *
Female	20	14	34	
Total	37	25	62	

* = not significant

Written consent was obtained from all subjects or their legal guardians (Appendix 1, p. 233). All patients in the study underwent an extensive clinical evaluation by a multi-disciplinary team. The team consisted of a neurologist specialising in the diagnosis and treatment of patients with early-onset dementia, a clinical psychologist registrar (the author), psychiatrist, speech pathologist, and social worker. All initial assessments for each patient occurred within a three-month time frame. Not all subjects were assessed by each member of the team. Assessments were conducted to assist with the clinical care of the patients and were not conducted primarily for research purposes. No additional assessments were performed beyond those routinely

administered by the hospital to enhance patient care. This was a requirement of the Murdoch University Ethics Committee to avoid placing families and carers under additional stress.

The team neurologist made referrals to members of the team for assessment and treatment. Full family and personal histories were taken from family members or primary carers. Semi-structured interviews were used to obtain the following information:

- Activities of daily living — self-care, orientation, communication, managing finances, using domestic appliances, using transport, concentration, coping with unfamiliar situations, participation in social activities, and planning ability.
- Age of onset.
- Education and vocational history.
- Family history of dementia or other neurological conditions.
- Psychiatric symptoms — paranoid and delusional ideation, hallucinations, activity disturbances, aggressiveness, diurnal rhythm disturbances, inappropriate activity, ritualistic behaviours, affective disturbance, fears, phobias and anxieties.
- Substance and alcohol usage history.
- Loss of insight. Patients were asked “Do you have an illness or a problem that requires medical attention?” “Is your behaviour significantly different now, compared to a few years ago?” and “Do family/friends think that you have an illness or that something is wrong with you?”.

Carers were used as a primary source of information about the patients. This was done as many of the patients, especially the Frontotemporal Dementia patients, had severe memory disturbance and/or behavioural disturbance combined with marked verbal and non-verbal communication deficits at the time of their initial presentation at the hospital. The Health Department of Western Australia provided long-term clinical services to all the patients, their families, and carers who took part in the study.

Patients were clinically assessed repeatedly during the study. Average length of time for neurological review was six months. Assessments were specifically designed for the provision of clinical services to the patients and their families.

Patients with long-term major psychiatric illnesses were excluded from the study (n = 3); one patient had a long-term diagnosis of bipolar disorder, and two patients had received long-term electroconvulsive therapy for depression.

Detailed case notes were kept for all patients. All patients underwent neurological examinations, electroencephalogram (EEG), computed tomography (CT) and/or magnetic resonance imaging (MRI). Forty-seven of the sixty two subjects underwent single photon emission computed tomography (SPECT).

All patients were administered routine screening blood tests.

All patients were assessed with a neuropsychological test battery (Table 5 p.27).

The neuropsychological tests were administered in a non-standardised manner due to the severe behavioural and/or memory disturbances exhibited by many of the patients and to minimize their discomfort. Neuropsychological assessment

was conducted primarily to assist with patient treatment and care, and not for research purposes. Due to the lack of adherence to standardised testing protocols, any statistical analysis of data must be treated with caution (Lezak, 1995; Stuss, 1996; Pasquier & Lebert et al. 1999).

Table 5: Neuropsychological tests used in study, number of subjects tested, and brief description of test.

Test	Brief Description of Test
<p>FAS verbal fluency test and Animal naming test (Lezak, 1995). FAS —FTD n = 28, AD n = 17; Animal Naming FTD n=20, AD n=10.</p>	<p>A test of ability to generate as many words as possible in four 60 second intervals starting with the letters “F”, “A”, & “S”, followed by animal names.</p>
<p>Tactile Finger Recognition Test (Reitan & Davison, 1974). FTD n = 20, AD n = 13</p>	<p>Part of Halsted-Reitan test battery. The examiner assigns a number to each finger. When subjects’ eyes are closed and hands extended, the examiner touches fingers in a predetermined order, and asks the subject to identify the touched finger by naming the finger by its assigned number. Subjects with verbal deficits can be asked to identify the finger by moving it or tapping it on the test table.</p>
<p>Purdue Pegboard Test (Purdue Research Foundation, 1968) FTD n = 24, AD n = 14</p>	<p>Test of manual dexterity requiring placing pegs in holes with left, right, and both hands in 30 second intervals.</p>

Table 5 continued: Neuropsychological tests used in study, number of subjects tested, and brief description of test.

Test	Brief Description of Test
Freehand clock drawing test (Borod, Goodglass & Kaplan, 1980). FTD n = 23 AD n = 15	A test of ability to draw a clock freehand, and set the hands at “10 past 11”.
Mini Mental State Exam (MMSE, Folstein, Folstein & McHugh, 1975) FTD n = 25 AD n = 14	A brief screening test for dementia that measures orientation, registration, attention and calculation, recall, and language.
Paired Associates Learning Task (PALT, Wechsler, 1944). FTD n = 26 AD n = 12	A paired-word learning test consisting of ten word-pairs, with six “easy” pairs, and four “hard” pairs.
Rey-Osterrieth Complex Figure Test (Bennett-Levy, 1984). FTD n = 27; AD n = 15.	A test of perceptual organisation and immediate and delayed visual memory. Subjects are asked to copy a complex figure using six coloured pens, and the examiner changes pens after each section is completed. An immediate recall trial is given after 60 seconds, and delayed recall after approximately 30 minutes.

Table 5 continued: Neuropsychological tests used in study, number of subjects tested, and brief description of test.

Test	Brief Description of Test
<p>Symbol Digit Modalities Test (SDMT, Smith, 1968) FTD n = 27; AD n = 12.</p>	<p>This test measures the ability to connect numbers to a series of different symbols. There are a maximum of 120 matches in a 90 second period. There is a written and oral component to the test. In one, the matching number must be written in the blank box directly below each symbol and in the other, the subject must say aloud which number matches each symbol. This is a measure of visual search and memory, fine motor control and concentration (Turner 1999).</p>
<p>The Wechsler Adult Intelligence Scale-111 (WAIS-111, Wechsler, 1997) FTD n = 26; AD n = 15</p>	<p>Intelligence test battery containing 13 subtests: Information, Comprehension, Arithmetic, Similarities, Digit Span, Vocabulary (measures of verbal skills), Digit Symbol-Coding, Picture Completion, Picture Arrangement, Block Design, Matrix Reasoning, Object Assembly, Symbol Search (measures of non-verbal skills).</p>

Table 5 continued: Neuropsychological tests used in study, number of subjects tested, and brief description of test.

Test	Brief Description of Test
<p>Wechsler Memory Scale Logical Memory and Visual Reproduction subtests (WMS, Wechsler, 1974)</p> <p>FTD n = 25; AD n = 15.</p>	<p>Visual Reproduction: a test of immediate and delayed visual recall. Three designs are shown for 5 seconds each, and subjects are asked to draw the design immediately then again after 20 minutes.</p> <p>Logical Memory: a test of immediate and delayed verbal recall. Two stories are read, and the subject is asked to recall as many details as possible. A delayed recall trial is given after 20 minutes.</p>

2.1.1 Diagnostic Criteria Employed in the Study

The patients in the study were given a diagnosis of Frontotemporal Dementia or Probable Alzheimer's Disease by the hospital neurologist. The diagnosis was made in line with the currently accepted international diagnostic criteria (see below).

Diagnostic Criteria for Probable Alzheimer's Disease

The diagnosis of probable Alzheimer's disease was made in accordance with the criteria published by the National Institute of Neurological and Communicative Disorders and Stroke/ Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA, McKhann et al. 1984). The NINCDS-ADRDA diagnostic criteria are the most widely accepted criteria for Alzheimer's Disease (Varma & Snowden et al. 1999; Storey, Slavin & Kinsella, 2002, see Table 1, p.9 for full NINCDS-ADRDA diagnostic criteria).

Diagnostic Criteria for Frontotemporal Dementia

The diagnosis of Frontotemporal Dementia was made in accordance with the criteria proposed by Neary and colleagues (1998). These criteria are the most commonly used by neurologists in the diagnosis of Frontotemporal Dementia (Chayer & Freedman, 2001). Subjects were diagnosed with Frontotemporal Dementia if all core diagnostic criteria listed were present (see Table 2, p.13 for full Frontotemporal Dementia diagnostic criteria).

Diagnostic Exclusion Features for Frontotemporal Dementia and Alzheimer's Disease

Patients were not included in the study if the following features were present.

1. Historical and Clinical

- Abrupt onset with ictal events.
- Head trauma related to onset.
- Logoclonic, festinant speech with loss of train of thought.
- Corticospinal weakness.
- Cerebellar ataxia.
- Choreoathetosis.

2. Neurological Investigations

- Brain imaging (CT, MRI, and SPECT) indicates predominantly postcentral structural or functional deficit, and/or multifocal lesions.
- Laboratory tests indicating brain involvement or inflammatory disorder such as Multiple Sclerosis, syphilis, AIDS or herpes simplex encephalitis.

3. Exclusion features

- Typical history of chronic alcoholism or drug use.
- Sustained hypertension.
- History of vascular disease (such as angina, claudication).

CHAPTER 3

NEUROLOGICAL AND

NEUROPATHOLOGICAL CHANGES IN

FRONTOTEMPORAL DEMENTIA AND

ALZHEIMER’S DISEASE

“The frontal lobes are relatively large. However, it is rare to find well-localised pathology in the frontal lobes. Due to the fact that the right and left frontal lobes are immediately next to one another, pathology that affects one frontal lobe tends to affect the other lobe”.

Stuss & Benson, 1986, p. 63

“In the past dementia was conceived as a non-specific decline in cognition associated with generalised atrophy. This is an outmoded notion and it is now clear that dementia is a generic term encompassing a number of specific neuropsychological syndromes, which are dictated by the regional distribution of pathology within the brain associated with particular disorders. Alzheimer’s Disease has an affinity with the limbic system and parieto-temporal association cortex.....Frontotemporal Dementia is associated with circumscribed atrophy of the frontal and temporal lobes”.

Snowden, Neary & Mann 1996, p. 176-177

3.1 NEUROPATHOLOGICAL CHANGES IN FRONTOTEMPORAL DEMENTIA & ALZHEIMER'S DISEASE

3.1.1 Introduction

Probable Frontotemporal Dementia is diagnosed when the neuropathological changes and atrophy accompanying the onset of the dementia occur primarily in the frontal and anterior temporal lobes, and the changes are not of the Alzheimer's Disease type (Neary & Snowden, 1996; Snowden & Neary et al. 2004). Although both Frontotemporal Dementia and Alzheimer's Disease are often diagnosed without autopsy-confirmation, autopsy remains the gold standard (Storey, Slavin, & Kinsella, 2002). Frontotemporal Dementia deterioration is often asymmetric, affecting differing regions of the right or left frontal and temporal lobes (Snowden & Neary et al. 1996; Miller et al. 1997; Varma, Adams, & Lloyd, 2002; Jeong & Song et al. 2005).

Atrophy of the basal ganglia and substantia nigra can also be characteristic features as the illness progresses. Neuropathological changes often include a combination of mild status spongiosus (irregular cavities in gliotic neuropil following extensive neuronal loss), gliosis of the cortical layers (gliosis is the production of a dense fibrous network and a proliferation of astrocytes associated with neurodegeneration), cell loss in the hypoglossal nucleus (this nucleus lies just off the midline beneath the floor of the fourth ventricle) and cell loss in the anterior horns of the spinal cord. The hippocampus is often relatively preserved, and where hippocampal atrophy is found it is generally focal. In Alzheimer's Disease hippocampal atrophy is generally

diffuse (Filley & Kleinschmidt-DeMasters, 1994; Laakso & Frisoni et al. 2000). There is often atrophy of the anterior cerebral cortex in Frontotemporal Dementia (Brun et al. 1994; Foster & Sima & Defendini et al. 1996; Neary et al. 1988; Neary & Snowden et al. 1990; Frisoni & Laakso et al. 1999).

Alzheimer's Disease is diagnosed when there is clear evidence from imaging of parietal and parieto-temporal atrophy (Duara & Barker et al. 1999).

Hippocampal and medial temporal lobe deterioration occurs early in the course of the illness, resulting in characteristic deterioration in verbal and visuo-spatial memory (Frisoni & Laakso et al. 1999). Significant loss of entorhinal cortex volume occurs early in the course of both Alzheimer's Disease and Frontotemporal Dementia (Frisoni & Laakso et al. 1999).

3.1.2 Evidence from Electroencephalogram (See Table 6 p.39 below for summary of neuropathological findings)

Electroencephalogram (EEG) Findings

In Frontotemporal Dementia, EEG findings generally have been found to change slowly during the course of the disease, with slowing of waveforms occurring in the late stages of the illness (Snowden & Neary et al. 1996; Pasquier & Petit, 1997). There is evidence that the accuracy of diagnosis of Frontotemporal Dementia can be enhanced utilizing quantitative EEG (Yener & Leuchter et al. 1996). Yenner and colleagues (1996) found that 85 per cent of Frontotemporal Dementia patients could

be distinguished from Alzheimer's Disease patients with quantitative evaluation of EEG recordings from the temporal region and parietal region.

Structural Imaging (Computed Tomography and Magnetic Resonance Imaging)

Structural imaging by Computed Tomography (CT) and magnetic resonance imaging (MRI) indicates frontotemporal atrophy is universally found in Frontotemporal Dementia patients (Snowden & Neary et al. 1996; Duara & Barker et al. 1999). CT scans also indicate that in conjunction with frontotemporal atrophy there can be cases of non-specific cerebral atrophy in Frontotemporal Dementia patients. It is not uncommon to find a pronounced widening of the interhemispheric and sylvian fissures (Snowden & Neary et al. 1996; Duara & Barker et al. 1999; Kaga & Nakamura et al. 2004).

Computed Tomography (CT) has also been found effective in differentially diagnosing Frontotemporal Dementia from subcortical white matter dementia (Sjogren, et al. 2000; Passant & Ostojic et al. 2004). CT and MRI scans are useful in differentially diagnosing Alzheimer's Disease from Frontotemporal atrophy. In contrast to the Frontotemporal Dementia changes noted above, CT and MRI imaging of Alzheimer's Disease patients has indicated primarily hippocampal, medial temporal, and tempoparietal lobe atrophy (Duara & Barker et al. 1999; Lavenu & Pasquier et al. 1997).

Single Photon Emission Computed Tomography (SPECT)

SPECT is not regarded as a highly sensitive indicator of Frontotemporal Dementia if used alone (Pasquier & Lebert et al. 1999). However, SPECT studies of Frontotemporal Dementia patients have become increasingly sophisticated, and provide significant assistance in the differential diagnosis of Frontotemporal Dementia from Alzheimer's Disease and other neurodegenerative conditions (Charpentier et al. 2000). Functional imaging by SPECT reveals a selective anterior hemisphere reduction in cerebral blood flow and reduced fronto-temporal tracer activity in patients with Frontotemporal Dementia (Read & Miller et al. 1995). SPECT studies have also found reduced regional cerebral blood flow measurements in the mesial superior frontal gyrus, near the *polus frontalis* in Frontotemporal Dementia patients (Sjogren & Gustafson et al. 2000). Mendez & Shapira (2005) reported that SPECT studies of Frontotemporal Dementia patients with marked loss of insight and lack of concern typically showed frontal lobe hypoperfusion and hypometabolism. SPECT studies of patients with Alzheimer's Disease show clear parietotemporal abnormalities. This result clearly contrasts with the Alzheimer's Disease SPECT profile outlined above (Duara & Barker et al. 1999). If SPECT indicates posterior cerebral uptake decrease, a diagnosis of Frontotemporal Dementia is excluded (Lebert & Pasquier et al. 1998).

Charpentier and colleagues (2000) found SPECT imaging used in conjunction with the Mini Mental State Exam (MMSE) to be effective in differentially diagnosing Frontotemporal Dementia and Alzheimer's Disease. Charpentier and colleagues were able to correctly classify 100 per cent of Frontotemporal Dementia patients (20/20), and 90 per cent of Alzheimer's Disease patients (18/20) with SPECT imaging and the MMSE.

Table 6: Summary of EEG and Imaging findings in Frontotemporal Dementia and Alzheimer’s Disease.

	Frontotemporal Dementia	Alzheimer’s Disease
Localisation	Deterioration in the frontal and anterior temporal lobes of the brain (Snowden & Neary et al. 1996).	Parietotemporal deterioration (Duara & Barker et al. 1999).
EEG	Changes in frontotemporal readings. Decrease in fast wave activity, with minimal increase in slow wave activity (Yenner & Leuchter et al. 1996; Lindau & Jelic et al. 2003).	Generalized slowing. Marked increase in slow wave activity (Yenner & Leuchter et al. 1996; Lindau & Jelic et al. 2003).
MRI & CT	Frontal and anterior temporal atrophy, non-specific atrophy, pronounced widening of the interhemispheric and sylvian fissures. Early entorhinal cortex atrophy (Frisoni & Laakso et al. 1999; Duara & Barker et al. 1999; Snowden, Neary & Mann, 1996)	Primarily parietal, hippocampal and medial temporal lobe atrophy (Duara & Barker et al: 1999; Frisoni & Laasko et al. 1999).
SPECT	Selective anterior hemisphere reduction in cerebral blood flow, reduced fronto-temporal tracer activity. Reduced regional cerebral blood flow measurements in the mesial superior frontal gyrus, near the polus frontalis (Duara & Barker et al. 1999; Read & Miller et al. 1995; Sjogren & Gustafson et al. 2000).	Clear Parietotemporal deficits (Curran & Murray et al. 1993; Duara & Barker et al. 1999).
Cerebrospinal Fluid (CSF)	Stable Neuropeptide Y CSF level. Increased Delta Sleep Inducing Peptide CSF level (Minthon & Edvinsson et al. 1990).	Reduced Neuropeptide Y and Delta Sleep Inducing Peptide CSF levels (Minthon & Edvinsson et al. 1990).

3.2 NEUROLOGICAL SIGNS IN FRONTOTEMPORAL DEMENTIA AND ALZHEIMER'S DISEASE

3.2.1 Neurological Signs in Alzheimer's Disease

In Alzheimer's Disease, neurological examination commonly indicates significant impairment of memory functioning on simple verbal recall tasks accompanied by impaired functioning on simple visuo-spatial tasks.

Disturbances of gait, tremor, akinesia, rigidity, or myoclonus typically increase as the disease progresses (Cummings & Benson, 1986; Tariot, 2003).

3.2.2 Neurological Signs in Frontotemporal Dementia

Neurological signs accompanying Frontotemporal Dementia are generally the primitive reflexes (involuntary muscular responses to sensory stimuli). These muscular responses include:

- Grasping.
- Pouting.
- Involuntary sucking.
- The extensor plantar response.

These primitive reflexes are also known as "infantile reflexes" as they occur in early childhood. The primitive reflexes gradually disappear during the course of a healthy childhood. If there is any re-emergence of these primitive reflexes it is typically a sign of significant neurological damage (Miller & Darby et al. 1997).

The extensor plantar response/reflex, or Babinski reflex, is an indicator of upper

motor neurone degeneration. If motor neurone functioning is healthy in an adult the extensor plantar response is automatically suppressed (Barraquer-Bordas, 1998).

In a small minority of Frontotemporal Dementia patients neurological signs may be absent even when gross behavioural and cognitive changes are evident (Miller & Ikonte et al. 1997). The opposite pattern has sometimes been found, with Frontotemporal Dementia patients remaining free from behavioural disturbances until there is evidence of significant neurological deterioration (Snowden & Neary et al. 1996).

In some cases of Frontotemporal Dementia clinical signs of striatal disorder become evident late in the course of the illness. The clinical signs associated with striatal disorder are akinesia (absence of movements), rigidity, and tremors (Miller & Ikonte et al. 1997).

3.3 NEUROLOGICAL IMAGING: RESULTS OF CURRENT STUDY

3.3.1 Collection of Neurological Imaging Data

Neurological imaging results were collected within an 18 month period of the initial assessment. Imaging studies were conducted in several different hospitals in Western Australia.

Table 7: Neurological Imaging and EEG results for Frontotemporal Dementia**Patients (n=37)**

Patient No.	CT	MRI	SPECT	EEG
1.	frontal lobe atrophy	frontal lobe atrophy	Frontal hypoperfusion	fronto-temporal slowing
2.	frontotemporal atrophy	fronto-temporal atrophy	fronto-temporal hypoperfusion	fronto-temporal slowing
3.	abnormal, clin. Signif	fronto-temporal atrophy	fronto-temporal hypoperfusion	temporal lobe slowing
4.	reduced attenuation in frontal lobes	frontal lobe atrophy	frontal hypoperfusion	generalised slow wave activity
5.	frontal lobe atrophy	frontal lobe atrophy	reduced activity	generalised slow wave activity
6.	reduced attenuation in frontal lobes	fronto-temporal atrophy	frontal hypoperfusion	generalised slow wave activity
7.	frontotemporal atrophy	fronto-temporal atrophy	no results	generalised slow wave activity
8.	frontal lobe atrophy	frontal lobe atrophy	generalized cerebral hypoperfusion	fronto-temporal slowing
9.	frontal lobe atrophy	frontal lobe atrophy	no results	fronto-temporal slowing
10.	frontotemporal atrophy	fronto-temporal atrophy	fronto-temporal hypoperfusion	diffuse slow wave activity
11.	frontotemporal atrophy	fronto-temporal atrophy	frontal hypoperfusion	short dysrhythmic bursts
12.	frontotemporal atrophy	frontal lobe atrophy	no results	nonspecific
13.	frontal lobe atrophy	frontal lobe atrophy	fronto-temporal hypoperfusion	temporal lobe slowing
14.	frontotemporal atrophy	frontal lobe atrophy	frontal hypoperfusion	generalised slow wave activity
15.	abnormal, clinically significant	fronto-temporal atrophy	fronto-temporal hypoperfusion	generalised slow wave activity
16.	frontal lobe atrophy	fronto-temporal atrophy	no results	generalised slow wave activity

Table 7 Continued: Neurological Imaging and EEG results for Frontotemporal Dementia Patients (n=37)

Patient No.	CT	MRI	SPECT	EEG
17.	abnormal, clinically significant	fronto-temporal atrophy	frontal hypoperfusion	fronto-temporal slowing
18.	frontal lobe atrophy	fronto-temporal atrophy	fronto-temporal hypoperfusion	short dysrhythmic bursts
19.	frontotemporal atrophy	frontal lobe atrophy	fronto-temporal hypoperfusion	fronto-temporal slowing
20.	frontotemporal atrophy	fronto-temporal atrophy	no results	fronto-temporal slowing
21.	frontotemporal atrophy	frontal lobe atrophy	frontal hypoperfusion	diffuse slow wave activity
22.	frontotemporal atrophy	frontal lobe atrophy	fronto-temporal hypoperfusion	generalised slow wave activity
23.	frontotemporal atrophy	frontal lobe atrophy	fronto-temporal hypoperfusion	fronto-temporal slowing
24.	frontal lobe atrophy	fronto-temporal atrophy	fronto-temporal hypoperfusion	fast wave activity
25.	frontal lobe atrophy	frontal lobe atrophy	no results	generalised slow wave activity
26.	frontotemporal atrophy	fronto-temporal atrophy	fronto-temporal hypoperfusion	fronto-temporal slowing
27.	frontotemporal atrophy	fronto-temporal atrophy	generalized cerebral hypoperfusion	generalised slow wave activity
28.	reduced attenuation in frontal lobes	frontal lobe atrophy	fronto-temporal hypoperfusion	fronto-temporal slowing
29.	frontal lobe atrophy	frontal lobe atrophy	frontal hypoperfusion	diffuse slow wave activity
30.	frontal lobe atrophy	fronto-temporal atrophy	frontal hypoperfusion	fronto-temporal slowing
31.	frontotemporal atrophy	fronto-temporal atrophy	no results	short dysrhythmic bursts
32.	abnormal, clinically significant	frontal lobe atrophy	generalized cerebral hypoperfusion	diffuse slow wave activity

Table 7 Continued: Neurological Imaging and EEG results for Frontotemporal Dementia Patients (n=37)

Patient No.	CT	MRI	SPECT	EEG
33.	frontotemporal atrophy	frontal lobe atrophy	fronto-temporal hypoperfusion	generalised slow wave activity
34.	frontal lobe atrophy	frontal lobe atrophy	frontal hypoperfusion	abnormal, clinically significant
35.	frontotemporal atrophy	fronto-temporal atrophy	frontal hypoperfusion	generalised slow wave activity
36.	abnormal, clinically significant	fronto-temporal atrophy	no results	generalised slow wave activity
37.	frontotemporal atrophy	fronto-temporal atrophy	fronto-temporal hypoperfusion	diffuse slow wave activity

Table 8: Neurological Imaging and EEG results for Alzheimer’s Disease Patients (n=25)

Patient No.	CT	MRI	SPECT	EEG
1.	parieto-temporal atrophy	cerebral atrophy	parietal hypoperfusion	temporal lobe slowing
2.	temporal lobe atrophy	cerebral atrophy	parietal hypoperfusion	generalised slow wave activity
3.	white matter changes	temporal lobe atrophy	temporal hypoperfusion	temporal lobe slowing
4.	parietal lobe atrophy	parieto-temporal atrophy	no results	generalised slow wave activity
5.	temporal lobe atrophy	temporal lobe atrophy	parietal hypoperfusion	diffuse slow wave activity
6.	ventricular dilation	ventricular dilation	no results	generalised slow wave activity
7.	cerebral atrophy	parieto-temporal atrophy	temporo-parietal hypoperfusion	tempoparietal slowing
8.	parieto-temporal atrophy	temporal lobe atrophy	generalized cerebral hypoperfusion	generalised slow wave activity
9.	temporal lobe atrophy	parieto-temporal atrophy	reduced activity	temporal lobe slowing
10.	parietal lobe atrophy	parietal lobe atrophy	temporo-parietal hypoperfusion	generalised slow wave activity
11.	parietal lobe atrophy	cerebral atrophy	generalized cerebral hypoperfusion	tempoparietal slowing
12.	parieto-temporal atrophy	parieto-temporal atrophy	no results	nonspecific
13.	parietal lobe atrophy	cerebral atrophy	no results	temporal lobe slowing
14.	temporal lobe atrophy	parieto-temporal atrophy	generalized cerebral hypoperfusion	diffuse slow wave activity
15.	parieto-temporal atrophy	parieto-temporal atrophy	no results	nonspecific

Table 8 Continued: Neurological Imaging and EEG results for Alzheimer's Disease Patients (n=25)

Patient No.	CT	MRI	SPECT	EEG
16.	temporal lobe atrophy	cerebral atrophy	generalized cerebral hypoperfusion	generalised slow wave activity
17.	abnormal, clin. Signif	cerebral atrophy	generalized cerebral hypoperfusion	nonspecific
18.	temporal lobe atrophy	cerebral atrophy	parietal hypoperfusion	tempoparietal slowing
19.	parieto-temporal atrophy	parieto-temporal atrophy	no results	diffuse slow wave activity
20.	parietal lobe atrophy	parieto-temporal atrophy	no results	generalised slow wave activity
21.	parietal lobe atrophy	cerebral atrophy	temporo-parietal hypoperfusion	generalised slow wave activity
22.	cerebral atrophy	temporal lobe atrophy	generalized cerebral hypoperfusion	nonspecific
23.	parietal lobe atrophy	temporal lobe atrophy	parietal hypoperfusion	temporal lobe slowing
24.	parieto-temporal atrophy	cerebral atrophy	temporo-parietal hypoperfusion	generalised slow wave activity
25.	temporal lobe atrophy	parieto-temporal atrophy	generalized cerebral hypoperfusion	generalised slow wave activity

Table 9: Summary of Frontotemporal Dementia and Alzheimer’s Disease Patients Neurological Imaging and EEG Results

CT & MRI IMAGING CATEGORIES	CT	MRI	SPECT IMAGING CATEGORIES	SPECT	EEG IMAGING CATEGORIES
FRONTOTEMPORAL DEMENTIA					
frontal lobe atrophy	12 (32.4%)	18 (48.6%)	frontal hypoperfusion	11 (29.7%)	Fronto-temporal slowing
frontotemporal atrophy	17 (45.9%)	19 (51.3%)	fronto-temporal hypoperfusion	14 (37.8%)	temporal lobe slowing
reduced attenuation in frontal lobes	3 (8.1%)	0	reduced activity	3 (8.1%)	generalised slow wave activity
abnormal, clinically significant	5 (13.5%)	0	generalized cerebral hypoperfusion	1 (2.7%)	Short dysrhythmic bursts
			no results	8 (21.6%)	diffuse slow wave activity
					fast wave activity
					abnormal, clinically significant
					nonspecific
TOTAL	37	37		37	
ALZHEMER’S DISEASE					
temporal lobe atrophy	7 (28%)	5 (20%)	parietal hypoperfusion	5 (20%)	temporal lobe slowing
parietal lobe atrophy	7 (28%)	1 (4%)	temporal hypoperfusion	1 (4%)	tempoparietal slowing
parieto-temporal atrophy	6 (24%)	9 (36%)	temporo-parietal hypoperfusion	4 (16%)	generalised slow wave activity
cerebral atrophy	2 (8%)	9 (36%)	generalized cerebral hypoperfusion	7 (28%)	diffuse slow wave activity
ventricular dilation	1 (4%)	1 (4%)	Reduced activity	1 (4%)	nonspecific
white matter changes	1 (4%)		no results	7 (28%)	
abnormal, clin. Signif	1 (4%)				
TOTAL	25	25		25	

3.4 NEUROLOGICAL IMAGING and EEG RESULTS DISCUSSION

3.4.1 Comparison of Imaging Techniques

Tables 7 and 8 (above) show the neurological imaging results for each Frontotemporal Dementia and Alzheimer's Disease patient. Table 9 (above) provides a summary of the neurological imaging results.

Although there were some differences in results between the various imaging modalities, direct comparison between the different imaging modalities was not possible, as neurological imaging assessments were not conducted at the same time for each patient. Generally patients were first assessed with CT scans. Other imaging assessments occurred up to 18 months after the initial CT scans. During this interval it is probable that further deterioration occurred, especially in this group of patients with the generally more aggressive forms of early-onset dementia.

3.4.2 Pattern of Imaging Results for Frontotemporal Dementia Patients

All Frontotemporal Dementia patients showed evidence of clear frontal or frontotemporal lobe neuropathological changes on at least two of the neuroimaging studies (see Table 7 above). Approximately 80 % of the Frontotemporal Dementia patients showed frontal or frontotemporal lobe atrophy with CT scans (see Table 9 above). All Frontotemporal Dementia patients showed frontal or frontotemporal lobe atrophy on MRI scans.

SPECT results showed approximately 80% of Frontotemporal Dementia patients had frontal or frontotemporal hypoperfusion. EEG imaging produced more varied findings. Approximately 30% of Frontotemporal Dementia patients showed frontotemporal lobe slowing. Approximately one third of patients were found to have generalised slow wave activity, and approximately 13% showed diffuse slow wave activity. Approximately 8% of patients exhibited short dysrhythmic bursts. Small numbers of patients were recorded with either temporal lobe slowing, fast wave activity, or classified as “abnormal, clinically significant”.

3.4.3 Pattern of Imaging results for Alzheimer’s Disease Patients

As shown in Tables 8 & 9 (see above), CT scans showed approximately 30% of Alzheimer’s Disease patients had temporal lobe atrophy, approximately 30% showed parietal lobe atrophy, and approximately 25% showed parieto-temporal atrophy. 8% of patients showed cerebral atrophy. Small numbers of Alzheimer’s Disease patients showed either ventricular dilation, white matter changes, or were classified as “abnormal, clinically significant”.

MRI results showed 20% of patients had temporal lobe atrophy, 36% showed parieto-temporal atrophy, and 36% showed cerebral atrophy. One patient showed ventricular dilation, and one patient showed parietal lobe atrophy.

EEG results showed approximately one third of Alzheimer's Disease patients had either temporal lobe slowing or tempo-parietal lobe slowing. 40% of Alzheimer's Disease patients showed generalised slow wave activity, and 12% diffuse slow wave activity.

SPECT results showed 40% of Alzheimer's Disease patients had parietal hypoperfusion, tempo-parietal hypoperfusion, or temporal hypoperfusion. Approximately 30% showed generalised cerebral hypoperfusion.

3.5 NEUROLOGICAL IMAGING CONCLUSIONS

The neurological imaging results (Tables 7, 8 & 9: CT, MRI, EEG, & SPECT) show that the Frontotemporal Dementia group and Alzheimer's Disease group exhibited clearly differentiated and clinically significant patterns of neuroradiological changes. The pattern of neurodegeneration detected in the Alzheimer's Disease patients involved primarily the temporal and parietal lobes. In marked contrast, the Frontotemporal Dementia patients imaging results showed primarily frontal and frontotemporal lobe degeneration. These findings are consistent with the findings of other researchers (e.g. Chan & Fox et al. 2001; Neary & Snowden et al. 1998; Pasquier & Delacourte, 1998) which have shown that neurological imaging studies are an essential component to assist with the differential diagnosis of Frontotemporal Dementia from Alzheimer's Disease.

The results indicate that the Frontotemporal Dementia and Alzheimer's Disease groups were clearly differentiated on neuropathological criteria, thus justifying further investigation in terms of neuropsychological function and behaviour.

3.6 AUTOPSY FINDINGS IN FRONTOTEMPORAL DEMENTIA AND ALZHEIMERS DISEASE

Autopsy studies of dementia patients revealed that a significant number of patients had definite non-Alzheimer's Disease pathology (Brun, 1987). More recent autopsy findings of patients with dementia have indicated that Frontotemporal Dementia may account for up to 20% of dementia cases (Gustafson, 1993; Lebert & Pasquier et al. 1998). Neuropathological changes in Frontotemporal Dementia patients noted at autopsy included non-specific frontal and temporal atrophy without the characteristic clumps and deposits of degenerating cells (amyloid plaques and neurofibrillary tangles) associated with Alzheimer's Disease changes (Lebert & Pasquier et al. 1998).

Autopsy studies have found that the majority of Frontotemporal Dementia patients have marked degeneration of the amygdala and hippocampus. These brain structures play a crucial role in memory functioning (Johanson & Hagberg, 1989). Frontotemporal patients who exhibited relatively well-preserved memories throughout the course of their illness were found to also have comparatively well-preserved hippocampal and amygdalar areas (Johanson & Hagberg, 1989; Neary & Snowden, 1996).

3.7 AUTOPSY RESULTS

Autopsy results were available for 4 of the 7 Frontotemporal Dementia patients who died after the 3-year follow-up. No autopsy results were available for the one Alzheimer's Disease patient who died during the course of this research. Nearly 20% of the Frontotemporal patients died during the course of this study compared with only 4% of the Alzheimer's Disease patients. This result is consistent with previous findings that have shown that Frontotemporal Disease patients have significantly shorter life spans after diagnosis than that of early-onset Alzheimer's Disease patients (Pasquier & Richard et al. 2004; Roberson & Hesse, 2005).

This finding has significant implications for caregivers as this result indicates that patients move through stages of their disease rapidly, and require flexible and rapid treatment if their care needs are to be met. This research indicates that a significant number of Frontotemporal Disease patients will require palliative care within 2 years of diagnosis. Traditional dementia services are designed for the slower progression of Alzheimer's Disease, and may not cope with the rapidly changing requirements of this group of Frontotemporal Dementia patients with early-onset dementia (i.e. Harvey, 1998; Tanabe & Ikeda et al. 1999).

Autopsy Results for “Ingrid”

Ingrid was diagnosed with Frontotemporal Dementia at age 60. She died 3 years later. The autopsy report showed narrowing of the gyri and widening of the sulci over the frontal lobes. The leptomeninges were thin and translucent. The brainstem and cerebellum were normal. The cranial nerves were normal.

Conclusion: Frontal lobe atrophy, pallor of the substantia nigra.

Autopsy Results for “Les”

Les was diagnosed with Frontotemporal Dementia at age 53. He died two years later. The autopsy finding showed unequivocal frontal lobe atrophy.

Conclusion: Frontotemporal Atrophy.

Autopsy Results for “Julie” (see Section 7.3.4, p. 208 for case study)

Julie was diagnosed with Frontotemporal Dementia with parkinsonism at age 46. She died 3 years later. The autopsy findings showed atrophy of frontal and temporal regions and pallor of the substantia nigra.

Conclusion not available.

Autopsy Results for “Ray”

Ray was diagnosed with Frontotemporal Dementia at age 57. He died 4 years later. The autopsy findings showed narrowing of the gyri and widening of the sulci over the frontal lobes. The leptomeninges were thin and translucent. The brainstem and cerebellum were normal. The cranial nerves were normal.

Conclusion: Frontal lobe atrophy, pallor of the substantia nigra.

Summary of Frontotemporal Dementia Patient Results

The autopsy results outlined above confirmed clear frontal and/or temporal lobe degeneration in all of the 4 patients diagnosed with Frontotemporal Dementia. Two of the 4 patients had pallor of the substantia nigra. This finding is consistent with previous research linking changes to the substantia nigra to Frontotemporal Dementia (Filley & Kleinschmidt-DeMasters, 1994; Laakso & Frisoni et al. 2000). None of the characteristic neuropathological changes associated with Alzheimer's Disease, the amyloid plaques and neurofibrillary tangles, were noted in the autopsy reports. These findings add support to the validity of Frontotemporal Dementia as a valid diagnostic category, and are consistent with a growing body of research (i.e. Rascovsky & Salmon, 2002).

CHAPTER 4

NEUROPSYCHOLOGICAL ASSESSMENT OF

FRONTOTEMPORAL DEMENTIA AND

ALZHEIMERS DISEASE

4.1 INTRODUCTION TO NEUROPSYCHOLOGICAL ASSESSMENT

OF FRONTOTEMPORAL DEMENTIA AND ALZHEIMER'S DISEASE

Neuropsychological tests have been widely utilised to assist with the clinical diagnosis of Frontotemporal Dementia (Snowden & Neary et al. 1996; Gregory & Hodges, 1996; Neary & Snowden et al. 1998; Miller & Diehl et al. 2003; Pasquier, 1999). Neuropsychological tests have been found to be a useful clinical tool in assisting with the differential diagnosis of Frontotemporal Dementia from Alzheimer's Disease, other forms of dementia, normal aging, and non-organic psychological problems (Pasquier, 1999; Gustafson & Brun, 1999; Neary & Snowden et al. 1998). Cognitive impairments identified by neuropsychological assessment in both Alzheimer's Disease and Frontotemporal Dementia have been found to have a high correlation with SPECT, MRI, and CT findings (Duara & Barker et al. 1999; Elfgren, Ryding & Passant, 1996).

Typically, neuropsychological assessment of Frontotemporal Dementia patients has produced a distinctive profile indicating relatively preserved visuospatial abilities combined with impaired verbal fluency, executive functions, and vocabulary (Johansen & Hagberg, 1989; Miller & Cummings et al. 1991; Elfgrén & Ryding et al. 1996; Lindau & Almkvist et al. 2000; Rascovsky & Salmon et al. 2002).

Several researchers have questioned the capacity of neuropsychological test batteries to discriminate Frontotemporal Dementia patients from Alzheimer's Disease patients (Kertesz & Davidson et al. 2003; Harciarek & Jodzio, 2005). Kertesz and colleagues (2003) assessed 52 Alzheimer's Disease patients and 52 Frontotemporal Dementia patients with a comprehensive battery of neuropsychological tests. They found that the majority of the neuropsychological tests were unable to discriminate between the two groups. Tests of memory were shown to be the most useful. Alzheimer's Disease patients produced lower scores on memory tasks than Frontotemporal Dementia patients, and Frontotemporal Dementia patients produced lower scores on verbal language tasks than Alzheimer's Disease patients. Kertesz and colleagues (2003) also found that analysis of the behaviour of the patients was significantly more effective in discriminating between the two groups. The majority of the subjects in this study subsequently had their diagnosis confirmed by autopsy.

A comprehensive review of the literature on the differential diagnosis of Frontotemporal Dementia from Alzheimer's Disease (Harciarek & Jodzio,

2005) indicated that most neuropsychological tests did not discriminate between the two groups. However, the researchers found that Alzheimer's Disease patients performed better on tests of executive functioning than Frontotemporal Dementia patients. Alzheimer's Disease patients were found to perform more poorly on tests of memory than Frontotemporal Dementia patients early in the course of the illness.

4.2 ROUTINE METHODOLOGICAL PROBLEMS ENCOUNTERED IN THE ASSESSMENT OF FRONTOTEMPORAL DEMENTIA PATIENTS

There are significant methodological problems when neuropsychological assessments are conducted with Frontotemporal Dementia patients and dementia patients generally (Pasquier & Lebert et al. 1995; Smeding & de Koning, 2000):

4.2.1 Multiple Task Demands

Most, if not all, neuropsychological tasks make multiple demands on cognition, often assessing a variety of cognitive functions including attention, receptive and expressive language, visuo-spatial abilities, organisation, planning, cognitive endurance, motor speed, speed of information processing, and abstraction (Lezak, 1995; Pasquier & Lebert et al. 1999). Therefore, it is possible that patients with differing forms of dementing illnesses will produce scores within the same range on the same test, but will have impairment in vastly differing areas of cognitive functioning (Lezak, 1995; Pasquier & Lebert et al. 1999).

4.2.2 Small Sample Sizes

An ongoing problem associated with the neuropsychological assessment studies of Frontotemporal Dementia patients has been small sample size (Stuss, 1993; Snowden & Neary et al. 1996; Marshall & Hutchinson, 2001). Stuss (1993), in a study of neuropsychological assessment of the frontal and anterior temporal lobes pointed to the fact that the majority of neuropsychological studies in this area relied on small sample sizes. Stuss (1993) cautioned that, due to the small sample sizes employed, most neuropsychological studies of frontal and anterior temporal lobe functioning had produced results of limited reliability and validity.

4.2.3 Behavioural Disturbance & Impoverished Communication Skills

Patients with Frontotemporal Dementia are typically difficult, if not impossible, to assess soon after the onset of the disease due to behavioural disturbance, wandering and pacing, lack of cooperation, loss of motivation, and mutism (Miller & Cummings et al. 1991; Pasquier, 1999; Smeding & de Koning; 2000; Snowden & Neary et al. 1996). The lack of capacity for concerted effort, combined with impoverished communication skills, are characteristic features of Frontotemporal Dementia. These characteristic deficits, and lack of concern about accurate test performance, invariably depress test scores on all neuropsychological measures (Snowden & Neary et al. 1996; Pasquier, 1999).

Some of the problems and dangers associated with the neuropsychological assessment of Frontotemporal Dementia patients were documented by Miller

and colleagues (1991) in a series of case studies. For example, one of the patients involved in their study left the assessment, and could not be stopped from leaving the hospital. He was found 18 hours later, having wandered twenty kilometres from the hospital.

Frontotemporal Dementia patients often become distracted by irrelevant visual stimuli in the test rooms, and commonly get out of their seats to investigate objects of interest to them (Snowden & Neary et al. 1996). Frontotemporal Dementia patients show marked perseverations (perseveration is the uncontrollable repetition of a particular response, such as a word, phrase, or gesture, despite the absence or cessation of a stimulus). Perseveration is an indicator that the patient has lost the ability to shift “mental set” (Lezak, 1995). Interference effects from previous tasks are common, and such interference effects are a form of perseveration (Snowden & Neary et al. 1996).

4.3 THE IMPORTANCE OF QUALITATIVE ASSESSMENT AND MISSING VALUES

Researchers (e.g. Elfgren, Passant, & Risberg, 1993; Gainotti, 1991; Johanson & Gustafson et al. 1986; Smeding & de Koning; 2000) have also highlighted the importance of qualitative as well as quantitative assessment of Frontotemporal Dementia patients.

Qualitative variables of particular note are degree of cooperation, loss of insight, speech abnormality, apathy, distractibility, flight reactions, and test strategies

(Gustafson & Brun, 1999; Diehl & Kurz, 2002; Gainotti, 1991; Johanson & Hagberg, 1989; Engelborghs & Martens, 2002; Rankin & Baldwin et al. 2005; Thompson & Stopford et al. 2005).

The difficulties invariably encountered in the assessment of Frontotemporal Dementia lead to many missing values in neuropsychological test results (Johanson & Hagberg, 1989; Smeding & de Koning; 2000). These researchers argue that it is important to evaluate the test behaviour responsible for the missing values, as this evaluation provides rich diagnostic information. Evaluation of such test behaviour highlights the cognitive and behavioural deficits that prevent the patients from successfully undertaking standard neuropsychological test batteries.

4.4 ASSESSMENT OF SPECIFIC NEUROPSYCHOLOGICAL SKILLS IN FRONTOTEMPORAL DEMENTIA AND ALZHEIMER'S DISEASE

4.4.1 Speech, Reading and Writing Skills

Although speech output is characteristically reduced, primary linguistic competence is usually preserved in the early stages of Frontotemporal Dementia (Diehl & Kurz, 2002; Snowden & Neary et al. 1996; Kertesz & Davidson et al. 2003). Frontal lobe dysfunction leads to economy of speech, perseverative speech, and marked reduction in speech output (dynamic aphasia), with mutism frequently occurring in the latter stages of the illness (Neary & Snowden et al. 1998; Snowden & Neary et al. 1996; Pasquier & Leber et al. 1999).

Impaired verbal fluency alone has been found to be a good indicator of frontal lobe dysfunction (Gregory & Hodges, 1993). In rare cases Frontotemporal Dementia is accompanied by a period of increased talking in the early stages of the illness (Gustafson & Brun, 1999). Patients with frontotemporal atrophy characteristically suffer a deterioration of both quality and quantity of language output early in the course of the illness (Miller & Darby et al. 1997; Johanson & Hagberg, 1989).

A characteristic feature of Frontotemporal Dementia patients is that they rarely initiate conversations. Responses to questions tend to be extremely brief and unelaborated. The speech patterns characteristic of Frontotemporal Dementia patients indicates minimal application of mental effort (Rosen & Gorno-Tempini et al. 2002). Health professionals assessing the Frontotemporal Dementia patient, caregivers and relatives are more likely to receive answers to questions that require only a single-word answer than to open ended questions that require generation and organisation of a complete sentence (Miller & Darby et al. 1995; Snowden & Neary et al. 1996).

Frontotemporal Dementia patients tend to overuse irrelevant and stereotypical remarks instead of meaningful conversation, and speech is often perseverative (Bathgate & Snowden et al. 2001). Over-learned repertoires are often repeated verbatim. Echolalia and verbal perseverations become more common in the middle stages of the disease (Bathgate & Snowden et al. 2001).

The increasing occurrence of echolalia and verbal perseverations reflects an increasing impoverishment in the patient's constructive and generative language. Patients are unable to generate, plan, and organise novel responses to questions. Utterances are usually grammatically correct, and word-finding performance is generally well preserved until the advanced stages of the illness. Over learnt, automatic language may persist long after spontaneous speech has disappeared (Gustafson & Brun, 1999; Bathgate & Snowden et al. 2001).

Loss of language output is more pronounced in patients with primarily left frontal deterioration (Miller & Darby et al. 1995). Patients with Frontotemporal Dementia often are unable to read silently, and make uncontrolled vocalisations when watching television or engaging in daily activities (Klinger, 2001).

Changes in writing include spelling errors, and speed of handwriting.

Alzheimer's Disease patients often have dysgraphic, error-filled handwriting, whereas Frontotemporal Dementia patients handwriting is often impoverished (Gustafson & Brun, 1999).

The cluster of language deficits occurring with Frontotemporal Dementia is known as the PEMA Syndrome: Palilalia, Echolalia, Mutism, and Amimia (see Table 27 p. 103, Guiraud, 1936). This syndrome is extremely rare in Alzheimer's Disease (Gustafson & Brun, 1999).

In comparison to Frontotemporal Dementia, speech in Alzheimer's Disease tends to be significantly less economical and concrete (Neary, 1988).

Speech in Alzheimer's Disease, particularly in the early course of the illness tends to feature a lack of meaningfulness and poor concept formation (Cummings & Benson, 1986).

4.4.2 Visual Perception and Spatial Skills

There is no convincing evidence of the common "parietal" type deficits associated with Alzheimer's Disease in Frontotemporal Dementia.

Frontotemporal Dementia patients, in the early stages of their illness, typically have little difficulty in the perceptual recognition of objects; do not make major perceptual errors on naming tests of line drawings, and generally use objects appropriately (Snowden & Neary et al. 1996; Rascovsky & Salmon et al. 2002).

In most cases Frontotemporal Dementia patients can accurately copy simple geometric designs when they are first assessed (Johanson & Hagberg, 1989; Snowden & Neary et al. 1996; Rascovsky & Salmon, 2002). This stands in marked contrast to Alzheimer's Disease patients, who generally exhibit impaired copying abilities at first assessment (Johanson & Hagberg, 1989; Fisher & Rourke et al. 1999).

Frontotemporal Disease patients generally experience little difficulty locating objects in their immediate environment, and can usually negotiate their way around their environment without becoming lost (Neary & Snowden et al. 1988;

Mathuranath & Nestor et al. 2000). However, due to loss of motivation, distractibility, and the tendency to perseverate on test instructions, patients may perform poorly on constructional tasks such as drawing and block constructions. Perseverations are common on drawing tasks, and on block design tasks blocks are often moved randomly (Snowden & Neary et al. 1996).

4.4.3 Memory

Reports of memory disturbance accompanying Frontotemporal Dementia are common. Memory of important episodes in a patient's life (episodic memory) is commonly relatively well-preserved in the early stages of the illness (Lindau & Almkvist et al. 2000). However, recent research has indicated that a significant number of Frontotemporal Dementia patients exhibit severe new learning deficits and impaired memory for recent events (anterograde amnesia) early in the course of Frontotemporal Dementia (Caine & Patterson et al. 2001; Graham & Davies et al. 2005). Frontotemporal Dementia patients perform poorly on standardised tests of memory for both recall and recognition (Johanson & Hagberg, 1989; Gustafson, 1993). Frontotemporal Dementia patients are often not clinically amnesic, and can be oriented for time and place, and can provide accurate information about current autobiographical events if given sufficient prompts (Snowden & Neary et al. 1996). Performance on tasks during a neurological examination can also generally be improved if specific, directive questions are used. Patients' memory performance also typically improves with frequent cues and with the provision of multiple-choice alternative responses (Snowden & Neary et al. 1996).

These findings suggest that Frontotemporal Dementia patients may have information available to them that they do not, or are unable to, access spontaneously. Patients appear to have difficulties with spontaneous information generation and organised searching.

There is no evidence of attempts to integrate information, or abstract the general thematic content. Delayed recall of a fable 1 hour later mirrored impaired immediate recall performance, with sporadic elements of the story given (Snowden & Neary et al. 1996).

Table 10: Major neuropsychological studies comparing Frontotemporal Dementia, Semantic Dementia & Alzheimer’s Disease patients.

No. of FTD, AD, & SD subjects in study.			Authors & Findings Summary
FTD	AD	SD	
16		6	Ikeda & Tanabe, 2000; neuro-psychological tests did not discriminate between FTD & AD*
12	12		Gregory & Orrell et al. 1997; neuro - psychological tests were poor discriminators between FTD & AD.*
52	52		Kertez & Davidson et al. 2003; most neuropsychological tests did not discriminate FTD from AD. Memory scores lower in AD and language scores lower in FTD*
14	28		Rascovsky & Salmon et al. 2002; AD verbal fluency scores higher than FTD. FTD visuospatial scores higher than AD.
51	69	13	Diehl & Monsch et al. 2005 A A combination of Animal Fluency and Boston Naming Test discriminated 90% of FTD patients from AD patients
14	14		Siri & Benaglio et al. 2001; most neuropsychological tests did not discriminate FTD from AD. AD verbal fluency scores higher than FTD. FTD visuospatial scores higher than AD.

* = behaviours good discriminators between FTD and AD

Neuropsychological studies of patients with Alzheimer's Disease and Frontotemporal Dementia (Table 10) have shown consistently that the majority of neuropsychological tests do not accurately discriminate between the two groups. Some visuospatial and verbal fluency tests have been found to discriminate between Frontotemporal Dementia and Alzheimer's Disease (Table 10).

4.5 PERFORMANCE ON STANDARD TESTS OF COGNITIVE

FUNCTIONING: MINI MENTAL STATE EXAM (MMSE, Folstein, Folstein, & McHugh, 1975)

The Mini Mental State Exam (MMSE) is a widely used dementia assessment and monitoring tool (Husain, 2003). Husain (2003) cautions that interpreting individual MMSE scores without clinical information about the patient can be misleading.

The MMSE has been found to have very limited capacity to detect executive functioning, abstract reasoning, and visuo-spatial construction deficits (Nys & Zandvoort et al. 2005). As noted above, executive functioning and abstract reasoning deteriorate in the early stages of Frontotemporal Dementia, and visuospatial constructional deficits occur in the early stages of Alzheimer's Disease. The MMSE's lack of sensitivity to these deficits may account for the fact that both Frontotemporal Dementia and Alzheimer's Disease patients have been found to produce scores within normal limits in the early stages of their

illnesses (Schmitt & Ranssen et al. 1989; Miller & Cummings et al. 1991).

Schmitt and colleagues (1989) found that dementia patients sometimes produced scores of 29 and 30.

Given the above, the MMSE has been found to have limited capacity to differentiate Frontotemporal Dementia from Alzheimer's Disease when used alone (Miller et al. 1991; Kertesz & Davidson et al. 2003; Diehl & Monsch et al. 2005). However, several researchers have incorporated the MMSE into brief and effective test batteries that accurately differentially diagnose Frontotemporal Dementia from Alzheimer's Disease (Mathuranath & Nestor et al. 2000; Diehl & Monsch et al. 2005). The MMSE scores have been found to deteriorate significantly faster in Frontotemporal Dementia patients than Alzheimer's Disease patients (Miller & Cummings et al. 1991; Pasquier & Lebert et al. 1999; Chow & Hynan et al. 2006).

4.6 MINI MENTAL STATE EXAM MMSE RESULTS

Table 11: Mini Mental State Exam Frequency table for Frontotemporal Dementia & Alzheimer’s Disease MMSE scores

MMSE Score	FTD	%	AD	%
6	2	5.4%		
10	3	8.1%	1	7.1%
11			1	7.1%
13	1	2.7%	1	7.1%
14	1	2.7%		
15			1	7.1%
16			2	14.3%
17	2	5.4%		
18			2	14.3%
19			1	7.1%
20	4	10.8%		
22	1	2.7%	1	7.1%
23	2	5.4%	1	7.1%
24	1	2.7%	1	7.1%
25	1	2.7%		
26	1	2.7%		
27	3	8.1%	1	7.1%
28	1	2.7%	1	7.1%
29	2	5.4%		
Total	25			14

Table 11 indicates a very broad range of scores on the MMSE for both Frontotemporal Dementia and Alzheimer’s Disease patients, with Frontotemporal Dementia MMSE scores falling between 6 and 29, and Alzheimer’s Disease MMSE scores falling between 10 and 28.

This finding is consistent with previous research (eg. Schmitt & Ranseen et al. 1989) that found dementia patients commonly produced a broad range of scores, with scores sometimes falling within normal limits.

Table 12: Mini Mental State Examination (MMSE) Results: Number of Frontotemporal Dementia & Alzheimer’s Disease subjects below and above the dementia cutoff score (23) and Chi Square result

MMSE Score	FTD	AD	Chi Square
≤ 23	16 (64%)	11 (78.6%)	.34 ^a
> 23	9 (36%)	3 (21.4%)	
Total	25	14	

^a not statistically significant

4.7 MMSE DISCUSSION

There was no significant difference between the number of Frontotemporal Dementia and Alzheimer’s Disease subjects falling below the dementia cutoff score of 23 (Table 12). A clinically significant number of patients in both groups (36% of Frontotemporal Dementia patients and 21% of Alzheimer’s Disease patients) produced scores above the dementia cutoff score of 23. This result indicates that patients with clear neuropathological deterioration consistent with either Frontotemporal Dementia or Alzheimer’s Disease can produce MMSE scores not necessarily indicative of dementia. This result supports previous research findings (Miller & Cummings et al. 1991; Snowden & Neary et al. 1996; Schmitt & Ranseen et al. 1989) that some Frontotemporal Dementia and Alzheimer’s Disease patients produced MMSE scores that were not markedly impaired in the early stages of their illness.

This result is consistent with previous research findings that have indicated the MMSE does not discriminate between Frontotemporal Dementia and Alzheimer's Disease patients (Miller & Cummings et al. 1991; Roberson & Hesse et al. 2005).

**4.8 PERFORMANCE ON STANDARD TESTS OF COGNITIVE
FUNCTIONING:THE WECHSLER ADULT INTELLIGENCE SCALE-
111 (WAIS-111, WECHSLER, 1997)**

Some Frontotemporal Dementia patients perform within normal limits on the Wechsler Adult Intelligence Scales (Neary & Snowden, 1996). However, performance is more commonly impaired, and becomes increasingly impaired as the disease progresses. There are typically depressed scores on the Wechsler Adult Intelligence Scales' Comprehension, Similarities, and Picture Arrangement subtests (Neary & Snowden, 1996; Zakzanis, Kiellar, Young, & Boulos, 2001). Comprehension scores tend to be depressed because Frontotemporal Dementia patients lose the ability to understand the underlying rules of sentence structure (Snowden & Neary et al. 1996, see Table 13 below for summary of Frontotemporal Dementia patients' performance on neuropsychological tests).

Table 13: Neuropsychological profile summary (Snowden & Neary et al. 1996)

Neuropsychological Profile Summary
Performance. Cursory responses, minimal effort, slowing of response initiation, perseveration
Language. Economy of speech, perseveration, echolalia, stereotypy, concreteness, late mutism.
Calculation. Impaired for mentally demanding tasks.
Perception. Preserved.
Spatial functioning. Preserved throughout disease. Errors of construction secondary to organisational deficits.
Memory. Variable, idiosyncratic day-to-day memory, preserved orientation in time and place, poor information retrieval, recall enhanced by cues and directional probes.
Planning and abstraction. Concrete responses, poor set shifting, organisational and sequencing failure, perseveration.

4.9 WAIS-111 RESULTS

Table 14: WAIS-111 IQ: Full Scale IQ, Verbal IQ, and Performance IQ scores and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment

	FTD			AD			Levene’s Test For Equality of Variance	t(df) sig
	N	Mean	Std. Dev	N	Mean	Std. Dev		
Verbal IQ	26	87.4	14.6	15	90.8	14.7	0.00	0.72(39)
Performance IQ	26	87	10.7	15	76.1	12.5	0.21	2.95(39) *
Full Scale IQ	26	86.3	12.1	15	83.5	12.9	0.01	0.71(39)

* = p < .01

Frontotemporal Dementia and Alzheimer’s Disease patients produced full scale IQ scores in the low-average range (see Table 14 above).

Both Frontotemporal Dementia and Alzheimer’s Disease Verbal IQ scores fell in the average to low-average range. Performance IQ scores for the Frontotemporal Dementia patients were significantly higher than the scores for Alzheimer’s Disease patients, with Frontotemporal Dementia Performance IQ scores falling in the low-average range and Alzheimer’s Disease Performance IQ scores falling in the borderline range. There was a large scatter of scores around the mean for both Frontotemporal Dementia and Alzheimer’s Disease subjects.

Table 15: WAIS-111 Verbal IQ (VIQ) subtest scores and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment

Verbal IQ scores	FTD			AD			Levene’s Test For Equality of Variance	t(df) ^a
	N	Mean	Std. Dev	N	Mean	Std. Dev		
Information	30	8.3	3.6	17	7.8	3.8	0.19	0.52(45)
Comprehension	26	6.6	3.5	17	8	3.7	0.02	1.3(41)
Similarities	31	6.3	3.1	17	6.9	2.5	0.13	0.78(46)
Arithmetic	26	7.7	3.1	16	6.8	2.6	0.69	0.97(40)
Digit Span	31	7.8	2.2	18	7.2	3.1	0.90	.74(26.9)
Vocabulary	27	7.3	3.2	16	9.1	3.3	0.29	1.76(41)

^a = none of the t-tests were statistically significant

All the Frontotemporal Dementia and Alzheimer’s Disease WAIS-111 Verbal IQ scores fell in either the low-average or borderline range (see Table 15 above). This result indicates that WAIS-111 Verbal IQ scores do not discriminate between Frontotemporal Dementia and Alzheimer’s Disease patients. This finding is consistent with previous research findings (Kertesz & Davidson et al. 2000).

Table 16: WAIS-111 Performance IQ (PIQ) scores and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment

Performance IQ scores	FTD			AD			Levene’s Test For Equality of Variance	t(df) sig
	N	Mean	Std. Dev	N	Mean	Std. Dev		
Object Assembly	26	6.8	2.9	15	5.1	2.9	0.00	1.75(39)
Block Design	30	7	3.3	17	4.4	2.9	0.21	2.74(45) *
Picture Arrangement	28	6.4	2.3	15	5.3	2.1	0.02	1.41(41)
Picture Completion	31	7.2	2.8	17	4.6	2.2	1.00	3.37(46) *

* = $p < .01$

All the Performance IQ subtest scores for Frontotemporal Dementia subjects fell in the borderline or low average ranges. Performance IQ scores for Alzheimer’s Disease subjects fell in the impaired/borderline range. Frontotemporal Dementia subjects mean scores for the Block Design and Picture Completion subtests were significantly higher than scores for Alzheimer’s Disease subjects.

4.9.1 WAIS-111 Results Summary

The above findings indicate that the WAIS-111 is an effective dementia assessment tool, with both the Alzheimer’s Disease and Frontotemporal Dementia groups producing results consistent with significantly compromised intellectual functioning. However, the results indicate that no WAIS-111 Verbal IQ subtests effectively discriminated between the Frontotemporal Dementia and

Alzheimer's Disease patient groups. Only two of the Performance IQ subtests, Block Design and Picture Completion, discriminated between the Frontotemporal Dementia and Alzheimer's Disease groups.

The pattern of WAIS-111 results, with Frontotemporal Dementia patients showing relatively preserved visuospatial skills in comparison to Alzheimer's Disease patients, is consistent with previous research (Johansen & Hagberg, 1989; Miller & Cummings et al. 1991; Elfgrén, Ryding & Passant, 1996; Lindau & Almkvist et al. 2000; Rascovsky & Salmon et al. 2002).

4.9.2 Subjective Assessment

Subjective assessment of the groups provided valuable clinical information. Only 26 of the 37 (84%) Frontotemporal Dementia patients and 15 of the 25 (72%) Alzheimer's Disease patients (Table 14) were able to complete all the WAIS-111 subtests. There were a number of reasons why patients were unable to complete the WAIS-111 including inability to understand test instructions, agitation, and patient distress. The large numbers of Alzheimer's Disease and Frontotemporal Dementia patients unable to complete the full WAIS-111 indicates that both groups of patients were significantly impaired.

4.10 PAIRED ASSOCIATES LEARNING TASK (PALT) RESULTS

Table 17: Paired Associates Learning Task (PALT) scores and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment.

Learning Task	FTD			AD			Levene’s Test For Equality of Variance	t(df) ^a
	N	Mean	Std. Dev	N	Mean	Std. Dev		
PALT Easy words trial 1	26	3.2	1.5	12	3.7	1.5	0.17	.27(36)
PALT Easy words trial 2	26	5	1.1	12	4.4	1.6	0.98	1.4(36)
PALT Easy words trial 3	26	5	1.2	11	5.3	0.8	1.90	0.6(35)
PALT Hard words trial 1	26	0.5	0.9	12	0.1	0.3	0.92	1.5(34)
PALT Hard words trial 2	26	1.1	1.3	12	0.4	0.8	2.60	1.7(36)
PALT Hard words trial 3	26	1.6	1.4	11	0.6	0.9	3.90	1.9(35)

^a = none of the t-tests were statistically significant

Scores for both Frontotemporal Dementia and Alzheimer’s Disease subjects fell in the impaired range for all Easy and Hard trials (see Table 17 above). There was no significant difference between the two groups of patients on any of the trials. Previous research has shown that Frontotemporal Dementia patients perform significantly better than Alzheimer’s Disease patients on the PALT (Lee & Rahman et al. 2003). The research by Lee and colleagues (2003) did not use early-onset dementia patients exclusively; therefore direct comparisons between their research findings and the current study are not possible.

4.11 PURDUE PEGBOARD TEST RESULTS

Table 18: Purdue Pegboard Test scores and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment

	FTD			AD			Levene’s Test For Equality of Variance	t(df) sig
	N	Mean	Std. Dev	N	Mean	Std. Dev		
Right hand	24	13.1	2.3	14	10.7	3.9	6.1 *	2.1(17.9)
Left hand	23	12.3	2.3	14	10.5	2.7	0.20	2.1(35) *
Both hands	17	9.6	2.5	11	7	.6	1.60	2.3 (26) *

* = p < .05

Scores for both Frontotemporal Dementia and Alzheimer’s Disease subjects indicated impaired performance with the exception of “Right Hand” for the Frontotemporal Dementia patient group. Frontotemporal Dementia patient scores were significantly higher than the Alzheimer’s Disease patient scores for the “Left Hand” and “Both Hands” components of the test. This finding indicates relatively preserved hand-eye coordination and manual dexterity in Frontotemporal Dementia patients. This test has not been used previously to assess Frontotemporal Dementia patients. The use of the Purdue Pegboard test with early-onset dementia patients warrants further research.

4.12 DIGIT SPAN TEST RESULTS (WAIS-111, WECHSLER, 1997)

Table 19: Digits Forward and Backward recalled. Scores and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment

	FTD			AD			Levene’s Test For Equality of Variance	t(df) ^a
	N	Mean	Std. Dev	N	Mean	Std. Dev		
Digits Forward	29	5.5	1.2	18	5.7	1.3	0.60	.4(45)
Digits Backward	29	3.6	1	18	2.9	1.4	0.60	1.9(45)

^a = none of the t-tests were statistically significant

The number of digits repeated verbatim and repeated in reverse order was impaired for both Frontotemporal Dementia and Alzheimer’s Disease groups, with no significant difference between the two groups.

4.13 WECHSLER MEMORY SCALE (WMS, WECHSLER, 1974) TEST

RESULTS

Table 20: Wechsler Memory Scale (WMS) Logical Memory and Visual recall scores and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment

Logical Memory	FTD			AD			Levene’s Test For Equality of Variance	t(df) sig
	N	Mean	Std. Dev	N	Mean	Std. Dev		
Immediate recall Story 1	29	6.3	3.4	18	4.5	3.2	0.10	1.7(45)
Immediate recall Story 2	29	6.1	3.8	18	3.9	3	0.60	2.1(45) *
Immediate recall Total	29	12.4	6.7	18	8.4	5.9	0.40	2.1(45) *
Delayed Recall Story 1	25	5.4	4.1	14	3.4	3.4	0.10	1.8(37)
Delayed Recall Story 2	25	4.5	3.6	14	3.7	3.7	0.10	1.5(37)
Delayed Recall Total	25	9.9	7.4	14	5.6	6.5	0.10	1.7(37)

* = $p < .05$

The Wechsler Memory Scale (WMS) scores were impaired for both Frontotemporal Dementia and Alzheimer’s Disease groups, and for both the immediate and delayed recall condition of the tests (see Table 20 above). The Frontotemporal Dementia group was able to recall significantly more of “Story 2” than the Alzheimer’s Disease group. Total Immediate Recall score was significantly higher for the Frontotemporal Dementia group than the Alzheimer’s Disease group. This finding is consistent with the findings of Kertez and colleagues (2003).

Table 21: Wechsler Memory Scale (WMS) scores and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment on the Visual Recall subtest

Visual Recall	FTD			AD			Levene’s Test For Equality of Variance	t(df) sig
	N	Mean	Std. Dev	N	Mean	Std. Dev		
Immediate Recall Design 1	28	2.1	0.9	15	1	0.9	0.10	3.8(41) *
Immediate Recall Design 2	28	2.1	1.5	15	1.1	0.8	6.7 *	2.7(40.9) *
Immediate Recall Design 3	27	2.2	1.8	15	0.6	0.8	12.3 **	3.9(38.8) **
Immediate Recall Total	27	6.6	2.9	15	2.7	2.2	1.40	4.6(41) **
Delayed Recall Design 1	25	1.4	1.2	11	0.5	0.9	6.9 *	2.8(28.1) *
Delayed Recall Design 2	25	1.8	1.5	11	0.6	1.1	3.60	3.0(28) **
Delayed Recall Design 3	25	1.7	1.9	11	0.5	0.8	11.0 **	2.7(33.9) *
Delayed Recall Total	25	4.9	3.2	11	1.5	2.1	0.50	3.3(34) **

* = $p < .05$; ** = $p < .01$

Both Immediate Recall and Delayed Recall scores fell in the impaired range for all visual designs for both Frontotemporal Dementia and Alzheimer’s Disease groups. Mean recall scores were significantly higher for the Frontotemporal Dementia group on all sections of the test.

This result indicates the Frontotemporal Dementia group has relatively preserved immediate and delayed visual memory for designs in comparison to the Alzheimer’s Disease group, and is consistent with previous research findings (Kertez & Davidson, 2003).

4.14 REY-OSTERRIETH COMPLEX FIGURE TEST RESULTS

Table 22: Rey-Osterrieth Complex Figure Test scores and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment

	FTD			AD			Levene’s Test For Equality of Variance	t(df) sig
	N	Mean	Std. Dev	N	Mean	Std. Dev		
Copy	27	32.7	6.2	15	24.3	10.1	7.3 *	2.8(19.5) *
Immediate Recall	20	12.6	6.9	10	6.2	6.1	0.40	2.4(28) *

* = p < .05

Both the Alzheimer’s Disease and Frontotemporal Dementia mean scores fell in the impaired range for both the “Copy” and “Immediate Recall” conditions of the test (see Table 22 above). The Frontotemporal Dementia group was able to recall significantly more details of the design at both conditions of the test. This result indicates that the Frontotemporal Dementia group had relatively preserved ability to copy and recall complex visuospatial designs compared to the Alzheimer’s Disease group. This finding is consistent with previous research (Edwards-Lee & Miller et al. 1997; Perri & Koch et al. 2005).

4.15 SYMBOL DIGIT MODALITIES TEST RESULTS

Table 23: Symbol Digit Modalities Test Scores (written component) and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment

	FTD			AD			Levene’s Test For Equality of Variance	t(df) sig
	N	Mean	Std. Dev	N	Mean	Std. Dev		
Written	27	27.6	11.9	12	21.5	9.7	2.20	2.1(23) *

* = p < .05

There were insufficient scores for the verbal component of the test for statistical analysis.

Both Frontotemporal Dementia and Alzheimer’s Disease groups produced scores in the impaired range on the Symbol Digit Modalities Test (SDMT, see Table 23 above). The Frontotemporal Dementia group score was significantly higher than the Alzheimer’s Disease group score. This result indicates relatively preserved capacity in the Frontotemporal Dementia group for completing a coding task with a significant complex scanning and visual tracking component in comparison to the Alzheimer’s Disease group. This finding is consistent with previous research (Ringholz & Appel et al. 2005).

4.16 TACTILE FINGER RECOGNITION TEST RESULTS

Table 24: Tactile Finger Recognition Test error-scores and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment

	FTD			AD			Levene’s Test For Equality of Variance	t(df) sig
	N	Mean	Std. Dev	N	Mean	Std. Dev		
Right Hand	20	1.1	1.7	13	4.8	3.8	9.3*	3.3(15.1)* *
Left Hand	20	1.3	1.5	13	4.2	5.4	25.1**	1.9(13.1)

* = $p < .05$; ** = $p < .01$

The Frontotemporal Dementia group produced scores within normal limits for both right and left hands (see Table 24 above). The Alzheimer’s Disease group produced results in the impaired range for both hands. The result for the left hand did not reach statistical significance due to the large variance in the Alzheimer’s Disease group. Many of the Alzheimer’s Disease subjects became disoriented during the test, and expressed discomfort at having to close their eyes and concentrate on their fingers. This result indicates that the Tactile Finger Recognition Test may be a simple, easy to administer test to assist with the differential diagnosis of Frontotemporal Dementia from Alzheimer’s Disease. There are no published studies that have used finger recognition tasks with Frontotemporal Dementia. The above results indicate that Frontotemporal Dementia patients are capable of maintaining orientation in the present with their eyes closed, whereas Alzheimer’s Disease patients appear more reliant of visual cues to remain oriented. The use of the Tactile Finger Recognition Test with early-onset dementia patients warrants further research.

4.17 FAS VERBAL FLUENCY AND ANIMAL NAMING TEST

RESULTS

Table 25: FAS Test of Verbal Fluency & Animal Naming Test scores and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment

	FTD			AD			Levene’s Test For Equality of Variance	t(df) ^a
	N	Mean	Std. Dev	N	Mean	Std. Dev		
F	28	8.7	4.6	17	9.7	4.1	.2	.7(43)
A	28	6.5	4.2	17	7.8	5.1	1.3	.9(43)
S	28	8.7	5.6	17	9.7	5.1	.2	.7(43)
Animals	20	11.9	5.1	10	10.8	5.1	.7	.5(28)

^a = none of the t-tests were statistically significant

Scores for both the Frontotemporal Dementia and Alzheimer’s Disease groups fell in the impaired range for the letters “F”, “A”, and “S”, and also for the animal-naming task (see Table 25 above). There was no statistical difference between the two groups. The animal naming result is inconsistent with the findings of Perri and Koch et al (2005) who found significantly lower animal naming scores in Frontotemporal Dementia patients than Alzheimer’s Disease patients. Perri and colleagues study (2005) included subjects over the age of 65, therefore direct comparison between the two groups is not possible.

4.18 FREEHAND CLOCK DRAWING TEST RESULTS

Table 26: Freehand clock drawing test scores and T-test scores for Alzheimer’s Disease and Frontotemporal Dementia patients at initial assessment

	FTD	AD	Chi Square
	N = 23	N = 15	
Impaired	9 (39%)	13 (87%)	8.42 *

* = $p < .05$

Both Frontotemporal Dementia and Alzheimer’s Disease groups showed significant impairment on the clock-drawing task (see Table 26 above). The Alzheimer’s Disease group was significantly more impaired, with all but 13% of the group unable to successfully complete the task. In contrast, 61% of the Frontotemporal Dementia group were able to successfully complete the task. This result provides further evidence that the Freehand Clock Drawing Test is a useful dementia screening tool. This result is consistent with previous research (Libon & Swenson et al. 1993; Juby & Tench et al. 2002; Tench, & Barker, 2003; Blair & Kertesz et al. 2006). The Freehand Clock Drawing Test is simple to administer and may assist with the differential diagnosis of Frontotemporal Dementia from Alzheimer’s Disease. Its use with early-onset dementia patients warrants further research.

4.19 NEUROPSYCHOLOGICAL RESULTS SUMMARY AND CONCLUSION

4.19.1 Non Standardised Assessment

Due to the advanced state of cognitive deterioration displayed by many of the patients, testing was not conducted in a standardised manner.

Neuropsychological assessment was conducted to assist with patient management, and not for research purposes. The assessments produced clinically useful information and outlined the relative strengths of each patient.

Due to the non-standardised use of neuropsychological tests the statistical analysis of the results in this study must be treated with some caution.

4.19.2 Summary

The neuropsychological assessment of the two groups of early-onset dementia patients produced variable results that generally support previous research in the area of early-onset dementia, with both the Frontotemporal Dementia and Alzheimer's patient groups producing below average to impaired results on all assessment measures. The Frontotemporal Dementia group had relatively preserved visuo-spatial skills compared to the Alzheimer's Disease group.

4.19.3 Task Failure

Significant numbers of both the Frontotemporal Dementia and Alzheimer's Disease group were unable to successfully complete many of the neuropsychological tests. For example, 16 % of the Frontotemporal Dementia

patients, and 28% of the Alzheimer's Disease patients were unable to complete the WAIS-111. The number of subjects who were unable to undertake standardised assessment tasks is an important result. The high percentage of task-failure indicates that the neuropsychological test results may be overestimates of the level of functioning for these two groups. The usual reasons for task failure were agitation, distress, distractibility, and inability to understand test instructions.

As a general rule distractibility and inability to understand test instructions appeared to be more common in the Frontotemporal Dementia patients, whereas distress and agitation appeared to be more common in the Alzheimer's Disease group. It was my impression that many of the Alzheimer's Disease group were aware of task failure, whereas the Frontotemporal Dementia patients generally appeared to be unaware of their deficits.

4.19.4 Effective Dementia Screening and Differential Diagnosis Instruments

All of the assessment measures were found to be effective tools that may assist with the assessment of dementia, but few of the verbal tests proved useful in the differential diagnosis of Frontotemporal Dementia from Alzheimer's Disease. The majority of measures that were found to have differential diagnostic potential with these groups did not require a verbal response. The measures

found to be effective were the WAIS-111 Block Design and Picture completion subtests, the Purdue Pegboard Test, the Tactile Finger Recognition Test, the Rey-Osterrieth Complex Figure Test, the Freehand Clock Drawing test, the written component of the Symbol Digit Modalities Test, and the Wechsler Memory Scale Visual Recall Test. The immediate recall condition of the Wechsler Memory Scale Logical Memory test was found to be the only subtest requiring a verbal response to discriminate between the two groups.

4.19.5 Ineffective Differential Diagnosis Instruments

The following tests did not discriminate between Frontotemporal Dementia and Alzheimer's Disease: the WAIS-111 Verbal IQ subtests, the Mini Mental State Exam, the Paired Associates Learning Task, Digit Span, the FAS and Animal Naming test. All of these tests, with the exception of some items on the Mini Mental State Exam, require verbal responses.

CHAPTER 5

CHARACTERISTIC BEHAVIOURAL AND

PSYCHIATRIC CHANGES

DIFFERENTIATING FRONTOTEMPORAL

DEMENTIA FROM ALZHEIMER'S DISEASE

“Personality changes in Alzheimer’s Disease are in keeping with, and perhaps to some extent the product of, preserved social awareness; personality changes in Frontotemporal Dementia reflect breakdown in social capacity. Frontotemporal Dementia patients are alienated early from relatives, because of loss of emotional rapport, resulting in relatively early admission of patients to permanent residential care.”

Snowden & Neary et al. 1996, p. 47

5.1 INTRODUCTION TO CHARACTERISTIC BEHAVIOURAL AND PSYCHIATRIC CHANGES DIFFERENTIATING FRONTOTEMPORAL DEMENTIA FROM ALZHEIMER'S DISEASE

Commonly, Frontotemporal Dementia is first noticed due to significant behavioural changes such as rapidly deteriorating social skills, loss of spontaneity, rudeness, and disregard for others (Brun & Englund et al. 1994; Walsh & Darby, 1999). The behavioural changes associated with Frontotemporal Dementia result in a rapid deterioration in occupational performance early in the course of the illness (Elfgren & Passant et al. 1993).

The rapid onset of behavioural and personality changes accompanying Frontotemporal Dementia stand in marked contrast to the comparatively mild personality and behavioural changes commonly accompanying the early stages of Alzheimer's Disease (Miller & Cummings et al. 1995; Trimble, 1991; Engelborghs & Martens, 2005). There is evidence that accurate differentiation between Frontotemporal Dementia and Alzheimer's Disease can be made solely on the retrospective analysis provided by primary carers of patient behaviours during the course of the illness (Barber, Snowden & Crausford, 1995).

Behavioural and psychiatric changes commonly associated with Frontotemporal Dementia and Alzheimer's Disease are described in detail below. A summary of the differential changes associated with each condition is summarised in Table 27 (p. 103).

5.1.1 Loss of Motivation/Apathy, and Clinical Depression in Frontotemporal Dementia and Alzheimer's Disease

Loss of motivation and depression commonly occur with both Frontotemporal Dementia and Alzheimer's Disease (Engelborghs & Martens, 2002; Van Reekumk, Stuss, & Ostrander, 2003; Mourik & Rosso et al. 2004; Diehl-Schmid & Pohl et al. 2006). There is a strong relationship between loss of motivation and depression, and the diagnostic criteria for these two syndromes have extensive similarities (Van Reekumk, Stuss, & Ostrander, 2003).

Although loss of motivation and depression commonly coexist, many patients with neurological conditions lose motivation and become apathetic, but do not develop other characteristics of depression (Levy & Cummings et al. 1998).

There are no longitudinal data on loss of motivation in Frontotemporal Dementia, and only one longitudinal study of Alzheimer's Disease patients. This study found that loss of motivation and apathy progressed steadily over a three year period (Petry & Cummings et al. 1989).

Loss of motivation has been found to occur more commonly early in the course of Frontotemporal Dementia than in early Alzheimer's Disease (Snowden &

Neary et al. 1996; Pasquier & Lebert et al. 1999). Frontotemporal Dementia patients commonly do not instigate activities unaided, and show lack of motivation in most situations (Pasquier & Lebert et al. 1999; van Reekum, Stuss, & Ostrander, 2003). In contrast, Alzheimer's Disease patients are more likely to become frustrated when they are unable to complete tasks, and engage in "covering up behaviour". That is, patients attempt to mask their underlying deficits, often by making excuses, or by minimising the behaviours (Barber, Snowden, & Craufurd, 1995; Binetti & Locascio et al. 2000).

The characteristic lack of motivation accompanying Frontotemporal Dementia has been mistaken for several other clinical conditions including menopause, depression and chronic fatigue syndrome (Pasquier & Delacourte, 1998). The loss of motivation commonly occurring in early Frontotemporal Dementia has been found by several researchers to make formal assessment difficult (Miller & Cummings et al. 1991; Smeding & de Koning; 2000; Snowden, Neary & Mann; 1996). In contrast, patients in the early stages of Alzheimer's Disease generally try to perform well on assessment tasks, and are aware of test-failure (Snowden & Neary et al. 1996).

5.1.2 Behavioural Changes Associated with Executive Function

Deterioration in Alzheimer's Disease and Frontotemporal Dementia

Executive functions are the cognitive abilities to successfully and independently engage in purposeful activities such as initiating activities, planning, self-regulation, and volition (Lezak, 1995). Frontotemporal Dementia patients rapidly lose these executive functions, which are controlled by the frontal lobes:

they become unconcerned, lack initiative, judgment and foresight (Mendez & Anderson et al. 2005). Personal responsibilities and self-care are generally neglected (Walsh & Darby, 1999; Diehl & Kurz, 2002). The loss of abstract thinking ability (or the manifestation of “concrete thinking”) is a universal feature of Frontotemporal Dementia. Patients with Frontotemporal Dementia tend to take objects at their face value, and lose the ability to dissociate themselves from their immediate environment. Ability to foresee consequences, effective planning and goal-directed behaviours therefore become increasingly rare (Walton, 1993; Gustafson & Brun, 1999).

5.1.3 Social Skills in Frontotemporal Dementia and AD

The early loss of executive functioning in Frontotemporal Dementia leads to rapid loss of social skills. Spatial skills, visual and auditory perception, motor skills, and memory, tend to be reasonably well preserved in the early stages of the illness. In marked contrast, Alzheimer’s Disease patients often experience deterioration of spatial skills, visual motor skills and memory, with relatively preserved social skills (Gustafson & Brun, 1999; Walsh & Darby, 1999). In Alzheimer’s Disease, social graces, manners, and courtesy often remain well preserved throughout the course of the illness (Bozeat & Gregory et al. 2000; Snowden & Neary et al. 1996).

5.1.4 Facade of Normality in Alzheimer’s Disease

Alzheimer’s Disease patients, through their preserved social skills, often attempt to maintain social relationships until the late stages of the illness, and are able to present and maintain a facade of normality in environments and familiar situations. This facade of normality, or “covering-up behaviour” masks the

patient's underlying deficits, and can often lead others who have not seen the Alzheimer's Disease patient in a variety of situations, to assume that there is no, or minimal deterioration (Rubin & Morris et al. 1987). This "facade of normality" generally becomes apparent when the Alzheimer's Disease patient is required to deal with novel situations, or tasks that they are unable to complete. In these situations the Alzheimer's Disease patient often becomes anxious, perplexed, and agitated as the "covering-up" behaviours are unable to meet the environmental demands (Cummings & McPherson, 2001; Mendez & Shapira, 2005).

5.1.5 Lack of Concern in Frontotemporal Dementia

In sharp contrast to the relatively preserved social skills and attempts to cover-up deficits that characterise many Alzheimer's Disease patients, Frontotemporal Dementia patients rarely show any evidence that they are aware of often profound social skills deficits. Frontotemporal Dementia patients typically appear unconcerned about breaches of social protocol and task failure (Cummings & McPherson, 2001; Mendez & Shapira, 2005). It is common for Frontotemporal Dementia patients to deny experiencing any difficulty or

decline in their level of social functioning, even when presented with clear evidence that there has been a dramatic change in functioning (Gustafson & Brun, 1999). Frontotemporal Dementia patients typically do not attempt to maintain social relationships. They show little or no distress or anxiety when unable to complete tasks that they had previously completed routinely, and do not attempt to mask social deficits (Snowden & Neary et al. 1996; Gustafson & Brun, 1999).

5.1.6 Neuropathology of Aggression in Frontotemporal Dementia

Some Frontotemporal Dementia patients exhibit aggressive behaviours that pose significant challenges to those involved in providing care for the patients (Tanabe & Ikeda et al. 1999). A significant association has been found between aggression and hypoperfusion in the left anterior temporal cortex and bilateral dorsofrontal cortex (Hirono & Mega et al. 2000; Miller & Darby et al. 1997). Increased levels of aggression have been linked to mutations in chromosome 17q21-22 (Heutkin & Stevens et al. 1997). Other researchers have highlighted the role of degeneration of frontotemporal regions in aggressive behaviour, in particular degeneration of the right frontotemporal region (Mychack & Kramer et al. 2001).

Several researchers have argued that it is probable that factors beyond pure neuropathology are involved in the manifestation of behaviours classified as “aggressive”. For example, quality of nursing care, behavioural management, support from primary carers, and medication, are all likely to reduce aggressive

behaviours (LaVigna, Willis, Shaull, Adebí & Sweitzer, 1994; Tanabe, Ikeda & Komori, 1999).

Overactivity

Hyperorality, Smoking and Alcohol Consumption

Dramatic excesses of eating and drinking are common early in the course of Frontotemporal Dementia (Miller & Darby et al. 1995; Ikeda & Brown et al. 2002). These changes are linked to hyperorality. Hyperorality is defined as excessive and indiscriminant eating, gluttony, preference for sweet food, and carbohydrate craving. Hyperorality is relatively common in Frontotemporal Dementia, but is rare in Alzheimer's Disease. Hyperorality is generally accompanied by rapid weight gain (Bathgate & Snowden et al. 2001; Miller & Darby et al. 1995).

The presence of hyperorality and associated gluttony and preference for sweet foods in dementia patients has been found to accurately discriminate Frontotemporal Dementia from Alzheimer's Disease (Miller & Darby et al. 1997; Bathgate & Snowden et al. 2001). In a study of 14 patients diagnosed with Frontotemporal Dementia and 14 patients diagnosed with Alzheimer's Disease, Miller and colleagues (1995) found that weight gain occurred in 64% of the Frontotemporal group, compared with only 7% in the Alzheimer's Disease group. Carbohydrate craving was found in 79% of the Frontotemporal group, but in none of the Alzheimer's group.

Smoking and alcohol consumption typically increases in the early stages of

Frontotemporal Dementia (Bathgate & Snowden et al. 2001). Alcohol abuse has, in some cases, resulted in patients being misdiagnosed with an alcohol-induced dementia (Gustafson, 1987).

Hypersexuality

Hypersexuality rarely occurs in Alzheimer's Disease (Dell & Halford, 2002). It is more common in Frontotemporal Dementia, and its occurrence can be extremely challenging for primary caregivers (Dell & Halford, 2002; Tang-Wai & Lewis et al. 2002; Higgins & Barker et al. 2004).

Restlessness & pacing

Restlessness, pacing, and apparently directionless wandering are commonly associated with Frontotemporal Dementia (Snowden & Neary et al. 1996; Snowden & Bathgate, 2001).

Stereotypical & Ritualistic Behaviours

Ritualistic and stereotypical behaviours are common in the early stages of Frontotemporal Dementia, and generally persist throughout the course of the illness. These behaviours generally occur only in the late stages of Alzheimer's Disease, and commonly do not occur throughout the course of the illness (Neary

& Snowden, 1996; Shigenobu & Ikeda et al. 2002; Nyatsanza & Shetty et al. 2003). Common stereotypical and ritualistic behaviours include behaviours such as collecting coupons or papers, spending many hours in the bathroom, or repetitive pacing (Gregory & Hodges, 1993; Pasquier & Delacourte, 1998; Bathgate & Snowden et al. 2001; Miller & Cummings et al. 1995). The behaviours associated with the reptilian brain are primarily ritualistic and stereotypical. These behaviours have commonly been associated with frontal lobar atrophy, and their presence assists in the differential diagnosis of Frontotemporal Dementia from Alzheimer's Disease (Miller & Darby et al. 1997; Tanabe & Ikeda et al. 1999).

Utilisation behaviour

Utilisation behaviour is the tendency to pick up and manipulate any object in the environment, and its appearance is an indicator of frontotemporal neurodegeneration. Utilisation behaviour is extremely rare in Alzheimer's Disease (Ikeda & Tanabe, 2000; Nyastanza & Shetty et al. 2003).

5.1.7 Psychiatric Symptoms Associated with Frontotemporal Dementia and Alzheimer's Disease.

The pattern of rapidly emerging "psychiatric" symptoms commonly accompanying the onset of Frontotemporal Dementia is markedly different from the relatively subtle, slow changes that generally occur with the onset of Alzheimer's Disease (Bozeat & Gregory et al. 2000). Due to the marked behavioural and personality changes associated with the early stages of

Frontotemporal Dementia, many Frontotemporal Dementia patients have been misdiagnosed with a psychiatric illness before they are diagnosed with Frontotemporal Dementia (Merriam & Aronson, 1988). In contrast, psychiatric symptoms rarely occur before cognitive and behavioural decline in Alzheimer's Disease (Merriam & Aronson, 1988).

Frontotemporal Dementia patients commonly experience affective disorders, radically altered emotional and social conduct, and transient psychiatric symptoms, including hallucinations, before or during the early stages of cognitive and behavioural decline (Elfgren & Passant et al. 1993; Lopez & Gonzalez et al. 1996; Neary & Snowden, 1996; Gallant & Muggier et al. 1998).

Acquired obsessive-compulsive disorder is common in Frontotemporal Dementia. Many patients develop compulsions as the disease progresses such as collecting meaningless objects and repetitive pacing (Pasquier & Delacourte, 1998).

5.1.8 Changes in Sleep Pattern

Sleeping patterns often change dramatically with the onset of Frontotemporal Dementia. Some patients become more lethargic, and spend up to 18 hours each day sleeping, while in others sleeping patterns become erratic (Harper & Stopa et al. 2001). In marked contrast, levels of nocturnal activity increase significantly in Alzheimer's Disease patients (Harper & Stopa et al. 2001).

Differential nocturnal activity levels between Alzheimer's Disease and Frontotemporal Dementia patients are accompanied by significant

neurochemical cerebrospinal fluid (CSF) differences (Minthon & Edvinson et al. 1990). Alzheimer's Disease patients showed significantly reduced Neuropeptide Y and Delta Sleep Inducing Peptide levels. In contrast, Frontotemporal Dementia patients showed no reduction in Neuropeptide Y levels, and increased Delta Sleep Inducing Peptide levels. Neuropeptide Y has a role in eating behaviour, circadian rhythms, and anxiety responses (Minthon & Edvinson et al. 1990). Delta Sleep Inducing Peptide is believed to assist with maintaining natural healthy sleep rhythms (Schneider-Helmert & Schoenenberger, 1983).

5.1.9 Additional Behaviours

Incontinence

Incontinence is relatively common in the middle and later stages of Frontotemporal Dementia. Incontinence often occurs within 18 months of diagnosis. In contrast, incontinence generally occurs in the later stages of Alzheimer's Disease (Nicolai & Lazzarino, 1992; Neary & Snowden et al. 1998; McKhann & Albert et al. 2002)

Pleasant Disposition and More Affectionate

Patients with Alzheimer's Disease often maintain premorbid personality characteristics until the late stages of the illness. If Alzheimer's Disease patients had previously had a pleasant disposition, they generally maintain these characteristics (Snowden & Neary et al. 1996; Harciarek & Jodzio 2005). No evidence was found in the literature of either Frontotemporal Dementia or Alzheimer's Disease patients becoming more affectionate during the course of their illnesses.

5.2 HUMOUR IN FRONTOTEMPORAL DEMENTIA AND ALZHEIMER'S DISEASE.

“Humour is a defining human attribute”

Shammi & Stuss, 1999

Humour plays an important part in all human interactions, helps build social groups, and assists in the communication of complex ideas and feelings (Brownell & Gardner, 1988). The role of the frontal lobes in processing humour has been well documented (e.g. Gardner & Ling et al. 1975; Lezak, 1995; Shammi & Stuss, 1999). The frontal lobes play a pivotal role in the integration of information from several different regions in the brain essential for the understanding of humour (Shammi & Stuss, 1999).

5.2.1 Neurological Underpinnings of Humour

Recent research has indicated that both right and left frontal lobes are involved in the understanding of humour (Moran & Wig et al. 2004; Shammi & Stuss, 1999). Moran and colleagues have also described the importance of the interaction between the frontal and temporal lobes, and the neural connections to the insular cortex and amygdala in the understanding of humour (Moran & Wig et al. 2004).

5.2.2 Cognitive Functions Involved in Humour

Humour is a higher cognitive function, and the understanding of humour uses a variety of cognitive processes: the ability to hold information in memory whilst it is being manipulated; the ability to change mental sets rapidly, and the ability to think abstractly (Shammi & Stuss, 1999).

5.2.3 Humour in Frontotemporal Dementia and Alzheimer's Disease

Any frontal lobe damage has been consistently found to cause deterioration in the ability to understand humour (Lezak, 1995). Humour in Alzheimer's Disease is generally well-preserved until late in the course of the illness (Buckwalter & Gerdner et al. 1995). Buckwater and colleagues (1995) found that patients with Alzheimer's Disease generally maintained their sense of humour, and they suggested that humour could be used as a therapeutic strategy for people with Alzheimer's Disease.

In marked contrast to the relatively well-preserved sense of humour in Alzheimer's Disease, Frontotemporal Dementia Patients rapidly lose their ability to understand humour. The loss of a sophisticated sense of humour is often replaced by the development of "Witzelsucht" – childish and inappropriate humour - and "slapstick humour". The development of the childish "Witzelsucht" in Frontotemporal Dementia is accompanied by a profound loss of ability to understand complex adult humour (Vardi & Finkelstein et al. 1994; Shammi & Stuss, 1999).

5.3 SUMMARY OF PSYCHIATRIC AND BEHAVIOURAL CHANGES

Table 27: Summary of psychiatric and behavioural changes

	Frontotemporal Dementia	Alzheimer's Disease
Eating and drinking	Hyperorality, excessive and indiscriminant eating, gluttony, preference for sweet food, carbohydrate craving, and weight gain (Bathgate & Snowden et al. 2001; Miller & Cummings et al. 1995; Ikeda & Brown et al. 2002).	Unchanged (Bathgate & Snowden et al. 2001; Miller & Cummings et al. 1995)
Motivation	Rapid loss of motivation and energy. Apathy, indifference, aspontaneity and inertia. Deterioration in occupational performance is common early in the course of the illness (Elfgrén & Passant et al. 1993; Pasquier & Delacourte, 1998; van Reekum, Stuss, & Ostrander, 2003; Diehl-Schmid & Pohl et al. 2006).	Slow loss of motivation throughout the course of the illness (Snowden & Neary et al. 1996; van Reekum, Stuss, & Ostrander, 2003).
Other behaviours	Motor and verbal perseverations and markedly reduced verbal fluency. Utilization behaviours, disabling compulsions, stereotypical and ritualistic behaviours such as collecting coupons or papers, spending many hours in the bathroom, or repetitive pacing (Gregory & Hodges, 1993; Bathgate & Snowden et al. 2001; Miller & Cummings et al. 1995; Shigenobu & Ikeda et al. 2002).	
Personal hygiene	Personal neglect, loss of interest in appearance. Incontinence as disease progresses may be a product of the patient's apathy (Nicolai & Lazzarino, 1991).	Often preserved until late in course of illness (Mace & Rabins, 1991).

Table 27 Continued: Summary of psychiatric and behavioural changes

Personality	Profound personality change in early stages. Disinhibited, loss of social awareness, impaired social skills, rudeness, emotional blunting, fatuous jocularity, disregard for others, breakdown of social communication (Brun & Englund et al. 1994; Kertesz, Davidson & Fox, 1997; Walsh & Darby, 1999).	Mild personality changes in early stages. Relatively preserved social graces. Manners and courtesy remain long-preserved (Snowden & Neary et al. 1996). Ability to present a facade of normality, hiding underlying deficits (Miller & Cummings et al. 1995; Rubin & Morris et al. 1987; Tanabe, Ikeda & Komori, 1999).
Planning	Retardation, mental rigidity, lack of initiative, judgment, and foresight. Personal responsibilities and self-care are generally neglected (Walsh & Darby, 1999).	More likely to become anxious, perplexed, and agitated in novel situations (Snowden & Neary et al. 1996).
Psychological/psychiatric symptoms	Depression, anxiety, excess sentimentality, early “psychotic” symptoms, hallucinations, disabling compulsions, repetitive pacing (Elfgren & Passant et al. 1993; Miller & Cummings, 1995; Spinnler & Della Salla, 1988).	Late onset psychosis, hallucinations, delusions. Depression (Cummings & McPherson, 2001; Gormley & Rizwan, 1998; Snow & Arnold, 1996).
Insight	Unaware of disability. Patients indicate little or no distress or anxiety when unable to complete tasks. Loss of ability to dissociate from immediate environment (Snowden & Neary et al. 1996; Gustafson & Brun, 1999; Mendez & Shapira, 2005; Rankin & Baldwin et al. 2005).	Variable. Often preserved until late in course of illness (Pasquier & Delacourte, 1998; Rankin & Baldwin et al. 2005)
Sleep	Increased sleeping (Harper & Stopa et al. 2001).	Increased nocturnal activity (Harper & Stopa et al. 2001)
Smoking and drinking	Increased smoking and alcohol consumption (Gustafson, 1987).	Unchanged (Gustafson, 1987).

Table 27 Continued: Summary of psychiatric and behavioural changes

Spatial skills, visual and auditory perception, motor skills, memory	Relatively preserved, can accurately copy simple designs early in the course of the illness (Gustafson & Brun, 1999; Johanson & Hagberg, 1989; Snowden & Neary et al. 1996).	Impaired copying ability at first assessment (Johanson & Hagberg, 1989).
Speech	Economy of speech, reduction in speech output, late mutism. PEMA Syndrome: Palilalia (repeating the same word over and over again), Echolalia (the involuntary copying of another's speech), Mutism, and Amimia (an aphasic symptom involving the loss of the power to use gestures and other pantomimic means of expression of thought) (Guiraud, 1936; Brun & Gustafson, 1999; Snowden, Neary & Mann 1996).	This syndrome is extremely rare in Alzheimer's Disease (Brun & Gustafson, 1999).
Spelling and handwriting.	Spelling errors, slowing of speed of handwriting (Gustafson & Brun, 1999).	Distinctive tempo-parietal dysgraphia characteristic of Alzheimer's Disease (Gustafson & Brun, 1999).
Thinking	Concreteness of thinking is common. Patients with FTD tend to take objects at their face value, and lose the ability to dissociate themselves from their immediate environment. Planning and goal direct behaviours therefore become increasingly rare (Gustafson & Brun, 1999).	Slow decline, concrete thinking late in course of illness (Cummings & McPherson, 2001).

5.4 TWO MODELS FOR UNDERSTANDING BEHAVIOURAL AND PSYCHIATRIC CHANGES IN FRONTOTEMPORAL DEMENTIA

The frontal and anterior temporal regions of the brain play a major role in the modulation of behaviour (Miller & Diehl et al. 2003). In Frontotemporal Dementia, the deterioration is often asymmetric, affecting differing regions of the right or left frontal and temporal lobes (Miller & Ikonte et al. 1997). The location of the deterioration is commonly related to the pattern of behavioural disturbances accompanying Frontotemporal Dementia (Snowden & Neary et al. 1996; Chow & Cummings, 1999). Any deterioration of the frontal and temporal areas of the brain invariably leads to some disruption in the conscious control of behaviour. The degree of disruption of normal pre-morbid behaviour is directly related to the level of neurodegeneration in the frontal and temporal lobes (Miller & Chang et al. 1993).

Two groups of researchers, Snowden & Neary et al. (1996), and Tanabe & Ikeda et al. (1999) have proposed comprehensive and clinically useful frameworks for understanding the behavioural syndromes accompanying Frontotemporal Dementia:

5.4.1 Snowden Neary, and Mann’s Model of Behavioural Syndromes

Associated with Frontotemporal Dementia

Snowden, Neary and Mann (1996) described three major behavioural syndromes observed in Frontotemporal Dementia patients. Table 28 (below) summarises the three behavioural syndromes and indicates the area of the brain commonly affected for each syndrome.

Table 28: Frontotemporal behavioural syndromes

Behavioural Syndrome	Associated area of brain
1. <i>A profile of overactivity, inattention, and disinhibition</i>	<i>orbitofrontal region</i>
2. <i>Retardation, apathy and withdrawal</i>	<i>Dorsolateral region</i>
3. <i>Stereotypic and ritualized behaviours</i>	<i>Associated with any frontotemporal lobar degeneration</i>

Overactivity, Inattention and Disinhibition

Overactivity, inattention and disinhibition are often most marked when patients are in the presence of others. Patients who display overactive, inattentive, and disinhibited behaviours usually lack motivation and do not instigate activities if left alone. Restlessness, pacing, and apparently directionless wandering are commonly associated with Frontotemporal Dementia (Snowden & Neary et al. 1996).

The first symptoms of Frontotemporal Dementia often include rudeness and lack of conformity to social conventions (Gregory & Hodges, 1996). Frontotemporal Dementia patients break social conventions without apparent awareness that

they are breaking the conventions (Gustafson & Brun, 1999). Examples of such behaviour include ignoring visitors, addressing people rudely, making tactless comments, or bumping into strangers without attempting to avoid colliding with them (Snowden & Neary et al. 1996). When dining out, patients may eat off others diners' plates, or drink from the wine bottle without apparent awareness that their behaviour is unusual. Shoplifting is not uncommon, but is always unplanned, and may be an example of environmental dependency syndrome ((Lhermitte, 1986; Miller & Darby, 1997). Patients may wander naked in front of strangers with no apparent awareness that they are breaking social rules. Overfriendliness and over-familiarity are common (Miller & Darby et al. 1995).

Although patients with Frontotemporal Dementia often engage in disinhibited and inappropriate behaviours, major incidents of law breaking are rare (Mychack & Kramer et al. 2001). There is no evidence of wilful attempts to flout social rules. The probable cause of the behaviours is a profound lack of awareness of social rules and constraints (Snowden & Neary et al. 1996).

Degeneration of the frontotemporal region is associated with high levels of socially undesirable behaviours (Mychack & Kramer et al. 2001).

Retardation, Apathy and Withdrawal

Loss of motivation, apathy and energy are common early in the course of the illness (Pasquier & Delacourte, 1998; Diehl-Schmid, J., C. Pohl et al. 2006).

These features have often been mistaken for menopause, depression and chronic

fatigue syndrome (Pasquier & Delacourte, 1998).

Personal hygiene is commonly neglected. Some patients show an aversion to water. Patients generally lose interest in their appearance, and sometimes dress in unusual combinations of clothing. Incontinence increases as the disease progresses, and may be a product of the patient's apathy rather than loss of control of their bodily functions (Nicolai & Lazzarino, 1991). Loss of libido (hyposexuality) is common in the early stages of the illness (Miller & Darby et al. 1995). However, a minority of patients exhibit a preoccupation with sex (Pasquier & Delacourte, 1998).

Stereotypical and Ritualised Behaviours

Patients become increasingly inflexible, and may adopt a fixed daily routine (Bathgate & Snowden et al. 2001; Shigenobu & Ikeda et al. 2002). Performing daily activities "by the clock" is common. If patients walk, they often follow an identical route every day (Mendez & Selwood et al. 1993). Patients regularly repeat the same sentence, phrase, puns, or ditty. This behaviour can mask the degree of impairment to others who do not see the patients regularly (Miller & Ikonte et al. 1997). Many patients develop disabling compulsions, such as collecting coupons or papers, spending many hours in the bathroom, or repetitive pacing (Miller & Ikonte et al. 1995).

5.4.2 MacLean's Triune Theory

Tanabe & Ikeda et al. (1999, see below) have provided a complex framework for understanding the behavioural changes accompanying Frontotemporal lobe degeneration. Tanabe and colleagues (1999) use Dr Paul MacLean's (1973, 1990) triune, or "three brains in one" neurological theory to provide a conceptual model for understanding typical behavioural changes accompanying the onset of Frontotemporal Dementia. The significant behavioural and personality changes associated with atrophy in the frontal and anterior temporal lobes are interpreted by studying the interaction between the basal ganglia, the limbic system, and the neocortex. MacLean's (1973, 1990) theory divides the brain into three interconnected hierarchical parts: the brain stem, the limbic system, and the neocortex. The parts are described in evolutionary terms, starting with the reptilian brain (brain stem), old mammalian (limbic system), and new mammalian (neocortex). There are no clear lines of separation between the three areas, with some brain-structures involved such as the thalamus being seen as part of both the reptilian brain and the old mammalian brain.

Reptilian Brain (Brain stem, basal ganglia, thalamus, globus pallidus, putamen)

The behaviours associated with the reptilian brain are the basic drives and instincts, needs and avoidances. These behaviours are primarily ritualistic and stereotyped. Behaviours controlled by the reptilian brain include mating rituals,

territoriality, rote behaviours, greeting rituals, the internal environment of the body, and various types of display. Tanabe (2000) noted that the structures of the reptilian brain have important connections to the orbitofrontal lobes and the anterior and medial temporal lobes. The basal ganglia are composed of the caudate, putamen, globus pallidus, and amygdala. The amygdala is the nucleus of the anterior temporal lobe, and is also part of the limbic system (Pinel & Edwards, 1998).

Old Mammalian Brain (limbic system, thalamus, hippocampus, amygdala)

The behaviours associated with the old mammalian brain are instinctive behaviours, emotions, and memory. Emotions are generated via the amygdala. The limbic system plays an important role in social bonding patterns, appropriate expressiveness, controls attention, and filters incoming and outgoing information. The limbic system is richly interconnected with the frontotemporal lobes.

New Mammalian Brain (neocortex, frontal, temporal, parietal, & occipital lobes)

The new mammalian brain, or neocortex, is the most recent evolutionary brain structure. The neocortex is the seat of the intellect and all thinking skills. The neocortex gives planning and adaptive functioning ability, and allows functional interactions with the external world. The neocortex allows for the understanding of metaphors, and models of understanding the world.

5.4.3 Tanabe, Ikeda, and Komori's Evolutionary and Developmental Model

The classification system of Tannabe and colleagues (Tannabe et al. 1999) builds on McLean's (1973, 1990) triune brain theory, and has many similarities to the model proposed by Snowden and colleagues (1996, see above) to help understand behavioural syndromes accompanying Frontotemporal Dementia. Behaviour changes are interpreted through an understanding of interactions between the basal ganglia, the limbic system, and the neocortex (the anterior and posterior association cortex).

Behaviours associated with Frontotemporal Dementia are classified as:

1. *Stimulus bound behaviour*
2. *Going My Way Behaviour*
3. *Stereotypical Behaviour*

Stimulus bound behaviour (also referred to as utilization behaviour and hypermetamorphosis)

Common stimulus-bound behaviours are: imitation behaviours (Shimomura & Mori, 1998), environmental dependency syndrome (Lhermitte, 1986), and utilization behaviours. Lhermitte (1986) described environmental dependency syndrome as a condition where a person is unable to control impulses to interact with the outside world. Utilisation behaviour is the tendency to pick up and manipulate any object in the environment. Stimulus bound behaviour is associated with damage to the dorsal frontal area of the brain causing an imbalance between the frontal and parietal lobes. Tanabe and associates (1999)

propose that degeneration or damage to the dorsal frontal area of the brain commonly results in the freeing up of parietal lobe activity. This pattern of damage leads to Frontotemporal Dementia patients' attention being absorbed by any environmental stimuli, without the moderating input from the frontotemporal regions of the brain.

It is common for Frontotemporal Dementia patients to inappropriately pick up, explore, and manipulate, random objects in their immediate environment. This tendency has been labelled "utilization behaviour" (Gustafson & Brun, 1999). This pattern of being "controlled" by the immediate sensory environment is extremely uncommon in patients diagnosed with Alzheimer's Disease (Snowden & Neary et al. 1996).

Going My Way Behaviour

"Going My Way" behaviour includes various forms of instinctive acts that are not mediated by rational thought, disinhibited and antisocial behaviours, impulsivity, and over familiarity (Tanabe, 1999). This behaviour stands in contrast to normal behaviour in Alzheimer's Disease, where patients are more likely to engage in "saving appearance" or covering up behaviour. Going my way behaviour is associated with damage to or degeneration of the orbitofrontal area of the brain. Damage to the orbitofrontal area commonly results in a loss of higher cortical control of the limbic system.

Stereotypic Behaviour

Examples of stereotypical behaviour are repetitive rubbing, stereotypical laughing, walking the same route every day, and adherence to a strict timetable. Stereotypical behaviour is associated with damage or degeneration to the frontal lobes leading to increased basal ganglia activity. The dorsal area of the basal ganglia controls simple stereotypies, such as knee rubbing. The ventral area of the basal ganglia controls more complex stereotypies, such as daily activities and complex rituals (Snowden & Neary et al. 2002).

5.5 LOSS OF “SELF” IN FRONTOTEMPORAL DEMENTIA AND ALZHEIMER’S DISEASE

The concept of “self” is inherently difficult to quantify. Nevertheless, the changes in “self” accompanying Frontotemporal Dementia are striking to carers, friends, and family members (Miller & Seeley et al. 2001). In marked contrast, relatives and friends commonly report relatively preserved characteristics of “self” in Alzheimer’s Disease. Relatives and friends of Frontotemporal Dementia patients report what they perceive as fundamental personality changes, with these changes often occurring rapidly early in the course of the illness (Miller & Seeley et al. 2001). Miller and colleagues (2001) have described the characteristic “loss of self” accompanying Frontotemporal Dementia. They define self as:

“The total, essential, or particular being of a person involving the essential qualities distinguishing one person from another”. (p 818)

The research by Miller and colleagues (2001) indicates that the frontal and anterior temporal lobes, especially the non-dominant hemisphere are responsible for what we perceive as a person's 'self'. Significant damage to the frontal and anterior temporal lobes results in the loss of a person's sense of self and previously learned self-concepts.

Lough & Gregory et al. (2001) have also studied changes to self typically accompanying Frontotemporal Dementia. They propose that Frontotemporal Dementia patients lose core social reasoning abilities, and in particular the ability to internally represent the thoughts and feelings of others. Lough and colleagues (2000) argue that this fundamental incapacity to internally represent the thoughts and feelings of others accompanying Frontotemporal Dementia patients invariably results in this group being viewed as fundamentally different to their previous self by others.

5.6 ASSESSMENT OF BEHAVIOUR

Clinical assessment of behavioural change is an essential component in the diagnosis of Frontotemporal Dementia, and assists in the differential diagnosis of Frontotemporal Dementia from Alzheimer's Disease (Miller & Cummings, 1991; Kertesz, Davidson, & Fox, 1997; Lebert & Pasquier et al. 1998). A few studies (Miller & Darby et al. 1997; Bozeat & Gregory et al. 2000; Shigenobu & Ikeda et al. 2002; Ikeda & Brown et al. 2002) found that analysis of behavioural variables without neuropsychological assessment was able to accurately differentially diagnose Frontotemporal Dementia from Alzheimer's disease.

5.6.1 Frontotemporal Dementia Behavioural Assessment Instruments

Kertesz & Davison et al. (1997) operationalised the behavioural criteria for Frontotemporal Dementia utilising the core features of the Lund/Manchester Frontotemporal Dementia consensus statement criteria (Brun & Englund et al. 1994; Kertesz & Nadkami et al. 2000), and their own clinical experience with twelve Frontotemporal Dementia patients. They constructed a 24 item inventory, the Frontal Behavioural Inventory (FBI). The FBI was designed to assist with the diagnosis of Frontotemporal Dementia, and to differentiate Frontotemporal Dementia from other forms of dementia and neurological conditions. In addition, the inventory was designed to provide information to increase understanding of the natural history of Frontotemporal Dementia. The items on the inventory were selected to represent two major behavioural styles, negative behaviours, and disinhibited behaviours. The items were designed to measure a patient's loss of social awareness, disinhibition, mental rigidity,

inflexibility, hyperorality, and perseverative behaviour, and distractibility, loss of insight, speech reduction, and impaired self-care.

5.6.2 Additional Important Behaviours for the Diagnosis of Frontotemporal Dementia.

Miller and colleagues (1997) reported that behavioural assessment alone could be used to accurately differentially diagnose Frontotemporal Dementia patients from Alzheimer's Disease patients. They found that five behaviours accurately discriminated all thirty Alzheimer's Disease patients from the thirty Frontotemporal Dementia patients in the study.

The five behaviours found to discriminate between the two groups were:

1. Stereotypical and ritualistic behaviours in Frontotemporal Dementia.
2. Loss of personal awareness in Frontotemporal Dementia.
3. Hyperorality in Frontotemporal Dementia.
4. Progressive reduction in speech output in Frontotemporal Dementia.
5. Impaired spatial orientation in Alzheimer's Disease.

Stereotypical and ritualistic behaviours or preserved spatial orientation were not included in the Frontotemporal Behavioural Inventory (see above).

Stereotypical and ritualistic behaviours have commonly been associated with frontal lobar atrophy, and were found to be among the five most important behaviours to discriminate Frontotemporal Dementia from Alzheimer's Disease (Miller & Darby et al. 1997; Shigneobu & Ikeda et al. 2002).

5.6.3 Standardised Interview

Lebert and colleagues (1998) produced a format for a standardised interview, the Frontotemporal Behaviour Scale, designed to monitor changes associated with frontal lobe dysfunction, and to differentially diagnose Frontotemporal Dementia patients from Alzheimer's Disease and Vascular Dementia patients. The Frontotemporal Behavioural Scale added several behaviours not included in the Frontotemporal Behaviour Inventory (Kertez, Davidson, & Fox, 1997). The additions were depressive symptomatology, perseveration, and ritualistic behaviours.

5.7 METHOD

5.7.1 Classification of Behaviours in Current Study

The criteria employed by Kertesz & Davidson et al. (1997) and Lebert et al. (1998) were used in the present study to classify the behaviours of the Alzheimer's Disease and Frontotemporal Dementia patients. Additional behaviours were recorded in their own categories (Table 29). The additional behaviours not measured by the above inventories were recorded to ensure that possible important behavioural changes associated with Frontotemporal Dementia were not overlooked.

In the current study, the files of patients were read thoroughly by the author, and each behaviour (see Table 29 below) recorded in the files by professionals (neurologists, clinical psychologists, speech pathologists, social workers, and psychiatrists), were recorded verbatim. All staff had extensive experience

working with Frontotemporal Dementia and Alzheimer's Disease patients, and were familiar with the behavioural profiles associated with these conditions. As part of the normal patient services, comprehensive case notes were recorded for each patient. The author recorded behaviours at two time intervals:

Time 1 Behaviour Recording Protocol

Consisted of behaviours recorded in patient files by the hospital neurologist, clinical psychologists, speech pathologists, or social workers that occurred in a six-month interval prior to first assessments, or during the first assessments.

Time 2 Behaviour Recording Protocol

Consisted of behaviours recorded in patient files by the hospital neurologist, clinical psychologists, speech pathologists, or social workers that occurred in a six-month interval between two years and nine months and three years and three months after the initial assessments. This time interval was chosen as the neurologist routinely reviewed patients at six-month intervals.

Patients were reviewed more frequently if additional clinical services were required, or if there were rapid changes or deterioration in the patient's condition. Patients were also routinely reviewed when carers required additional assistance with patient care.

All behaviours indicating a change in the patient's behaviour, including positive changes and stable personality traits, were recorded. This was done to provide

a comprehensive profile of the common and uncommon behaviours associated with Frontotemporal Dementia and Alzheimer's Disease.

The above method of obtaining behavioural change data was employed to ensure that families were not burdened with test-material and interviews in addition to the routine hospital procedures and the often overwhelming demands of caring for a relative or partner with early-onset dementia. It is important to note that the behaviours recorded in the files do not necessarily represent all behaviours observed. The behaviours may have been misidentified or misrepresented by the team member who recorded the behaviours in the file notes.

5.7.2 Criteria for extracting behaviours from patients' files

The following criteria were adapted by the author from Kertesz & Davidson et al. (1997) and Lebert et al (1998).

Table 29: Criteria used to extract behaviours from files and for calculating inter-rater reliability

Development of Childish humour	The patient has markedly changed, with the development of childlike humour.
Clinical Depression.	Patients with depression were given a diagnosis of clinical depression by a psychiatrist, and treated with antidepressants and/or Cognitive Behaviour Therapy.
Confabulation	The patient has started fabricating stories in response to questions.
Echolalia	The patient immediately and involuntarily repeats words or phrases spoken by others
Increased emotional indifference.	The patient has increasingly shown emotional flatness, and has lost emotional responsiveness, especially for family members.
Hallucinations	The patient has described hallucinations they have experienced. There is documented evidence of hallucinations.
Hiding food or clothes	The patient has recently begun hiding food or clothing.
Hyperorality.	The patient's eating habits have dramatically changed. The patient has started eating and drinking more, eating excessively, or putting non-food objects in their mouth.
Hypersexuality	The patient's levels of sexual activity have become abnormally high.

Table 29 continued: Criteria used to extract behaviours from files and for calculating inter-rater reliability

Impaired Judgment	The patient has lost their ability to plan and organise activities, and is unable to complete tasks without prompting and assistance
Impaired object recognition	Patient has lost ability to recognise some common objects such as cooking utensils, and common household items.
Increased impulsivity.	The patient has become more impulsive, and acts or speaks without apparent regard for the consequences.
Increased inattention and distraction	The patient has increasingly failed to pay attention to their environment, has become easily distracted, and loses track of conversations or instructions. In the extreme, the patient does not follow conversations or instructions at all.
Incontinence.	The patient has begun experiencing urinary and/or fecal incontinence.
Increased anxiety/panic attacks.	The patient has become increasingly anxious about a range of issues, such as their food, money, and times of meals. The patient has started experiencing panic attacks.
Increased Concrete Communication	The patient increasingly understands only the concrete meaning of what is being said. The patient's expressive language has become increasingly concrete.
Increased incidents of aggression.	The patient has become more aggressive, with documented incidents of verbal and/or physical abuse directed towards primary caregivers.
Increased Inflexibility.	The patient has become increasingly stubborn and rigid in their behaviour to the degree that their stubbornness and rigidity has caused significant difficulties for primary caregivers.
Increasingly disinhibited	The patient has begun displaying disinhibited behaviours in more than one situation.

Table 29 continued: Criteria used to extract behaviours from files and for calculating inter-rater reliability

Increasingly getting lost	The patient has lost their sense of direction, and has started getting lost in previously familiar environments.
Increasing errors of speech	The patient has increasingly made grammatical errors of speech and/or begun slurring
Increasingly sparse speech	Sparse grammatically correct speech.
Increased Jealousy	The patient has increasingly become jealous, and has displayed uncharacteristic jealousy.
Loss of Humour	The patient has lost their characteristic sense of humour.
Loss of Insight *	The patient has marked deterioration in insight in speech and actions.
Loss of motivation.	The patient has lost interest in friends and former daily activities. The patient does not instigate actions without prompting. The patient has a tendency to sleep unless stimulated. The patient has become increasingly indifferent to others.
More Affectionate	The patient has become more affectionate.
Paranoia	The patient has developed significant paranoid ideation and behaviour.
Perseverative Speech	The patient has started uncontrollably repeating particular responses such as words, phrases or gestures despite the absence or cessation of stimuli.
Pleasant Disposition	The patient displays a pleasant disposition towards primary carers.
Problems Dressing	The patient has developed problems dressing.

Table 29 continued: Criteria used to extract behaviours from files and for calculating inter-rater reliability

Increased restless and pacing.	The patient has become more restless or hyperactive. The patient paces apparently without direction
Ritualistic behaviours.	Ritualistic behaviours include repeating socially inappropriate routines such as collecting a set number of objects and placing them in a specific spot without apparent reason.
Stealing	Patient has begun taking the property of others without permission.
Unable to recognise own reflection	The patient has lost the ability to recognise their own reflection.
Utilisation behaviour.	The patient has begun automatically feeling, examining, picking up and manipulating objects in the environment.

5.7.3 Inter-Rater Reliability Coefficients — Calculating Inter-Rater Reliability

Inter-reliability was calculated on 11 randomly selected behaviours using Cohen’s kappa. This statistic measures the agreement between the evaluations of two raters when both are rating the same categorical variables. A value of 1 indicates perfect agreement. A value of 0 indicates that agreement is no better than chance (Coakes & Lyndall, 1999). The author and a postgraduate psychology student rated the behaviours independently using the criteria in Table 29. Behaviours were rated as either “Yes” (the behaviour occurred) or “No” (the behaviour did not occur). The data was entered in SPSS Version 7.5.1 for each variable and the reliability coefficients were calculated using the “Crosstabs” Kappa function.

Table 30: Inter-rater reliability coefficients (valid cases = 62)

Variable name	Kappa Coefficient Value
Apathy time 1	.777
Apathy time 2	.839
Clinically depressed time 1	.943
Clinically depressed time 2	.924
Concreteness time 1	.850
Concreteness time 2	.832
Errors of speech and/or slurring time 1	.621
Errors of speech and/or slurring time 2	.545
Indifference Time 1	.750
Indifference time 2	.719
Inflexibility time 1	.757
Inflexibility time 2	.803
Loss of insight time 1	.751
Loss of insight time 2	.868
Loss of sense of humour time 1	.924
Loss of sense of humour time 2	.897
More affectionate time 1	1.000

Table 30 continued: Inter-rater reliability coefficients (valid cases = 62)

Variable name	Kappa Coefficient Value
More affectionate time 2	1.000
Poor judgment time 1	.737
Poor judgment time 2	.834
Restlessness pacing time 1	.955
Restlessness pacing time 2	.931

Cohen’s kappa values were interpreted using the following table, Table 31 (Altman, 1991).

Table 31: Cohen’s kappa interpretation table

Value of K	Strength of agreement
< 0.20	Poor
0.21 — 0.40	Fair
0.41 — 0.60	Moderate
0.61 — 0.80	Good
0.81 — 1.00	Very good

All Cohen’s kappa coefficient values (Table 30) fell in either the “good” or “very good” range (Table 31), with the exception of “Errors of Speech and Slurring – Time 2” which produced a result in the “Moderate” range. The Cohen’s kappa results indicate acceptable levels of inter-rater reliability for the variables used in the study.

5.8 BEHAVIOURAL RESULTS

The results are presented below in tables. It is important to note that the behaviours reported below are the behaviour recorded by team members in file notes and, as noted above, do not necessarily represent all behaviours observed.

The results under “Initial Assessment” are for the full groups of Alzheimer’s Disease and Frontotemporal Dementia patients. The results under “Additional cases at 3-year follow-up” involve the subset of Alzheimer’s Disease and Frontotemporal Dementia patients who were without the specified features at the initial assessment:

5.8.1 Loss of Motivation/Apathy & Clinical Depression

Table 32: Percentage and Chi Square significance of difference between Frontotemporal Dementia & Alzheimer’s Disease patients reported in file notes with loss of motivation and apathy at initial assessment and additional cases at 3-year follow-up

BEHAVIOURAL SYNDROMES	Cases at Initial Assessment			Additional Cases at 3-Year Follow-up		
	FTD	AD	chi square	FTD	AD	chi square
Loss of Motivation/Apathy	12/37 (32.4%)	5/25 (20%)	1.2	14/25 (56%)	3/20 (15%)	7.9 *

* = p < .05

Loss of Motivation/ Apathy (Table 32)

Both Frontotemporal Dementia and Alzheimer’s Disease subjects exhibited high, clinically significant rates of loss of motivation at their initial assessments. After an interval of three years there was a marked deterioration in the Frontotemporal Dementia patient group with significantly less deterioration in the Alzheimer’s Disease group. At the second assessment a total of 70.2% of Frontotemporal Dementia patients were recorded with the behaviours compared with only 32% of Alzheimer’s Disease patients. None of the Frontotemporal

Dementia or Alzheimer’s Disease patients were noted to have any improvement in motivation or decrease in apathy over the 3-year time interval.

This result is consistent with previous research findings that have shown consistently rapid deterioration of motivational abilities in Frontotemporal Dementia patients (Diehl-Schmid & Pohl et al. 2006). In contrast, Alzheimer’s Disease patients have been found to undergo a less insidious, gradual loss of motivation (Elfgrén & Passant et al. 1993; Pasquier & Delacourte, 1998; Snowden & Neary et al. 1996).

5.8.2 Behavioural Changes Associated with Loss of Executive Functions

Table 33: Percentage and Chi Square significance of difference between Frontotemporal Dementia & Alzheimer’s Disease patients reported in file notes with behavioural changes associated with loss of executive functions

BEHAVIOURAL SYNDROMES	Cases at Initial Assessment			Additional Cases at 3-Year Follow-up		
	FTD	AD	chi square	FTD	AD	chi square
Increased Concrete Communication	12/37 (32.4%)	0/25	10.1 **	6/25 (24 %)	2/25 (8 %)	2.4
Increased Inflexibility	16/37 (43.2%)	1/25 (4%)	11.6 **	1/21 (4.8 %)	2/24 (8.3 %)	5.3
Loss of Insight	21/37 (56.8%)	0/25	21.5 ***	13/16 (81 %)	4/25 (16 %)	17.1 ***
Emotional Indifference	1/37 (2.7%)	0/25	0.91	10/36 (27.7 %)	3/25 (12 %)	4.7 *

* = p < .05; ** = p < .005; *** = p < .0005

Increased Concrete Communication (Table 33)

A significantly large number of the Frontotemporal Dementia group had become increasingly unable to understand complex speech, and were able to understand only the concrete meaning of conversations. Their expressive communication had become similarly concrete. In marked contrast, no Alzheimer's Disease patients were recorded with this impairment at the initial assessment. After an interval of three years 18 of the 37 Frontotemporal Dementia patients (49%) were recorded with concrete patterns of thinking. In contrast, only 8% of Alzheimer's Disease patients were reported with increased concreteness of thinking.

These findings are consistent with previous research that has indicated that Frontotemporal Dementia patients rapidly begin to take objects at face-value. In marked contrast concrete thinking in the Alzheimer's Disease patients has been found to slowly increase late in the course of the illness (Gustafson & Brun, 1999; Cummings & McPherson, 2001).

Increased Inflexibility (table 33)

At the initial assessments a large number of the Frontotemporal Dementia group had become increasingly stubborn and rigid in their behaviours, and this deterioration in behaviour had led to significant problems for the patient's primary caregivers. In contrast, only one Alzheimer's Disease patient had

developed this pattern of behaviour. After an interval of three years nearly half the Frontotemporal Dementia patients had become increasingly inflexible, compared with only twelve percent of Alzheimer's Disease patients.

This result is consistent with previous research findings that show rapid deterioration in Frontotemporal Dementia patients' ability to think and behave flexibly. In contrast, Alzheimer's Disease patients have been found to lose flexible thinking skills relatively slowly (Gustafson & Brun, 1999; Cummings & McPherson, 2001).

Loss of Insight (table 33)

Over half of the Frontotemporal Dementia patients were reported to have significant loss of insight in their speech and actions at their initial assessment. No Alzheimer's Disease patients were recorded with this deficit. After an interval of three years, all but 8% of the Frontotemporal Dementia patients were reported to have lost insight. In comparison, only 16% of Alzheimer's Disease patients had lost insight at the final assessment, as documented in the case notes.

The results are consistent with previous research which has found rapid early loss of insight in Frontotemporal Dementia patients, with typically relatively slow loss of insight over many years in Alzheimer's Disease patients.

Frontotemporal Dementia patients have been found to rapidly lose awareness of their deficits, and generally appear unaware that they are failing at tasks or

breaking social rules. In contrast, Alzheimer's Disease patients have been found to generally retain awareness of their deficits, and are able to follow social rules until late in the course of their illness (Rubin & Morris et al. 1987; Snowden & Neary et al. 1996; Gustafson & Brun, 1999; Bozeat & Gregory et al. 2000; Mendez & Shapira, 2005; Rankin & Baldwin et al. 2005).

Emotional Indifference (table 33)

Only one Frontotemporal Dementia patient displayed emotional indifference at the initial assessment, with no Alzheimer's Disease patients recorded with this deficit. After an interval of three years nearly 30% of the Frontotemporal Dementia had become emotionally "flat" and had lost emotional responsiveness when dealing with family members. In contrast, a total of 12% of the Alzheimer's Disease group had become emotionally indifferent by the end of the second time-interval.

This finding is consistent with previous research that has found emotional indifference more common amongst patients with Frontotemporal Dementia early in the course of the illness, whereas Alzheimer's Disease patients deteriorate later and more slowly (Elfgren & Passant et al. 1993; Pasquier & Lebert et al. 1998; Snowden & Neary et al. 1996).

Implications for providing care

The rapid loss of insight associated with Frontotemporal Dementia, and the relatively well-preserved insight associated with Alzheimer's Disease has major implications for caregivers. Alzheimer's Disease patients generally appear keenly aware of any loss of ability, and of task failure. Alzheimer's Disease patients generally attempt to maintain social relationships and conceal any deficits (Bozeat & Gregory et al. 2000).

In marked contrast, Frontotemporal Dementia patients are often unaware that they are failing at tasks, have any deficits, or are breaking social rules (Bozeat & Morris et al. 2000; Gustafson & Brun, 1999). This pattern of markedly different levels of insight between the groups indicates that individualized care-plans can assist with the maintenance of dignity amongst dementia patients by providing services and activities that do not needlessly expose their deficits. The relatively preserved visuo-spatial skills amongst the Frontotemporal Dementia group, combined with their profound loss of insight and social skills, indicates they may benefit from structured physical activities such as outdoor activities and simple board games (e.g. Tanabe & Ikeda et al.1999).

5.8.3 Speech and Language Changes

Table 34: Percentage and Chi Square significance of difference between Frontotemporal Dementia & Alzheimer’s Disease patients reported in file notes with behavioural changes associated with deterioration of speech and language ability at initial assessment and after three years

BEHAVIOURAL SYNDROMES	Cases at Initial Assessment			Additional Cases at 3-Year Follow-up		
	FTD	AD	chi square	FTD	AD	chi square
Echolalia	1/37 (2.7%)	0/25	0.7	2/36 (5.5 %)	0/25	1.5
Errors of speech/slurring	7/37 (18.9%)	1/25 (4%)	2.9	4/30 (13.3 %)	7/24 (29.2 %)	2.1
Increasingly sparse speech	15/37 (40.5%)	0/25	13.4 **	11/22 (50 %)	1/25 (4 %)	13.1 **
Perseverative Speech	10/37 (27%)	0/25	8.1 *	12/27 (44.4 %)	0/25	14.5 **

* = p < .01; ** = p < .001

Echolalia (table 34)

At the initial assessment one of the Frontotemporal Dementia group demonstrated echolalia (the immediate and involuntary repetition of words or phrases spoken by others). Two more Frontotemporal Dementia subjects developed this impairment over the following three years. None of the Alzheimer’s Disease group developed Echolalia during the course of the study. This result is consistent with previous research (Gustafson, 1987; Bathgate & Snowden et al. 2001).

Errors of speech and slurring (table 34)

At the initial assessment approximately 19% of the Frontotemporal Dementia group and 4% of the Alzheimer’s Disease group had increasing grammatical

errors of speech and/or slurring. After an interval of three years nearly 30% of both Alzheimer's Disease and Frontotemporal Dementia groups exhibited this speech deficit. There is no previous research that has examined the comparative increase in errors of speech in Frontotemporal Dementia and Alzheimer's Disease over time.

Increasingly sparse speech (table 34)

At the initial assessment approximately 40% of the Frontotemporal Dementia group exhibited increasingly sparse, grammatically correct speech. None of the Alzheimer's Disease group exhibited sparse speech. After an interval of three years speech had become sparse, but had retained its grammatical correctness in nearly 70% of the Frontotemporal Dementia group. Only one of the Alzheimer's Disease group had developed this verbal deficit. This finding is consistent with previous research which has found that Frontotemporal Dementia is very commonly associated with sparse, correct speech early in the course of the illness, with this trend continuing often to the point of mutism as the disease progresses. In contrast, speech in Alzheimer's Disease patients rarely becomes sparse until the late stages of the illness (Galton & Patterson, 2000; Bathgate & Snowden et al. 2001; Flaherty, 2005).

Perseverative Speech (table 34)

At the initial assessment nearly 30% of the Frontotemporal Dementia group were reported to have started uncontrollably repeating particular responses such as words, phrases or gestures, despite the absence or cessation of external stimuli. After an interval of three years nearly 60% of Frontotemporal Dementia patients had developed this speech deficit. In contrast, no Alzheimer's Disease

patient developed perseverative speech at either the initial assessment, or after an interval of three years. This pattern of marked increase in perseverative speech amongst Frontotemporal Dementia patients, but little or no perseverative speech in Alzheimer's Disease until the late stages of the illness, is consistent with previous research (Kertesz & Davidson et al. 1997; Smeding & de Koning, 2000).

5.8.4 Visuo-spatial Skill Changes

Table 35: Percentage and Chi Square significance of difference between Frontotemporal Dementia & Alzheimer’s Disease patients reported in file notes with behavioural changes associated with deteriorating visual recognition and visuo-spatial abilities at initial assessment and after an interval of three years

BEHAVIOURAL SYNDROMES	Cases at Initial Assessment			Additional Cases at 3-Year Follow-up		
	FTD	AD	chi square	FTD	AD	chi square
Increasingly getting Lost	0	5(20%)	8.1 **	0	2(8%)	4.3
Impaired object recognition	0	0		0	4(16%)	6.3 *
Unable to recognise own reflection	0	0		0	1(4%)	1.5

* = $p < .01$; ** = $p < .001$

Increasingly getting lost (table 35)

At the initial assessment, and after an interval of three years, none of the Frontotemporal Dementia group was reported to have started getting lost in previously familiar environments. In comparison, 20% of the Alzheimer’s Disease group were reported to have started getting lost. After an interval of three years a total of nearly 30% of the Alzheimer’s Disease group were getting lost. This finding is consistent with previous research that has found Frontotemporal Dementia patients rarely become lost. In marked contrast, Alzheimer’s Disease patients experience increasing difficulties finding their way (Barber, Snowden, & Craufurd, 1995; Pasquier & Richard et al. 2004). This finding has important implications for caregivers of Alzheimer’s Disease patients, as the inability to negotiate successfully through previously familiar environments requires high levels of supervision to ensure patient safety.

Impaired object recognition (table 35)

None of the Frontotemporal Dementia patients were found to have impaired recognition of common objects at either the initial or 3-year follow-up assessment. No Alzheimer's Disease patients had this deficit at the initial assessment, but after an interval of three years 16% of the Alzheimer's Disease group had impaired object recognition. Previous research has shown that Alzheimer's Disease patients develop object recognition deficits more rapidly than Frontotemporal Dementia patients (Brun & Passant, 1996; Kramer & Jurik et al. 2003). The Frontotemporal Dementia patients that were studied for longer than three years (see case studies p. 173) developed impaired object recognition for some common objects. The results show a pattern of differential deterioration of object recognition skills, with Frontotemporal Dementia patients having relatively preserved abilities in this area.

Unable to recognise own reflection (mirror sign) (table 35)

At the initial assessment none of either the Frontotemporal Dementia or Alzheimer's Disease group were reported to have lost the ability to recognise their own reflection. After an interval of three years one of the Alzheimer's Disease patients had developed this deficit. The development of the "mirror sign" in Alzheimer's Disease is rare, and its onset signals a poor prognosis for the patient (Breen & Caine et al. 2001).

Summary

Table 35 shows that over a three year period there was no deterioration in visual recognition and visuo-spatial abilities in the Frontotemporal Dementia group. In marked contrast, significant numbers of Alzheimer's Disease patients exhibited marked impairment in these areas. This result indicates preserved visuo-spatial abilities in the Frontotemporal Dementia group, and marked visuo-spatial processing deterioration in the Alzheimer's Disease group. These findings are consistent with previous research (Johansen & Hagberg, 1989; Miller & Cummings et al. 1991; Elfgren & Ryding et al. 1996; Lindau & Almkvist et al. 2000; Rascovsky & Salmon et al. 2002). The results, showing differential deterioration in each group, are consistent with the loci of neurological deterioration associated with Frontotemporal Dementia and Alzheimer's Disease (see Chapter 3).

5.8.5 Inattention and Judgment

Table 36: Percentage and Chi Square significance of difference between Frontotemporal Dementia & Alzheimer’s Disease patients reported in file notes with behavioural changes associated with inattention at initial assessment and after three years

BEHAVIOURAL SYNDROMES	Cases at Initial Assessment			Additional Cases at 3-Year Follow-up		
	FTD	AD	chi square	FTD	AD	chi square
Inattention/Distractio	18/37 (48.6%)	0/25	17.1 ***	6/19 (31.6 %)	4/25 (16 %)	0.6
Impaired Judgment	16/37 (43.2%)	0/25	14.6 ***	10/21 (47.6 %)	1/25 (4 %)	11.9 **

** = p < .001; *** = p < .0001

Inattention/Distractio (table 36)

At the initial assessment nearly half the Frontotemporal Dementia group were experiencing difficulties paying attention to their environment, losing track of conversations, were easily distracted, and not following instructions. None of the Alzheimer’s Disease group were reported to have this cluster of problems. After an interval of three years nearly sixty-five percent of the Frontotemporal Dementia group had deficits of attention. In contrast, sixteen percent of the Alzheimer’s Disease group had developed impairment in this area. This finding, showing a marked increase of inattention and distractio in the Frontotemporal Dementia patients, and relatively slow development of attentional difficulties in the Alzheimer’s Disease group, is consistent with previous research (Snowden & Neary et al. 1996; Binetti & Locascio, 2000; Geschwind & Robidoux, 2001).

Impaired Judgment (table 36)

At the initial assessment almost half of the Frontotemporal Dementia group had lost their ability to plan and organise activities, and required assistance and prompting to complete tasks. None of the Alzheimer's Disease group were reported with this deficit. After an interval of three years almost 70% of the Frontotemporal Dementia group had impaired judgment. During this time only one of the Alzheimer's Disease group were reported to have developed deficits in their judgment. This result is consistent with previous research that has shown marked deterioration of judgment in Frontotemporal Dementia, and relatively preserved judgment in the early years of Alzheimer's Disease (Gustafson, 1993). Other researchers have found that judgment in certain areas reliant on calculation ability may be more impaired in Alzheimer's Disease than in Frontotemporal Dementia (Mendez & Doss et al. 1998).

The combination of attention and judgment deficits at the initial assessment and increasing deficits over a period of three years in the Frontotemporal Dementia group compared with the Alzheimer's Disease group has major implications for management strategies for each group. These implications will be fully explored below in Chapter 7.

5.8.6 Disinhibition

Table 37: Percentage and Chi Square significance of difference between Frontotemporal Dementia & Alzheimer’s Disease patients reported in file notes with behavioural changes associated with Disinhibition at initial assessment and after three years

BEHAVIOURAL SYNDROMES	Cases at Initial Assessment			Additional Cases at 3-Year Follow-up		
	FTD	AD	chi square	FTD	AD	chi square
Aggression	12/37 (32.4%)	3/25 (12%)	3.4	0/25	4/22 (18.1 %)	7.2 *
Disinhibition	10/37 (27%)	0/25	8.1 **	9/27 (33.3 %)	0/25	8.1 **
Impulsivity	12/37 (32.4%)	0/25	10.1 **	13/25 (52 %)	3/25 (12 %)	4.2 *
Stealing	3/37 (8.1%)	0/25	2.1	3/34 (8.8 %)	3/25 (12%)	0.2

* = $p < .05$; ** = $p < .01$

Aggression (table 37)

At the initial assessment there were clinically significant numbers of both Frontotemporal Dementia and Alzheimer’s Disease patients directing verbal and/or physical abuse toward their primary caregivers. There was no statistical difference between the two groups. Rates of aggression were significantly higher amongst Alzheimer’s Disease patients after three years. Previous research has shown that aggression is commonly associated with both Frontotemporal Dementia and Alzheimer’s Disease, with higher rates of aggression associated with Frontotemporal Dementia (Miller & Darby et al. 1997; Hirono & Mega et al. 2000). The current study indicates that aggression is common in both Frontotemporal Dementia and Alzheimer’s Disease in the initial stages of the

illness. This finding has important implications for the clinical management of early-onset dementia, as resources may be required at the age of onset to effectively manage incidents of aggression.

Disinhibition (table 37)

At the initial assessment over one quarter of the Frontotemporal Dementia group were exhibiting disinhibited behaviours. After an interval of three years approximately 50% of the Frontotemporal Dementia group was exhibiting disinhibited behaviours. In marked contrast, none of the Alzheimer's Disease group were reported with disinhibited behaviours at either time interval. This finding is consistent with previous research that has shown patients with Frontotemporal Dementia often engage in disinhibited and inappropriate behaviours, whereas disinhibition is rarely associated with Alzheimer's Disease (Brun & Englund et al. 1994; Kertesz & Davidson et al. 1997; Walsh & Darby, 1999; Snowden & Bathgate et al. 2001).

Impulsivity (table 37)

At the initial assessment approximately one third of the Frontotemporal Dementia group were demonstrating impulsive behaviours. After an interval of three years over two-thirds of the Frontotemporal Dementia group had developed impulsive behaviours. In contrast, at the initial assessment no Alzheimer's Disease patient was reported with impulsive behaviours, and after an interval of three years only 12% of the Alzheimer's Disease group had developed impulsive behaviours. Rapid increases in impulsive behaviours

amongst the Frontotemporal Dementia patients, and relatively slow increases in impulsivity as the disease progresses in Alzheimer's Disease patients, are consistent with the findings of previous research (Kertesz & Davidson et al. 1997; Chow, 2000; Kertez & Nadkarni, 2000; Passant & Ostojic, 2004).

Stealing (table 37)

At the initial assessment approximately 8% of the Frontotemporal Dementia group had started stealing. No Alzheimer's Disease patients were reported to have started stealing. After an interval of three years a total of 16% of the Frontotemporal Dementia group were reported to have started stealing. 12% of the Alzheimer's Disease group were reported to have started stealing in the three year period after the first assessment. Previous research has shown that stealing is commonly associated with Alzheimer's Disease and Frontotemporal Dementia (Harwood & Ownby, 1998; Mendez & Chow et al. 2000).

Although the numbers are relatively small, stealing can pose a challenge to carers, and can bring patients suffering from dementia into contact with the police. Management strategies that provide unobtrusive monitoring and direction of behaviour may assist with this problem.

5.8.7 Humour

Table 38: Percentage and Chi Square significance of difference between Frontotemporal Dementia & Alzheimer’s Disease patients reported in file notes with changes in humour at initial assessment and after three years

BEHAVIOURAL SYNDROMES	Cases at Initial Assessment			Additional Cases at 3-Year Follow-up		
	FTD	AD	chi square	FTD	AD	chi square
Loss of Humour	8/37 (21.6%)	0/25	6.2 *	5/29 (17.2 %)	0/25	4.8 *
Development of Childish humour	1/37 (2.7%)	0/25	0.7	7/36 (19.4 %)	0/25	5.3 *

* = p < .05

Loss of Humour (table 38)

Approximately twenty-two percent of Frontotemporal Dementia patients had lost their characteristic sense of humour at the time of the initial assessment. After an interval of three years a total of approximately thirty-five percent of Frontotemporal Dementia patients had lost their sense of humour. In marked contrast, no Alzheimer’s Disease patients were reported to have lost their sense of humour at either time interval.

Development of Childish Humour (table 38)

At the initial assessment one of the Frontotemporal Dementia group had developed childish humour. After an interval of three years approximately twenty-three percent of the Frontotemporal Dementia group had developed childish humour. None of the Alzheimer’s Disease group developed childish humour at either time interval.

Summary

The results support previous findings which have consistently shown rapid loss of the ability to understand humour in Frontotemporal Dementia subjects and relatively preserved humour ability in Alzheimer's Disease patients (Lezak, 1995; Moran et al. 2004; Shammi & Stuss 1999). The current study is also consistent with previous research that has found the loss of ability to understand humour in Frontotemporal Dementia is often replaced by childish humour (Shammi & Stuss 1999).

The results provide support for previous research findings that indicate that humour ability relies on the healthy functioning of the frontotemporal lobes, and undamaged connections between these areas and subcortical regions of the brain (Shammi & Stuss, 1999; Moran et al. 2004).

Implications for Management

The rapid loss of humour in Frontotemporal Dementia patients, and the preserved sense of humour in Alzheimer's Disease patients, has significant implications for the differential clinical management of these groups. For Alzheimer's Disease patients, their relatively preserved humour allows them to understand many human interactions, and humour can be used as a therapeutic tool (e.g. Buckwalter & Gerdner et al. 1995). Preserved humour allows Alzheimer's Disease patients to understand the subtleties of conversation, and benefit from therapies such as "reminiscence therapy" (e.g. Moss & Polignano

et al. 2002). In contrast, the profound loss of humour accompanying Frontotemporal Dementia indicates that this group is unlikely to respond positively to verbally-based therapies.

5.8.8 Overactivity

Table 39: Percentage and Chi Square significance of difference between Frontotemporal Dementia & Alzheimer’s Disease patients reported in file notes with behavioural changes associated with overactivity at initial assessment and after three years

BEHAVIOURAL SYNDROMES	Cases at Initial Assessment			Additional Cases at 3-Year Follow-up		
	FTD	AD	chi square	FTD	AD	chi square
Hyperorality	7/37 (18.9%)	0/25	5.3 *	10/30 (33.3 %)	0/25	8.1 **
Hypersexuality	1/37 (2.7%)	0/25	0.7	1/36 (2.8)	0/25	0.7
Restlessness/ Pacing	14/37 (37.8%)	0/25	12.2 ***	6/23 (26.1 %)	4/25 (16 %)	0.7

* = p < .05; ** = p < .01; *** = p < .001

Hyperorality (table 39)

Nearly 20% of the Frontotemporal Dementia group’s eating habits had dramatically changed at the initial assessment. The patients had started eating and drinking more, eating excessively, and putting non-food objects in their mouths. After an interval of three years nearly half of the Frontotemporal Dementia group had developed these hyperoral behaviours. In contrast, none of the Alzheimer’s Disease group were reported with this pattern of deficits at either the initial assessment, or after an interval of three years. This finding is

consistent with previous research that has shown that hyperorality often accompanies the onset of Frontotemporal Dementia, and hyperoral behaviours rapidly increase as the disease progresses.

Previous studies reported 100% of Frontotemporal Dementia cases and 58.1% of Alzheimer's Disease cases showed at least one abnormal eating behaviour in various disease stages (Ikeda & Brown et al. 2002). Hyperoral behaviours are associated with human Kluver-Bucy syndrome (Lily, Benson & Frakel, 1983; Aggleton & Mishkin, 1990; Clarke & Brown, 1990; Heutink & Stevens et al. 1997; Spillantini & Murrell et al. 1998). Hyperoral behaviours are discussed further in Chapter 7, and illustrated with case studies.

Hypersexuality (table 39)

One Frontotemporal Dementia patient was reported to have abnormally high levels of sexual activity at the initial assessment, accompanied by disinhibited and inappropriate sexual acts. This patient continued to be sexually disinhibited during the 3-year assessment period. None of the Alzheimer's Disease patients were reported with unusually high levels of sexual activity at either assessment. One Frontotemporal Dementia patient became increasingly sexually active and inappropriate over the following 3 years.

Restlessness/Pacing (table 39)

At the initial time assessment nearly 40% of the Frontotemporal Dementia group had become more restless or hyperactive, and had started "pacing" – walking without apparent direction. After an interval of three years

over half of Frontotemporal Dementia group were reported to have developed “Restlessness/Pacing behaviours. In contrast, no Alzheimer’s Disease patients were reported with this deficit at the initial assessment. After an interval of three years 16% of Alzheimer’s Disease patients had developed “Restlessness/Pacing behaviours.

For purposes of clinical management it is important to note that although there were significantly greater numbers of Frontotemporal Dementia patients with this cluster of deficits than Alzheimer’s Disease patients, the Frontotemporal Dementia patients were not getting lost as a result of this restlessness and pacing. Allowing Frontotemporal Dementia patients access to areas where they can safely walk may be a useful means of providing healthy, socially appropriate activities, and may also assist in the control of weight gain. This is discussed further in Chapter 7.

5.8.9 Other Behaviours Associated with Frontal Lobe Deficits

Table 40: Percentage and Chi Square significance of difference between Frontotemporal Dementia & Alzheimer’s Disease patients reported in file notes with stereotypical and ritualised behaviours at initial assessment and after an interval of three years

BEHAVIOURAL SYNDROMES	Cases at Initial Assessment			Additional Cases at 3-Year Follow-up		
	FTD	AD	chi square	FTD	AD	chi square
Hiding Food or Clothes	0/37	0/25		2/37 (5.4 %)	0/25	1.4
Ritualistic Behaviours	4/37 (10.8%)	0/25	2.9	5/33 (15.2 %)	0/25	3.7
Utilisation Behaviours	11/37 (29.7%)	0/25	9.1 **	3/26 (11.5 %)	0/25	3.1

** = p < .01

Hiding Food or Clothes (table 40)

No Frontotemporal Dementia or Alzheimer’s Disease patients hid food or clothing at the initial assessment. During the following three years two of the Frontotemporal Dementia patients developed this behaviour. None of the Alzheimer’s Disease patients developed this behaviour at either time interval. Hiding food and clothing is a form of hoarding behaviour, and has been frequently noted in Frontotemporal Dementia patients (Lynch & Marder et al. 1994; Neary & Snowden, 1996).

Ritualistic Behaviours (table 40)

At the initial assessment approximately 11% of the Frontotemporal Dementia group had developed ritualistic behaviours including socially inappropriate routines such as collecting a set numbers of objects and placing them in a specific spot without apparent reason. After an interval of three years nearly quarter of the Frontotemporal Dementia group had developed ritualistic behaviours. None of the Alzheimer's Disease group were reported to have developed these behaviours at either time interval. This finding is consistent with previous research that has reported ritualistic behaviours are common at the onset of Frontotemporal Dementia, and that these behaviours increase as the disease progresses. The research also indicates that ritualistic behaviours are extremely rare in Alzheimer's Disease (Neary & Snowden, 1996; Nyatsanza & Shetty et al. 2003; Pasquier & Delacourte, 1998; Bathgate & Snowden et al. 2001; Miller & Cummings et al. 1995).

The clinically significant (25%) of ritualistic behaviours that developed in the Frontotemporal Dementia group over 3 years, and the absence of these behaviours in Alzheimer's Disease, suggests that management strategies for the two groups of patients need to be significantly different, with some researchers proposing that behavioural changes associated with Frontotemporal Dementia can be utilised to assist with patient care (Tanabe, Ikeda, & Komori, 1999).

This is discussed further in Chapter 8.

Utilisation Behaviours (table 40)

At the initial assessment nearly 30% of the Frontotemporal Dementia group had developed “utilisation behaviours”. These behaviours involved the patients automatically feeling, examining, picking up and manipulating objects in the environment. After an interval of three years nearly 40% of the Frontotemporal Dementia group had developed utilisation behaviours. No Alzheimer’s Disease patient developed these behaviours at either time interval. This finding is consistent with previous research which has found utilisation behaviours are common in Frontotemporal Dementia, and rarely occur in Alzheimer’s Disease (Ikeda & Tanabe, 2000; Nyastanza & Shetty et al. 2003).

5.9 PSYCHIATRIC SYMPTOMS

5.9.1 Confabulation, Anxiety/Panic Attacks, Hallucinations, & Paranoia

Table 41: Percentage and Chi Square significance of difference between Frontotemporal Dementia & Alzheimer’s Disease patients reported in file notes with psychiatric symptoms at initial assessment and after an interval of three years

PSYCHIATRIC SYMPTOMS	Cases at Initial Assessment			Additional Cases at 3-Year Follow-up		
	FTD	AD	chi square	FTD	AD	chi square
Anxiety/Panic Attacks	5/37 (13.5%)	1/25(4%)	1.5	2/32 (6.3 %)	1/24 (4.2 %)	0.1
Confabulation	0/37	1/25 (4%)	1.5	0/37	1/24 (4.2 %)	1.6
Clinical Depression	7/37 (18.9%)	4/25 (16%)	0.09	3/30 (10%)	2/21 (9.5%)	0.1
Hallucinations	4/37 (10.8%)	1/25(4%)	0.9	0/33	2/24 (8.3 %)	2.8
Paranoia	7/37 (18.9%)	0/25	5.3 *	0/30	5/25 (20 %)	11.5 **

* = p < .05; ** = p < .01

Anxiety/Panic Attacks (table 41)

Anxiety and panic attacks occurred in approximately 13% of the Frontotemporal Dementia patients, and one Alzheimer's Disease patient at the initial assessment. A total of approximately 19% of Frontotemporal Dementia patients and 8% of Alzheimer's Disease patients had experienced anxiety/panic attacks after an interval of three years. The results are inconsistent with previous research which has indicated little or no anxiety and panic associated with Frontotemporal Dementia, with higher rates of anxiety and panic associated with Alzheimer's Disease (Snowden & Neary et al. 1996; Gustafson & Brun, 1999; Pasquier, 1999; Cummings & McPherson, 2001; Mendez & Shapira, 2005).

The previous studies did not examine the natural histories of patients with Frontotemporal Dementia. As the incidents of anxiety/panic were generally of short duration, and did not continue for the course of the illness, it is possible that such incidents were not detected in previous studies. Also, as noted above, all research in this area has used relatively small sample sizes. Therefore the results of the current study need to be treated with caution.

Confabulation (table 41)

None of the Frontotemporal Dementia patients exhibited confabulation at either the initial assessment, or after an interval of three years. One Alzheimer's Disease patient exhibited confabulation at time one, with a total of two Alzheimer's Disease patients exhibiting this behaviour after three years. This

finding is consistent with previous research that has found confabulation rarely occurs in Frontotemporal Dementia, and is more commonly associated with Alzheimer's Disease (Merriman & Aronson, 1988; Pasquier, 1999).

Clinical Depression (table 41)

A significant and similar number of both Frontotemporal Dementia and Alzheimer's Disease patients were diagnosed with depression at their initial assessments. Rates of increase of depression were low for both groups over three years. Similar rates of depression between Frontotemporal Dementia and Alzheimer's Disease groups have been found by other researchers (Cummings & McPherson, 2001; Elfgren & Passant et al. 1993; Gormley, & Rizwan, 1998; Miller & Cummings et al. 1995; Snow & Arnold, 1996).

Hallucinations (table 41)

Approximately 11% of Frontotemporal Dementia patients had experienced hallucinations at the time of the initial assessment. All of these patients had hallucinations for less than three months duration. The pattern of hallucinations was different in both groups, with more Frontotemporal Dementia patients with hallucinations at the initial assessment, and more Alzheimer's Disease patients than Frontotemporal Dementia patients with hallucinations after a three year interval. Although the result was not statistically significant, the result has important implications for clinical management due to the behavioural disturbances commonly associated with hallucinations. In the two Alzheimer's

Disease patients, hallucinations continued as the patients deteriorated. Previous research has found that hallucinations in Frontotemporal Dementia are associated with motor neuron disease (FTD/MND, see Chapter 6) (Dickson & Horoupian et al. 1986; Lopez & Gonzalez et al. 1996; Nitrini & Rosemberg, 1998). Three of the four Frontotemporal patients with hallucinations were diagnosed with FTD/MND. The current research supports previous findings that indicate that hallucinations are an indicator of rapid deterioration, as all Frontotemporal and Alzheimer's patients with hallucinations deteriorated rapidly, and exhibited severe behavioural disturbances.

A case study presented below (7.2.3 p. 193) details the rapid deterioration of a man who experienced disturbing hallucinations early in the course of his illness. This man developed a severe behavioural disturbance, and died approximately seven years after first showing signs of dementia.

Paranoia (table 41)

Paranoia was common in the Frontotemporal Dementia group at the initial assessment, whereas no Alzheimer's Disease patient exhibited paranoia. In contrast, no additional Frontotemporal Dementia patients developed paranoia over three years whereas 20% of Alzheimer's Disease patients developed paranoia by the final assessment. This research is consistent with previous findings that have indicated paranoia often occurs early in the course of

Frontotemporal Dementia, and develops more slowly in Alzheimer’s Disease (Merriman & Aronson, 1988; Harwood & Ownby, 1998; Snowden & Neary, 1999).

5.10 OTHER BEHAVIOURS: INCONTINENCE, MORE AFFECTIONATE & PLEASANT DISPOSITION

Table 42: Percentage and Chi Square significance of difference between Frontotemporal Dementia & Alzheimer’s Disease patients reported in file notes with other behaviours

	Cases at Initial Assessment			Additional Cases at 3-Year Follow-up		
	FTD	AD	chi square	FTD	AD	chi square
Incontinence	2/37 (5.4%)	0/25	1.4	12/35 (34.3 %)	3/25 (12 %)	3.4
More affectionate	1/37 (2.7%)	0/25		2/36 (5.5 %)	0/25	1.4
Pleasant disposition	3/37 (8.1%)	7/25 (28%)	4.4 *	0/34	0/18	

* = p < .05

5.10.1: Incontinence, More Affectionate, & Pleasant Disposition.

Incontinence (table 42)

A small number of Frontotemporal Dementia patient were incontinent at the initial assessment, with no incontinent Alzheimer’s Disease patients. At the final assessment a total of 37.8% of Frontotemporal Dementia patients were incontinent, with 12% of Alzheimer’s Disease patients becoming incontinent over a period of three years. This finding is consistent with previous research

that has shown incontinence commonly occurs within 18 months of diagnosis in Frontotemporal Dementia, and develops more slowly in Alzheimer's Disease (Nicolai & Lazzarino, 1992; Neary & Snowden et al. 1998; McKhann & Albert et al. 2002). The rates of incontinence in this study suggest that incontinence management is an important component of early-onset dementia care.

More affectionate (table 42)

No Alzheimer's Disease patient was reported to have become more affectionate at the initial assessment, but one Frontotemporal Dementia patient was reported to have become more affectionate. A total of three Frontotemporal Dementia patients were reported to have become more affectionate at the final assessment. All three Frontotemporal Dementia patients who became more affectionate were given the additional diagnosis of Frontotemporal Dementia/Primary Progressive Aphasia (FTD/PPA) after the initial assessment. FTD/PPA is a form of Frontotemporal Dementia with severe language deterioration, and less severe behavioural disturbances (Kertesz & Martinz-Lage, 2000).

Pleasant disposition (table 42)

The three Frontotemporal Dementia patients reported to have a pleasant disposition at the initial assessment were the same patients who were given a diagnosis of FTD/PPA by the final assessment. A large number of Alzheimer's Disease patients were reported to have a pleasant disposition at the initial assessment, and this disposition appeared to be stable over the 3-year assessment period.

CHAPTER 6

FRONTOTEMPORAL DEMENTIA AND

CONNECTED CONDITIONS

6.1 CONDITIONS ASSOCIATED WITH THE ONSET OF

FRONTOTEMPORAL DEMENTIA

Frontotemporal Dementia is commonly diagnosed in conjunction with a range of neurological conditions such as Human Klüver-Bucy Syndrome; Corticobasal Degeneration Syndrome/ Parkinsonism, and Motor Neurone Disease (Foster & Wilhelmsen et al. 1997; Gustafson, Brun & Passant, 1992; Lebert & Pasquier et al. 1998; Mathuranath & Xuereb et al. 1999; Davies & Hodges et al. 2005).

6.1.2 Human Klüver-Bucy Syndrome

“Dementia is always hard on the spouse but Frontotemporal Dementia is particularly trying because of the symptoms, which may be extremely difficult to cope with. The fact that Frontotemporal Dementia also affects younger people who may have dependant children makes the disease so much more devastating”.

Passant & Elfgren et al. 2005, p. 17

Human Klüver-Bucy Syndrome is an extremely rare medical condition. The majority of human Klüver-Bucy Syndrome cases involve patients who have suffered severe damage to the bilateral anterior temporal lobes, and specifically the amygdala (Anson & Kulman, 1993; Conlon, 1988; Hayman & Rexer et al. 1998; Cummings & Duchon, 1981; Filley & Cullum, 1993; Nahm, 1997). Human Klüver-Bucy Syndrome is associated with profound behavioural changes. These changes are detailed below in Table 43. All recorded cases of Human Klüver-Bucy Syndrome have been associated with a combination of aphasia, amnesia, or dementia (Lilly & Cummings et al. 1983; Janita, 1985).

There are no universally accepted diagnostic criteria for human Klüver-Bucy Syndrome, and published diagnostic criteria vary widely (Hayman & Rexer et al. 1998). Human Klüver-Bucy syndrome is, in most cases, associated with progressive or chronic neurological disorders. It is probable that human Klüver-Bucy Syndrome is a result of combined frontal and temporal deficits.

Table 43: Behaviours associated with Human Klüver-Bucy syndrome

Behaviour	Description
Extreme sexual behaviour	Including public and excessive masturbation, and the inappropriate touching of others. Inappropriate sexual remarks and gestures are frequent (Lily & Benson et al. 1983; Boller & Kim et al. 1984; Hayman & Rexer et al. 1998; Jha & Patel, 2004). Changes in sexual preferences and paedophilia have also been reported (Mendez & Chow et al. 2000).
Environmental dependency syndrome	Utilization behaviour or stimulus-bound behaviour (Hashimoto & Yoshida et al. 1995). This cluster of behaviours bears striking similarities to the “hypermetamorphosis” described in rhesus monkeys by Klüver and Bucy (1939). Klüver and Bucy defined hypermetamorphosis as “the irresistible tendency of the monkeys to pick up and manipulate objects in their environment”. This tendency is often an early sign of Frontotemporal Dementia, and has been linked to neuronal loss in the frontal and fronto-thalamic regions of the brain (Hashimoto & Yoshida et al. 1995).
Hyperorality	The exploration of the environment with the mouth, and an urge to put all kinds of inedible objects into the mouth (Clarke & Brown, 1990; Lily & Benson et al. 1983). Lesions in both the inferior temporal cortex and the superior temporal polysensory area mimic the deficits observed after amygdala ablation, implying that these two regions supply the amygdala with information that identifies objects as being edible or inedible (Aggleton & Mishkin, 1990).

Table 43 continued: Behaviours Associated With Human Klüver-Bucy syndrome

Behaviour	Description
Appetite	An almost uncontrollable appetite for food and drink. This often manifests itself with the eating of food off other people’s plates, and stealing food (Mendez & Foti, 1997).
Memory loss	(Hayman & Rexer et al. 1998; Lily & Benson et al. 1983).
Blunted affect	Emotional unresponsiveness, indifference, apathy, and even pet-like compliance. This cluster of behaviours may be due to damage to the amygdala. Such damage invariably results in loss of ability to make emotionally meaningful discriminations between stimuli (Boller & Kim et al. 1984).
Visual agnosia	Visual agnosia associated with human Klüver Bucy Syndrome is characterized by the inability to distinguish friends, relatives and strangers (Hayman & Rexer et al. 1998; Goscinki & Kwiatowski et al. 1997). Disorders of facial recognition in humans have been seen following bilateral amygdalotomy (Jacobson, 1986). It has been shown repeatedly in animal studies that bilateral lesions in the amygdala by themselves will produce the visual agnosia component of Klüver —Bucy Syndrome (Zola-Morgan & Squire et al. 1989).

Table 43 continued: Behaviours Associated With Human Klüver-Bucy syndrome

Hyperactivity and distractibility	Lesions in the Frontotemporal system can disrupt access to learned emotional associations and responses, including inhibitory social restraints (Shoenbaum & Chiba et al. 2000). Shoenbaum and associates (2000, 2001) have described the critical importance of the interconnections between orbitofrontal cortex and baso-lateral amygdala for encoding and using information about the motivational significance of stimuli. Damage to this system results in lack of access to learned responses. The result of damage to orbitofrontal cortex/basolateral amygdala system is commonly hyperactive non-specific undirected exploration of the environment.
Loss of fear	LeDoux (1992) has demonstrated the role of the amygdala in fear conditioning and in learning about the emotional significance of social interactions. Damage to the amygdala results in loss of fear and inability to learn through fear conditioning.

6.1.3 Corticobasal Degeneration Syndrome/ Parkinsonism

Corticobasal Degeneration (CBD) and Frontotemporal Dementia (FTD) have historically been viewed as two distinct neurodegenerative processes (Kertez, 2000). Recent research has seriously challenged this view, and established clear connections between the two conditions (Kertez & Martinez-Lange et al. 2000; Mathuranath & Xuereb et al. 2000).

Corticobasal Degeneration refers to a neurodegenerative process affecting the fronto-parietal regions of the cortex and the basal ganglia (Mathuranath & Xuereb et al. 2000). Corticobasal Degeneration (CBD) has similarities to Pick's disease due to the focal cortical atrophy and the ballooned neurons characteristically associated with Pick's Disease. Corticobasal Degeneration Syndrome (CBDS) is characterized by extrapyramidal signs, including slowness, clumsiness and stiffness, starting on one side of the body, predominantly in the arms or legs. Other features of the illness include dysphasia (difficulty with speech generation), dysarthria (difficulty with articulation), difficulty controlling the muscles of the face and mouth, swallowing difficulties, and loss of balance. Patients have often been first diagnosed in movement disorder clinics.

Corticobasal Degeneration Syndrome is associated with Motor Neurone Disease/Frontotemporal Dementia and Frontotemporal Dementia (Kertez & Martinez-Lange et al. 2000). The rigidity, poor motor control, loss of balance, and slow movements associated with Corticobasal Degeneration Syndrome are a form of Parkinsonism (Chow & Miller et al. 1999).

Studies of the natural history of Frontotemporal Dementia indicate that in some cases Corticobasal Degeneration Syndrome develops as the disease progresses (Mathuranath & Xuereb et al. 2000; Wenning & Litvan et al. 1998).

6.1.4 Tau Mutations: A Link Between Frontotemporal Dementia and Corticobasal Degeneration Syndrome

TAU is an important protein that assists with neuronal communication, and supports neuronal survival (Hong & Zhakareva et al. 1998). Tau protein mutations have been found in Frontotemporal Dementia and Corticobasal degeneration (Poorkaj & Grossman et al. 2001). Identical Tau protein mutations in one family have been found in family members with both Frontotemporal Dementia and Corticobasal degeneration (Bugiani & Murrell et al. 1999). Bugiani and colleagues (1999) suggest that the finding of identical Tau protein mutations in both Corticobasal degeneration and Frontotemporal Dementia indicates that Tau mutations can, in some families, result in either Frontotemporal Dementia or Corticobasal degeneration, and that there is an underlying connection between the two conditions.

6.1.5 Frontotemporal Dementia and Motor Neurone Disease (FTD & MND)

Frontotemporal Dementia (FTD) and Motor Neurone Disease (MND) often co-exist, and the inter-related disease processes represent a pathological continuum (Mitsuyama, 1984; Bak & Hodges, 1999; Brun & Passant, 1996; Neary & Snowden et al. 1990; Neary & Snowden, 1996; Nitri & Rosemberg, 1998;

Talbot & Goulding et al. 1995). When Frontotemporal Dementia occurs in conjunction with motor disturbance, the term FTD/MND is now commonly accepted (Barson & Kinsella et al. 2000). Amyotrophic Lateral Sclerosis and Motor Neurone Disease (ALS/MND) is a widely used term describing motor neuron degeneration. For the purposes of this research the term “MND” is used to describe “ALS/MND” and all motor neurone diseases.

Patients often present with Frontotemporal Dementia symptomatology, including significant behavioural and cognitive changes, before they develop Motor Neurone Disease (Bak & Hodges, 1999). Barson and colleagues (Barson & Kinsella et al. 2000) studied 69 patients diagnosed with Motor Neurone Disease. They found that when dementia was also diagnosed in the patients, the dementia could be accurately classified as Frontotemporal Dementia.

In conjunction with the characteristic changes in the frontal and temporal lobes associated with Frontotemporal Dementia, Frontotemporal Dementia/Motor Neurone Disease patients also exhibit a cluster of additional neurological changes. These changes commonly include bulbar atrophy, status spongiosus (widespread neuronal death and collapse of the cerebral cortical cytoarchitecture), gliosis (i.e., the production of a dense fibrous network consisting of a proliferation of astrocytes resulting from neurodegeneration), hypoglossal cell loss and atrophy of the anterior temporal horns of the spinal cord (Brun & Englund et al. 1994; Neary & Snowden et al. 1990; Neary,

Snowden, & Mann, 2000). The link between Motor Neurone Disease and Frontotemporal Dementia has been further established through SPECT studies (Talbot & Snowden et al. 1995). Talbot and colleagues (1995) found that the SPECT findings of FTD/MND patients and Frontotemporal Dementia patients showed a similar pattern of cerebral involvement.

The prognosis for patients diagnosed with FTD/MND is very poor, with rapid deterioration and death generally occurring within five years of diagnosis. FTD/MND is commonly accompanied by severe behavioural and psychiatric symptoms (Barson et al. 2000; Nitrini & Rosemberg, 1998). Hallucinations and other psychotic symptoms are not common in Frontotemporal Dementia (Lopez & Gonzalez et al. 1996). However, in FTD/MND psychotic symptoms and hallucinations are common, and often occur early in the course of the illness (Dickson & Horoupian et al. 1986; Nitrini & Rosemberg, 1998). Nitrini & Rosemberg (1998) have hypothesised that when psychotic symptoms occur in conjunction with FTD/MND the temporal lobes are affected early in the course of the illness.

6.1.6 Increased Artistic Ability and Frontotemporal Dementia

Miller and colleagues (Miller & Ponton et al. 1996; Miller & Cummings et al. 1998) described a series of Frontotemporal Dementia patients who exhibited heightened artistic ability at the onset of their Frontotemporal Dementia. Miller and Cummings et al. (1998) presented case studies of 5 Frontotemporal

Dementia patients. The patients were selected from a group of 69 patients diagnosed with Frontotemporal Dementia because of their heightened interest in art. The patients all became interested in art in the early stages of their illness. The patients began painting obsessively and attending art classes after previously showing no artistic inclination. SPECT studies revealed that the patients had significant anterior temporal lobe atrophy and relatively spared dorsolateral frontal cortex. The patients all demonstrated profound personality change, with impaired speech and social skills. Miller and colleagues (1998) hypothesised that the anterior temporal lobe atrophy may have facilitated the patient's artistic skills. No published follow-up studies have as yet replicated the above findings linking increased artistic creativity to Frontotemporal Dementia.

Observations from the Current Study

In the current research there was no reported increase in artistic creativity in any of the Frontotemporal Dementia or Alzheimer's Disease patients. Two of the Frontotemporal Dementia patients worked in creative fields (graphic design and architecture). Both experienced marked deterioration in their ability to draw before diagnosis, and one began producing child-like drawings.

6.2 CASE STUDIES – GLORIA, MICHAEL, STEVEN, JULIE

Four case studies are presented below. The first case study is an Alzheimer's Disease patient (See "Gloria", section 6.2.1 below). This patient exhibited the most extreme behaviours by far of any of the Alzheimer's Disease group, and was in no way typical of the Alzheimer's group. This patient's profile was presented to illustrate the complex care requirements of some early-onset Alzheimer's Disease patients. The next case studies, a patient with Frontotemporal Dementia (See Michael, section 6.2.2 below) and a patient with Frontotemporal Dementia with Motor Neurone Disease (FTD/MND, see "Steven", section 6.2.3 below) are presented to illustrate the behaviours associated with these conditions. Both these patients displayed extremely difficult behaviours. Frontotemporal Dementia patients displayed behaviours of varying intensity. A profile of a Frontotemporal Disease patient with parkinsonism with some of the least severe behavioural problems (see "Julie" 6.2.4 below) is also presented to illustrate the range of behaviours associated with this condition.

6.2.1 Alzheimer's Disease Case Study 1: "Gloria" – Mirror Sign

Age: 58

Gloria was initially referred to a neurologist by her doctor who had become increasingly concerned about her rapid decline in functioning in all areas of her life. She was seen by the team neurologist with her husband. Her husband stated that he had become increasingly concerned that she had been developing a medical or psychiatric disorder for approximately ten years. Gloria was unable to give a coherent life history.

Her husband stated that her memory and general functioning had deteriorated steadily over the past 10 years, and she now needed help with many activities of daily living. For example, she required assistance to cook simple meals, to organise her clothing, and to dress. He stated that she increasingly fabricated stories, and provided numerous examples. Approximately four years previously he stated that she had become progressively more “unreasonable and disorientated”. She had acted erratically, and made some disastrous business decisions. She unexpectedly and uncharacteristically left her children with her husband and went travelling for twelve months. When Gloria returned from her travels, her husband reported that she had deteriorated further.

He stated that, due to her steady deterioration in functioning, he had taken over all domestic duties gradually over the past 10 years. For the previous four years he had completed all domestic duties. He reported that Gloria was still able to perform some tasks if he supervised her closely, such as washing clothes. He stated that over the past 12 months she had completely lost her sense of direction, and frequently got lost, even in familiar environments such as her local shopping centre. She often became distressed if she had to leave her home. She reported frequent headaches.

Gloria still attempted to iron, but had difficulties working out how to place the clothing on the ironing board. Her husband stated that he had to help her dress as she had problems doing up zips and belts, and was unable to tell if she had put her clothes on incorrectly. Gloria was clearly distressed during the interview, and was frequently tearful. She was sensitive to her failures when

asked to perform tasks. For example, Gloria was unable to successfully write a simple sentence, and cried, stating “My writing is terrible now, it used to be good”, and “I used to be clever once, I can’t believe I have ended up like this”. She appeared anxious and agitated throughout the assessment.

Age: 58 years 6 months.

Gloria was seen by her neurologist accompanied by her husband. They were told that she had “probable Alzheimer’s Disease”:

EEG: Abnormal, showing a slowing of the background rhythms and is compatible with an encephalopathy of any cause.

MRI: Parietal and occipital lobes show extensive enlargement of the cortical sulci. Frontal lobes relatively spared, but these show some degree of atrophy.

SPECT: Appearance supports the diagnosis of Alzheimer’s Disease.

Gloria’s husband reported that there had been acceleration in her rate of deterioration over the past six months. She had become increasingly confused and unable to cope. She had forgotten how to do all household tasks, and required assistance with all activities of daily living, including toileting. Her speech was normal, but her memory was impaired. She was unable to recall what she had done a few hours previously, and did not know where she was. She was distressed, agitated, and tearful throughout the assessment.

Age: 58 years 8 months

Gloria was assessed by a speech pathologist at home. The speech pathologist reported adequate reading skills for single words, but difficulties with comprehension of more complex written and spoken material.

Age: 59 Years 2 Months

Gloria was seen for neurological review. Her husband reported that she no longer recognised herself in the mirror (mirror sign, concrete thinking, see above p.130), and talked to her reflection, believing it was someone else. She had lost the ability to put on even a dressing gown without assistance, and frequently attempted to put clothes on the wrong way. For example, she would try to put a t-shirt on upside down. Her inability to perform such simple actions caused her great distress. Her memory continued to deteriorate, and she was constantly confused, distressed, and anxious.

Age: 59 Years 5 Months.

Gloria's husband reported that she had continued to believe her reflection was someone else, and argued with him if he tried to explain that the reflection was her image. She had recently started having arguments with her reflection, and had hit out and spat at the mirror. She had lost the ability to recognise her friends and family, and occasionally didn't recognise her husband. Gloria had become increasingly disoriented, and often became lost in her own house. She was often frustrated, and had become verbally and physically aggressive. Friends and family members rarely visited due to her deteriorated condition. Her husband described his wife as "extremely difficult to care for". At times

she would throw household objects at him without apparent reason. At other times she would “switch back to her old pleasant self” for short periods of time.

Age: 59 Years 8 months.

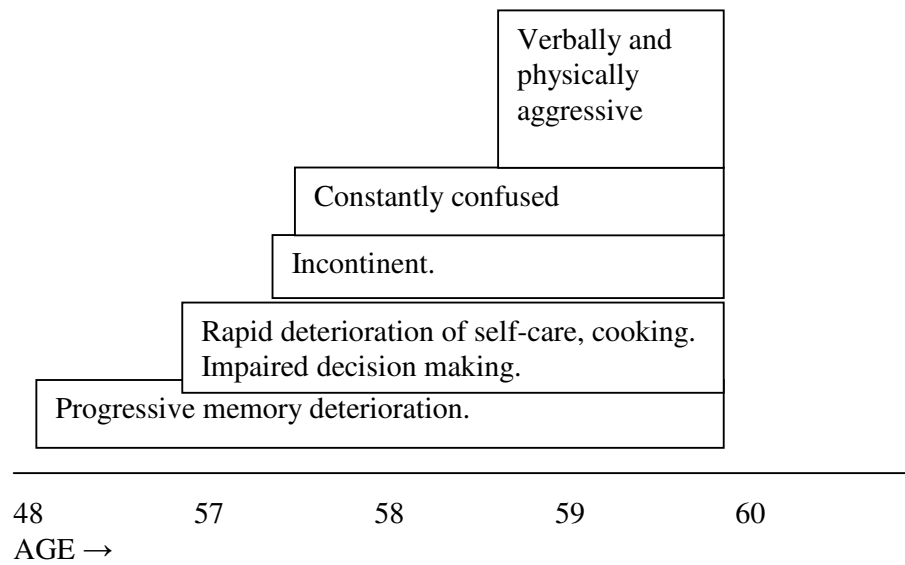
Gloria’s husband telephoned Gloria’s social worker to inform her that he was no longer able to cope with his wife’s behaviour, and she had been placed in a nursing home.

Age: 60 Years.

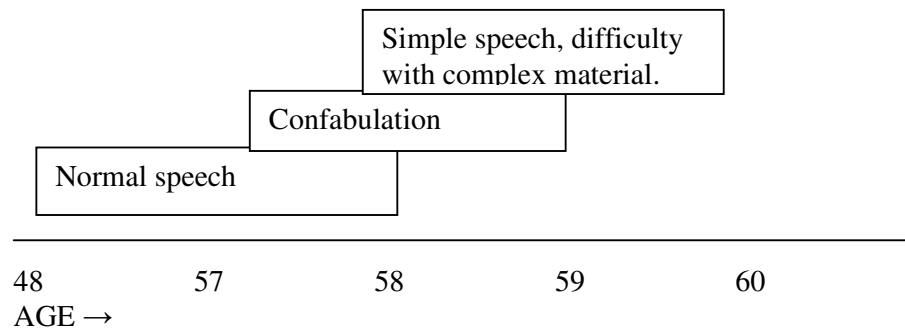
Gloria died in her sleep in the nursing home.

Gloria's Timelines: Each bar indicates the length of time (years) each event occurred.

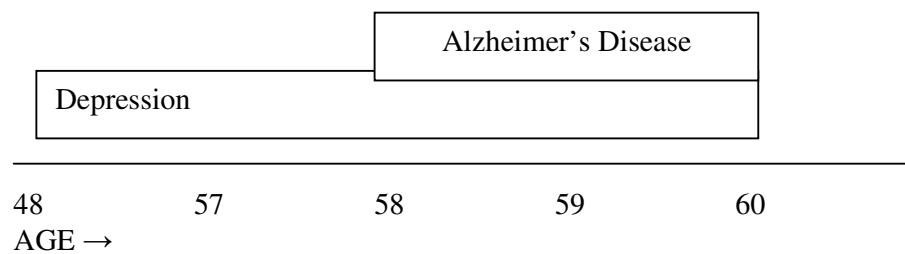
Timeline 1: Behaviours



Timeline 2: Speech



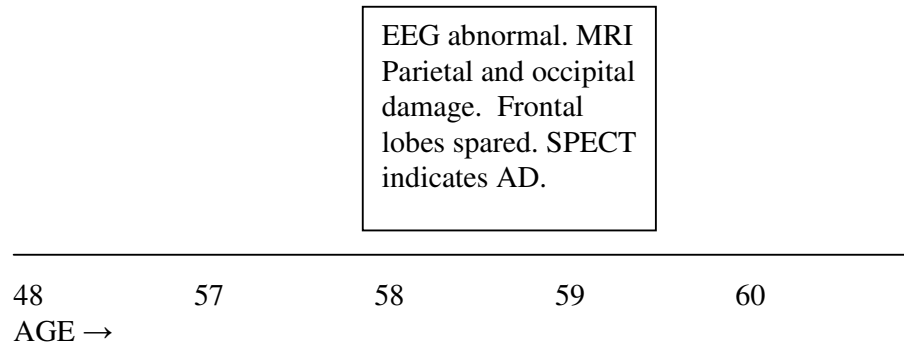
Timeline 3: Diagnoses.



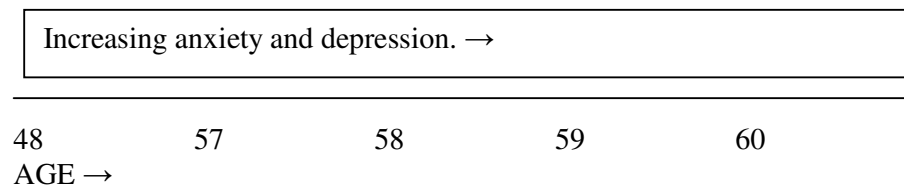
Timeline 4: Syndromes



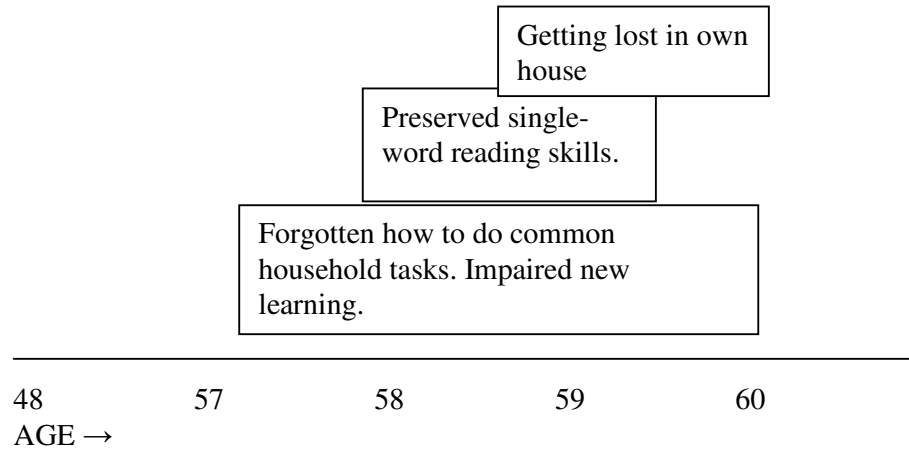
Timeline 5: Imaging results



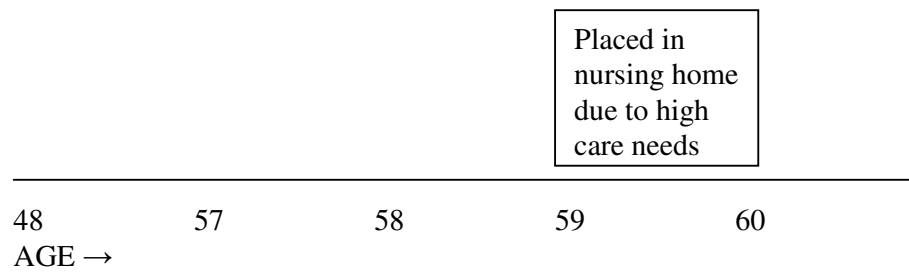
Timeline 6: Affective conditions



Timeline 7: Memory & preserved skills.



Timeline 8: Hospital & Residential Services



6.2.2 Frontotemporal Dementia Case Study 2: “Michael”

Age: 47

Michael first presented to his doctor with a list of problems at age 47. The doctor’s report indicated he was well groomed. Michael reported increasing difficulties following conversations, and often forgot what he wanted to say. He was a self-employed small businessman, and reported problems running his business. The doctor stated that he appeared to have “lost all conversational skills”, and noted that Michael exhibited “mild levels of anxiety and depression”. His depression and anxiety were treated for twelve months with an SSRI antidepressant, with no improvement noted in his depression. He had recently divorced, but denied being concerned about this.

He was subsequently referred by his doctor to a psychiatrist. The psychiatrist reported that Michael was unable to give an accurate history. He scored 28/30 on the Mini Mental State Exam. The psychiatric exam indicated mild depression with no psychotic features. Michael stated that he was doing his job well, but stated that his family were “concerned about me”. He believed his work output was a little slower, but he did not think he was making errors of judgement. The psychiatrist noted paucity of thought and language, with accompanying memory and concentration difficulties. The psychiatrist queried early onset dementia, and referred him for neurological and neuropsychological investigations. A CT scan performed at this time was reported to be within normal limits.

Age: 51 years 2 months

He was seen for neuropsychological assessment at age 51. He was accompanied by his sister, who provided answers when Michael was unable to do so. At the neuropsychological assessment he reported that he was “only able to do one thing at a time”, and had difficulty concentrating, following television plots, and stated “I forget everything”. Michael’s sister reported that she had noticed subtle changes perhaps two years previously, with a gradual loss of motivation, and rapid deterioration in his expressive language. Michael’s tennis partners had contacted his sister to express their concern about his increasingly disinhibited behaviour.

Michael denied any worsening of his symptoms, but did not elaborate. He had recently “retired” from work due to inability to cope. He denied being concerned about this. His sister also noted that he now experienced difficulty recognizing friends, and no longer read after being a big reader. She noted that Michael had become increasingly self-absorbed, appeared unable to make decisions, and would try to argue a point, but would immediately forget why he was arguing. She stated that he had become increasingly indifferent to his obvious difficulties.

His verbal fluency was noted to be “severely defective” throughout the assessment. However, he appeared to enjoy the assessment tasks, and followed task instructions eagerly. He persevered on tasks even if he was experiencing difficulty completing a task.

Age: 51 years 8 months.

He was seen for neuropsychological review six months later. He was again accompanied by his sister. At that time his condition had deteriorated markedly. He was very slow completing tasks, and rapidly forgot information. He required constant prompting to complete most tasks. His spontaneous verbal recall was impaired. However, with prompting, he was able to recall some significant points from the stories read to him. He exhibited severe word retrieval difficulties throughout the assessment. Unlike the previous assessment, he was passive and disinterested, and showed no spontaneous actions. His visuospatial skills, although falling well below normal limits on standardised tasks, remained relatively intact in comparison to his verbal skills.

Age: 51 years 10 months

He was seen for neurological assessment two months later, accompanied by his sister. She stated that her brother was rapidly deteriorating, and had become increasingly childlike. He had lost all motivation, and was now totally reliant on friends and family members. He “shadowed” his sister and her husband around, and appeared happy to do this.

He stated cheerfully “my brain is awful”. His sister had met with other family members due to her concern about her brother, and had compiled a list of changes family and friends had noted in her brother’s behaviour over the past two years:

- Frequently crying for no apparent reason.
- Loss of interest in all activities after being previously highly motivated, and actively involved in social and sporting groups.
- Was now “a different person”.
- He was formerly polite and had a sharp sense of humour. He was now usually rude and humourless. Complete loss of interest in friends.
- If friends visit, he usually leaves the room without explanation, without apparent awareness that this behaviour is unusual.
- If questioned about his behaviour he usually stated, “I don’t like people”.
- He was now “self-centred”, after being “a kind and sensitive man”.
- Michael had started eating compulsively, eating any food in front of him, and eating off others’ plates. This was a drastic change in his eating behaviour, as he had previously shown “impeccable manners”.
- Inability to keep still, with increasing pacing and wandering. He had never become lost.
- Slow to respond to any stimulus.
- Rapid deterioration over the previous year.

The neurological examination revealed slowness of mental activity, speech and motor function.

Age: 52 years 1 month.

A family meeting was held with a clinical psychologist and social worker. The family had requested the meeting due to a rapid deterioration in Michael's condition. They reported difficulties managing his behaviours. Michael had developed a range of obsessive and ritualistic behaviours. He constantly swept certain parts of the house, and sorted out rubbish, stating that he knew the right way to do it. He collected specific objects from the house and placed them in a designated spot in the garden. He appeared happy doing this, and if he gave any explanation at all said, "This is my job".

When not engaged in the above activities, he constantly shadowed people he was familiar with. He avoided or was rude to old friends. He made sexually inappropriate remarks and advances. His sexually disinhibited behaviour had resulted in family members being concerned about him being around his grandchildren. His speech output was dramatically reduced. Michael constantly interrupted family members, but appeared confused when he attempted to communicate.

Age: 52 years 4 months.

Michael was assessed at home by the author. His brother was present at the meeting. His brother reported that Michael had continued to deteriorate. He tired easily. If friends came over, he made an effort to play card games with them. He no longer understood the rules of the card games, but enjoyed playing

according to what appeared to be his own idiosyncratic rules. His appetite had continued to increase. If Michael was not constantly monitored he would constantly drink very strong coffee, any alcohol he could find, or soft drinks.

Michael increasingly disliked leaving home, and didn't like to be alone. This placed an enormous strain on his family, as he constantly "shadowed" the person looking after him. If asked if he wanted to do anything, such as going for a walk, or to town, he always stated that he was "sorting things out". By this he meant he was moving certain objects from the house that appeared to have significance to him and placing them in the garden in designated spots, or he swept patches of the floor. He also obsessively polished certain cupboards and appeared to get great satisfaction from washing the dishes. His brother stated that he did a good job of washing the dishes. Michael stated that he didn't like going out because people "talk too much".

Throughout his illness Michael had continued to show an interest in his dress, and always ensured that he was shaved and well dressed. Apart from his interest in his appearance, he had lost all concern about his public presentation. He urinated in public places, and showed no concern or shame. He had become stubborn, and demanded immediate attention. If he wasn't given attention, he became loud and verbally aggressive.

He enjoyed helping in the kitchen, and made simple meals for himself and others, such as cereals and coffee, or toast. Michael constantly paced, and liked

to constantly move objects from one place to another, without apparent reason. His comprehension was extremely limited, and he did not appear aware of others.

Age: 52 years 6 months

Michael was seen by his neurologist with his sister and brother. Michael was given a diagnosis of Frontotemporal Dementia, in line with the test results:

CT: clear symmetrical cortical atrophy of the frontal lobes.

SPECT: Predominant bilateral frontal lobe perfusion abnormality, and most marked posteriorly in keeping with frontal lobe degeneration.

EEG: showed non-specific slowing of the cerebral rhythms in the frontal and temporal regions bilaterally

Michael appeared to be very well physically. He spoke briefly when addressed, but initiated no conversation. With extensive prompting, he stated that he had lost interest in any activities other than drawing, and this does not bother him. His brother and sister reported further deterioration. He was constantly shadowing those he knew well, and became extremely anxious when he was not in their company. Michael showed total loss of interest in all activities except his ritualistic behaviours. He continued to performed tasks such as helping in the kitchen if requested. He showed no distress or unhappiness, and appeared

unaware and/or unconcerned about his lack of interest.

His sister and brother reported that Michael was becoming increasingly irritable and verbally aggressive. He had lost the ability to correctly verbally identify common objects. He was unable to label a ruler, a chair, and a door. His sister stated that he had recently forgotten how to dress properly, and would place his singlet over his shirt. He had begun regular respite care, which he apparently enjoyed. She described him as “worse than a three year old”, and stated that his friends had commented that he had become childlike.

Age: 53 Years 1 month.

Michael was visited at home by a clinical psychologist and social worker. His sister and son were present. He wandered around during the visit, and ate constantly. His son reported that his father enjoyed going out now, and particularly liked going for drives and walks. Michael’s sister stated that he used to enjoy drawing, but had stopped drawing after his drawings had become increasingly childlike. He was often irritable, and verbally aggressive. His appetite had increased “enormously”, and the family had to hide food and drinks from him. He continued to “shadow” family members, and appeared scared when left alone, even for short periods of time. He answered questions appropriately with either “yes” or “no”, but did not use sentences. He continued to move objects from the house and place them in seemingly designated positions in the garden. He also repeatedly polished the same object,

sometimes 10 times in a row. He appeared to enjoy these activities, and became verbally aggressive if interrupted.

Age: 53 Years 4 months

Michael was visited at home by a clinical psychologist and social worker. He was seen with his son and sister. They reported that he was “driving them crazy”, shadowing them around, and requiring constant prompting to complete even the simplest of tasks. His speech had deteriorated further, and his sentences were apparently meaningless. For example “is my car in billiards room”. He also often asked apparently meaningless questions. The family were also experiencing difficulties with what they described as “interruptive behaviours” that he used to gain attention, such as becoming enraged and verbally aggressive.

There had been some incidents of physical aggression, and his sister stated that she had been scared on several occasions. He had started hurling objects at family members and carers when angry. He still enjoyed going for drives with family members, but refused to get out of the car.

He still enjoyed playing games with playing cards, although the “games” had no discernable logic to anyone else. At the time of the visit Michael was well groomed, and “a picture of health”. His sister stated that he still enjoyed being well dressed, but required some assistance to organise his clothing.

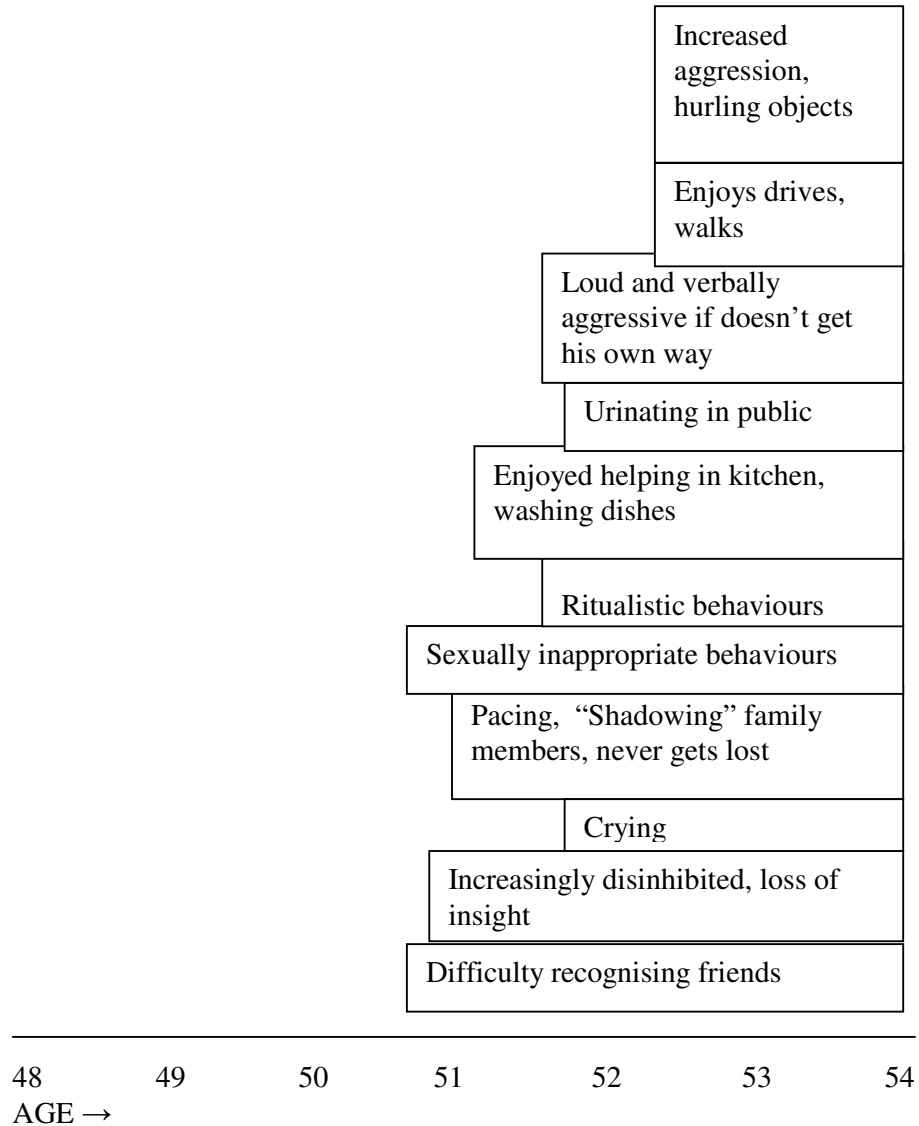
Age: 53 years 6 months

Michael was placed in nursing home due to severe behavioural problems. The nursing home reported difficulties managing his behaviours. He refused to allow staff to wash him, and washed ritualistically with a small amount of water and soap. He wandered constantly, and had lost the ability to recognise all but his closest family members. He refused to believe that his friends were really his friends, but called them “people from overseas”.

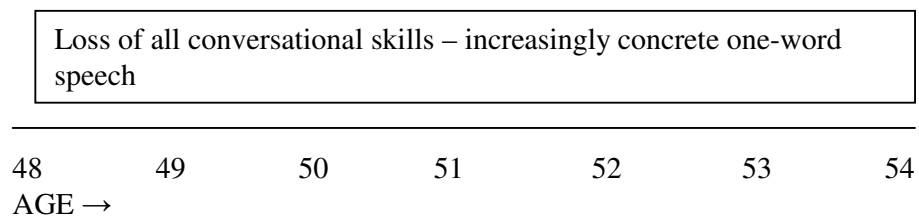
He urinated in his room, and around the nursing home, and did not care if he was in the sight of others. The nursing home also reported that he had damaged computers and kitchen appliances attempting to “fix them”. He continued to enjoy card games and outings. He enjoyed visits from family members, and happily played card games with them.

Michael's Timelines: Each bar indicates the length of time (years) each event occurred.

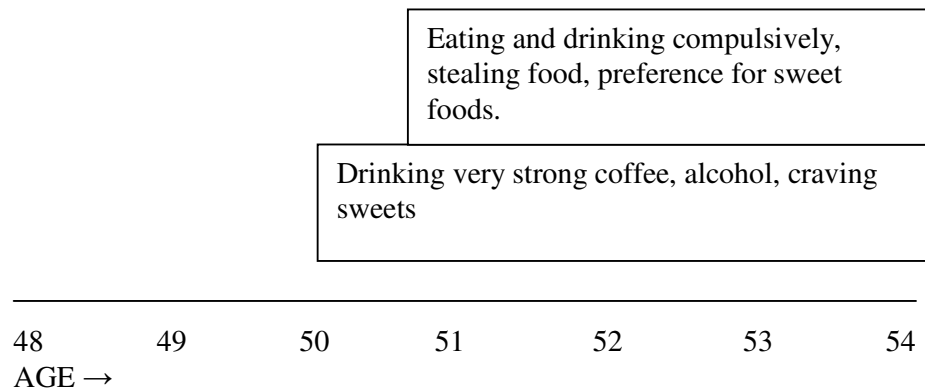
Timeline 1: Behaviours



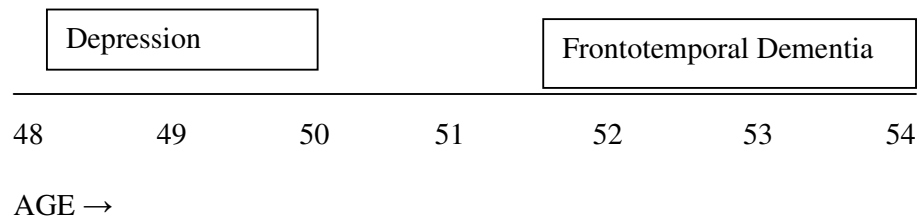
Timeline 2: Speech



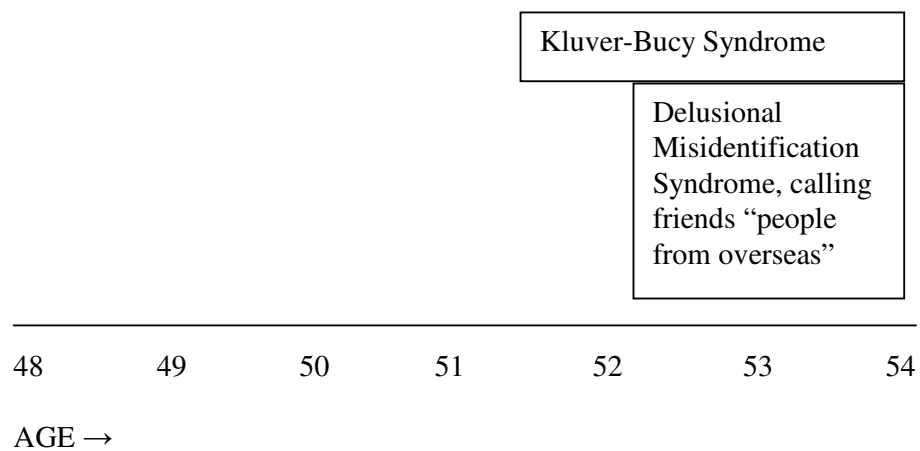
Timeline 3: Eating & Swallowing.



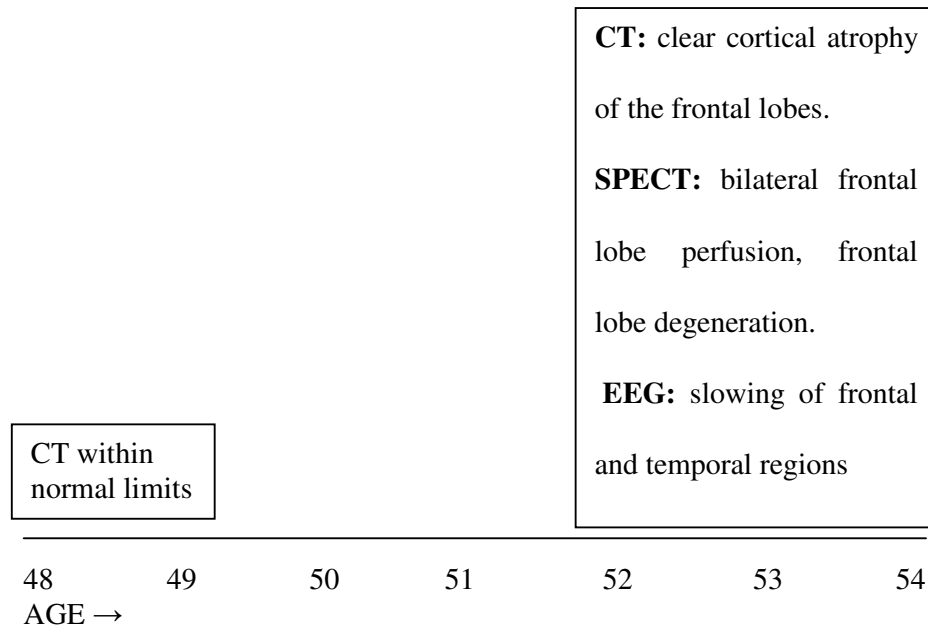
Timeline 4: Changing diagnoses.



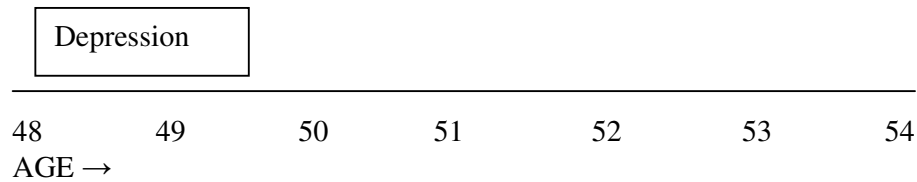
Timeline 5: Syndromes



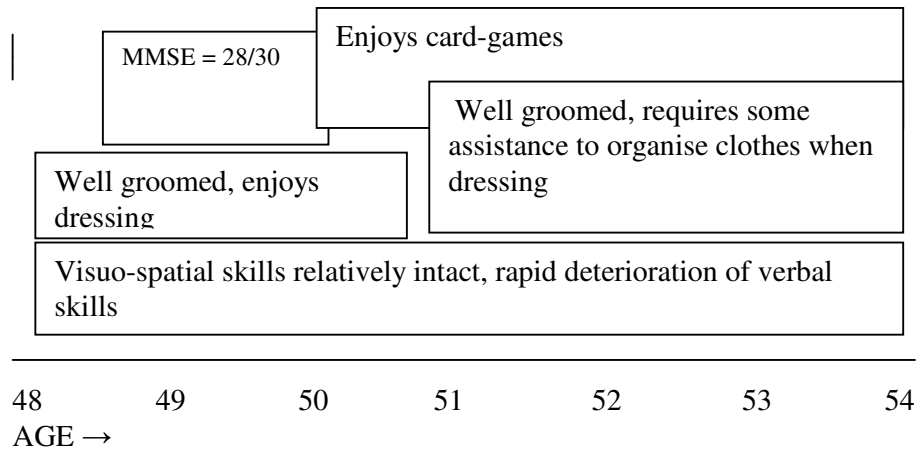
Timeline 6: Imaging results



Timeline 7: Affective conditions



Timeline 8: MMSE, memory & preserved skills.



Timeline 9: Hospital & Residential Services



6.2.3 Frontotemporal Dementia Case Study 3 “Steven”

Age: 48

Steven, a 48 year old tradesman, first presented for assessment at hospital after being arrested for a very minor shoplifting offence. The police had been unable to successfully interview him, and contacted his wife. Shortly after this incident his family contacted his doctor who admitted him to hospital. After being admitted to hospital he showed no interest as to why he had been hospitalised, ate and drank excessively, and did not socialize. Staff reported that he did not appear depressed in hospital and there was no evidence of psychotic symptoms. He slept through the days, becoming active only at night.

Steven’s wife gave a history of progressive memory deterioration over 3 years, with increased emotionality, and increasingly disinhibited socially inappropriate behaviours. Family members reported no history of depression or psychiatric illness. On the contrary, family and friends indicated he had previously been a well-balanced, active member of the community, with excellent social skills. His wife reported increasing memory lapses and incidents where he would forget social and work engagements.

Two years before presenting at the hospital she reported a marked increase in her husband’s level of anxiety, and incidents when he would cry for no obvious reason. He was seen by a psychiatrist at this time. Steven was diagnosed with depression and prescribed antidepressants. There was no noticeable change in his mood or memory associated with the medication. He was subsequently

referred to a neurologist who suggested his problems were of psychiatric or psychological origin.

His family and friends noticed increasing incidents of rudeness and lack of motivation. He stopped playing sport, and stopped reading. He had been a heavy smoker, but had virtually stopped smoking. He had become increasingly impulsive, spontaneously flying interstate, and walked aimlessly for long distances. He did not get lost at any time. He scratched his genitals in company, and appeared to enjoy burping and farting in public.

Six months before initially presenting at the hospital, family members and friends reported a marked deterioration in Steven's overall level of functioning. He had increasingly gone for long walks without explanation, and paced aimlessly around the house. His sleep pattern had become erratic, and he sometimes went into town in the middle of the night. Incidents of unusual behaviour increased, with friends reporting that he had visited them and had not talked to them. He reported increased headaches at this time.

Over the six months before presenting at hospital, Steven's eating habits had completely changed. Previously he had been conscious of his diet, and ate healthy foods. He now compulsively ate any food he could find, and particularly sought out sweet foods. He had rapidly gained weight. Friends reported that he had "become childlike". His memory had continued to deteriorate, and he now was rarely able to remember friends' names. He often said he missed his mother, and became scared when left alone. His wife stated that he was always anxious unless he was by her side.

Shortly before his admission to hospital his wife took him to see his psychiatrist. He reported to the psychiatrist that he had “seen things”, including seeing a headless man with a long neck and holes for eyes and nose and mouth. He did not realise that this was illogical. He had told his wife that his friends were “doubles” of people he knew (this is a classic Delusional Misidentification Syndrome, as first described by Pick, 1903). The psychiatrist reported a strong compulsive element in his behaviours accompanied by memory deficits.

While in hospital he was given a comprehensive neurological work-up:

MMSE = 28/30

CT of cranium: - Slight prominence of the anterior and temporal horns of the lateral ventricles bilaterally and also the 3rd ventricle.

Conclusion: Possible early atrophy.

EEG: Grossly abnormal with poorly organised activity. Diffuse slowing dominated by theta waves. Short dysrhythmic bursts with sharply contoured potentials in the frontal and temporal regions.

Short dysrhythmic bursts are commonly found in patients with delusional misidentification syndromes (Chistodoulou & Malliara-Loulakaki, 1981).

Previous CT and EEG scans completed twelve months previously were reported to have been normal.

He was given a neuropsychological assessment shortly after admission to hospital. He was superficially cheerful and compliant throughout the assessment. He showed no curiosity as to why he was being assessed, and

asked no questions. He denied any problems, and said he was “good”. There was little spontaneous speech. He needed continual breaks during the assessment.

He denied any symptoms of depression. He picked up a range of non-test materials during the assessment, including the psychologist’s diary. He looked through without permission, and appeared unaware that his behaviour was unusual. At times he stood up and walked around the office touching and examining various objects.

He was seen for neuropsychological review three months later. He was again cooperative, superficially cheerful, with a bland facial expression. He was restless and fidgeted throughout the assessment. He denied any problems, and was unaware of test failure. He compulsively picked up test materials and wandered around the room, examining objects. The clinical psychologist thought a psychiatric diagnosis was the most likely cause of his behaviour.

Further imaging studies were conducted three months after his admission to hospital:

MRI: - frontotemporal atrophy, pronounced symmetrical temporal lobe and inferior frontal lobe atrophy, and anterior basal ganglia atrophy.

CT: - Mild frontal lobe atrophy, and pronounced relatively symmetrical temporal and inferior basal ganglia atrophy. The degree of atrophy was found to be unusually severe for his age.

SPECT: - unequivocal frontal lobe hypoperfusion. He was extremely agitated before the study, which showed symmetrical hypoperfusion in both frontal lobes plus mesial portion of right temporal lobe.

Conclusion: Results typical of frontotemporal dementia.

MMSE = 25

Electron microscopy:

- The axons showed wrinkling, - an axonopathy.
- Mitochondrial paracrystalline inclusions.
- Chronic denervation with reinnervation
- Chronic neuropathy

After the neurological work-up he was given the diagnosis of Frontotemporal Dementia by the hospital neurologist.

Three months after his admission to hospital, staff reported increasing swallowing problems, and coughing during fluid intake. His self-care had

deteriorated markedly. He now dribbled when drinking, and appeared unaware when he had spilled food or drink on himself, and made no attempt to clean himself up.

Steven was seen for neuropsychological review 12 months after his initial hospitalisation. He was slightly agitated during assessment, and showed no insight. He did not speak unless prompted, and then only gave occasional one or two word answers. He was perseverative and impulsive during the assessment. He drew the same design three times, and continually attempted to read the psychologist's notes, despite being asked not to.

Age: 48 years 7 months

Approximately five months after admission to hospital he had begun exposing himself. This behaviour was noted to be associated with increasingly disinhibited groping of staff. He was medicated with Depo Provera, Thioridazine, and Clonazepam. No improvement was noted in his behaviour.

Age: 49 years 6 months

Steven was seen by his neurologist 16 months after first being hospitalised. He was unable to describe his problems, answered questions with short phrases such as "being here", "the other day", "not particularly interested". Steven told the neurologist that he fed animals when asked what he did. When prompted

repeatedly he replied “particularly birds”. He was unable to give any details of his history. He was unable to give his own name.

Nursing staff had reported that Steven was often found crying, but was unable to give reasons for his sadness, except to say, “need to be held”. He often cried when listening to music. He increasingly liked to hold on to, and cuddle people. He also cuddled a range of objects, including pillows and blankets. He sometimes “howled” for up to ten minutes, and was unable to tell staff why he was upset, or even if he was upset.

His gait had become unsteady, and he had developed a range of unusual movements, and performed rapid alternating movements with his legs. He had become doubly incontinent and required assistance with all activities of daily living. His days were spent watching television, and he often turned the volume up excessively.

Steven’s weight had continued to increase, and he had become clinically obese. Hospital staff reported that he “guzzled food and drink” without chewing. He attempted to eat large pieces of food without chewing them, including whole biscuits. He had started eating off his plate without using his hands. His eating and drinking had recently been assessed by a speech pathologist, and he was placed on a soft diet due to incidents of choking. His eating was noted to improve if he was given constant prompts to chew his food, but regressed to his

“gulping” food down and coughing as soon as the prompts ceased. He was diagnosed with Frontotemporal Dementia with Motor Neurone Disease (FTD/MND).

Age: 49 years 8 months

Approximately 18 months after his hospital admission his medication was changed by a psychiatrist:

Anti depressant — Sertraline 50 mg per day

Anti psychotic — thioridazine 500 mg per day

No improvement was noted in his behaviour.

Staff reported that he had continued to deteriorate. He urinated anywhere, sometimes on the floor. His rate of urination increased. He began to exhibit increasingly sexually inappropriate behaviours, including exposing himself to staff and visitors, and touching female staff on their breasts and buttocks. He also showed sexual interest in visitors’ pets.

He appeared briefly pleased if family or friends visited, but would go back to watching television after a few minutes. He frequently wandered, randomly turning on and off of any switches he could find. The hospital attempted to place him in a nursing home. This failed due to inappropriate behaviour, including public masturbation and “bear hugging” women.

Age: 49 years 10 months

Approximately 20 months after admission to hospital he developed diabetes mellitus. He now rarely cried, and spent most of his time watching children's television, which he watched for hours at a time, and appeared to enjoy. He actively avoided washing or showering. He began to make numerous loud animal-like noises, and frequently touched objects that he appeared to find visually appealing. Staff stated that he had settled well, and despite his unusual behaviours, appeared to enjoy the hospital routine, and had become easier to manage.

Age: 50 years

Two years after his admission to hospital he was placed in a nursing home. He continued to grope female staff if he had the opportunity, and often masturbated in public. He continued to enjoy watching children's television programs.

Age: 50 years 3 months

Twenty-seven months after his admission to hospital he continued to deteriorate. He continued to crave sweets, and ate and drank compulsively. He had started stealing food from other residents' rooms, and from their plates in the dining room. His favourite things to steal were sweets and biscuits. He cried frequently, and repeated numbers out loud.

His movement disorder worsened, and he now exhibited marked tremor, and

was “wobbly” on his legs. He was able to answer concrete questions that required only one-word answers accurately. For example, if he was asked what he had eaten for breakfast he was able to respond “toast” or “cereal”. He had lost the ability to brush his teeth, and required extensive prompting for all daily activities. Staff in the nursing home found his behaviour increasingly difficult to manage, and complained that they were not sufficiently resourced to manage someone with his complex behavioural and medical problems. The staff stated that he required one-to-one male 24 hour supervision, but they were unable to supply this. He paced around the nursing home constantly and other residents complained about his behaviour. He constantly attempted to fondle female staff and pinch their bottoms.

Steven remained oriented to his immediate environment, and despite his constant pacing and wandering, did not get lost. His daily activities consisted of pacing around or watching children’s programs on television. He enjoyed colouring in children’s colouring books, and would spend long periods of time colouring in. He enjoyed praise for his work. He was still able to play dominoes, and enjoyed counting the small sums of money he was given. He regularly looked through the daily paper, and especially enjoyed looking at the car and travel sections. He was able to communicate through writing better than through speech, which had continued to deteriorate. He enjoyed being well groomed, and appeared pleased when others commented on his appearance. If given one-to-one attention, he was compliant, and was capable of remaining on task for up to two hours if being assessed by an occupational therapist or speech

pathologist. His limited speech consisted of perseverative, syntactically correct, one or two word utterances.

Age: 50 years 6 months

Two and a half years after his initial hospitalisation his condition continued to worsen. He wrote long letters, composed of the same line repeated over and over. He was reviewed by his neurologist who noted a further reduction in speech output. He continued to grope females, and had begun smearing his excreta on walls. He enjoyed farting and blowing bubbles throughout the assessment.

Despite his deterioration, he continued to enjoy family visits, and board games. He enjoyed going for drives with family members, and exhibited no behavioural problems at these times.

Age: 50 years 10 months

He was assessed by the neurologist and the author. He was difficult to assess. He responded to questions by looking briefly at the neurologist, and making brief grunts. He showed no sign of distress, and repeatedly wandered out of the room. On one occasion he took himself to the toilet and returned without assistance. He ate biscuits continually, played with his genitals, and smelled his fingers. He did not use any discernible words throughout the assessment.

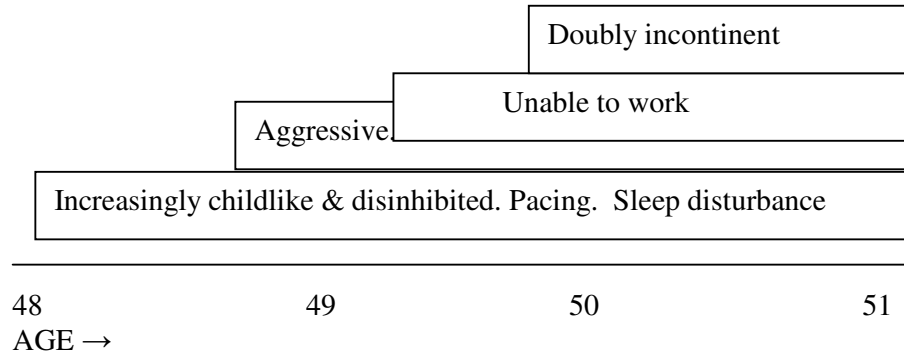
Staff at the nursing home reported that they were increasingly alarmed by his behaviours, and felt that he was a risk to himself and others. He was placed on a

combination of Clonazepam, Thioridazine, and Cyproterone. Staff reported that the medication did not change his behaviour. Shortly after the introduction of the above medication he became more aggressive, and began pushing residents and staff. There were insufficient staff to implement behavioural interventions, and no staff with psychiatric nursing experience.

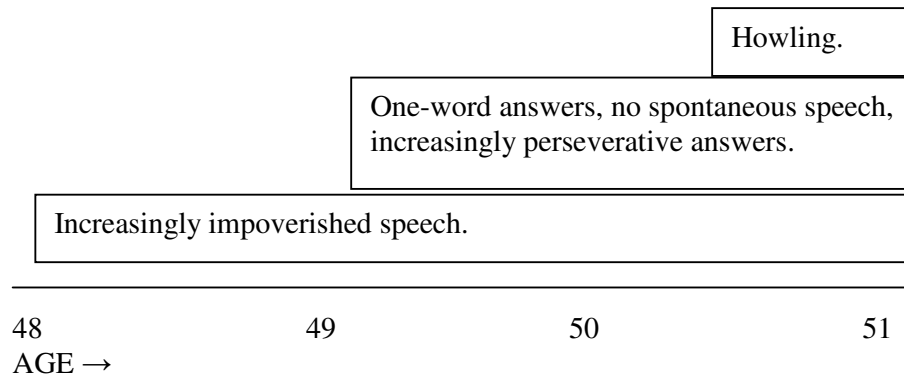
Staff at the nursing home reported that Steven was spending much of his time sleeping with brief periods of hyperactivity. During his hyperactive periods he grabbed the breasts of staff and patients, and howled. He was medicated with Olanzapine. He died in his sleep 3 weeks later.

Steven's Timelines: Each bar indicates the length of time (years) each event occurred.

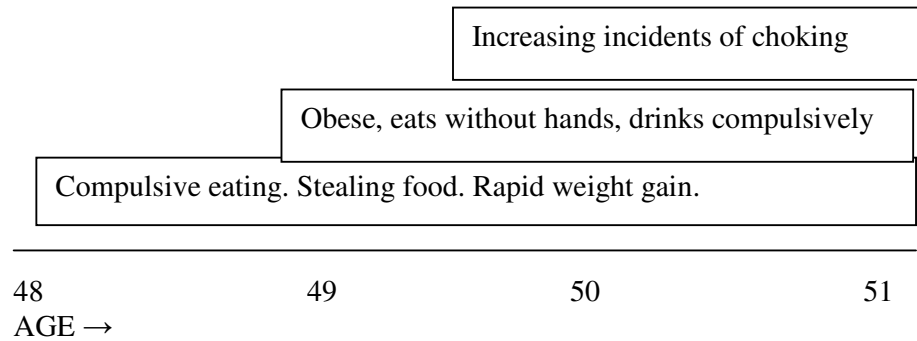
Timeline 1: Behaviours



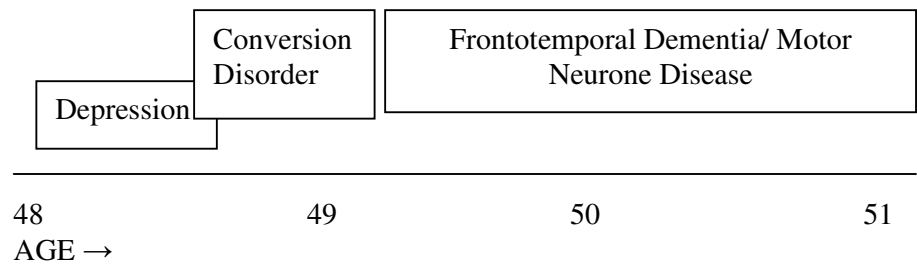
Timeline 2: Speech



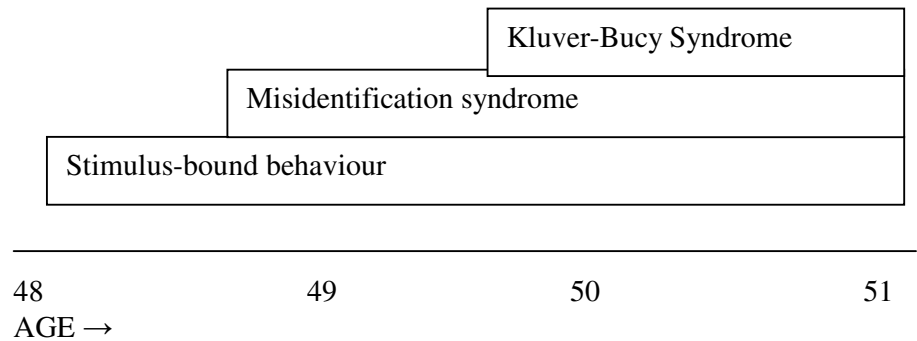
Timeline 3: Eating & Swallowing.



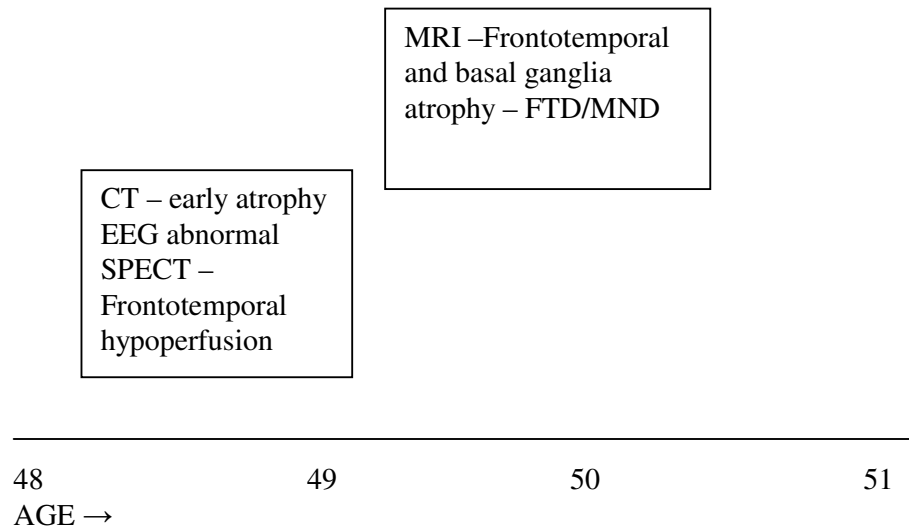
Timeline 4: Changing diagnoses.



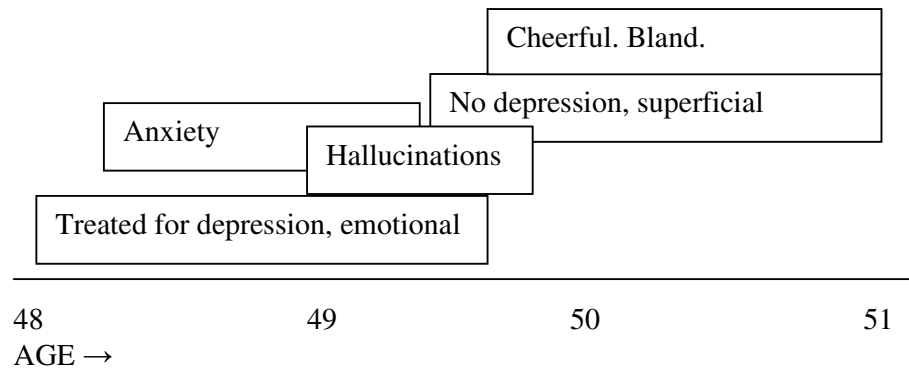
Timeline 5: Syndromes



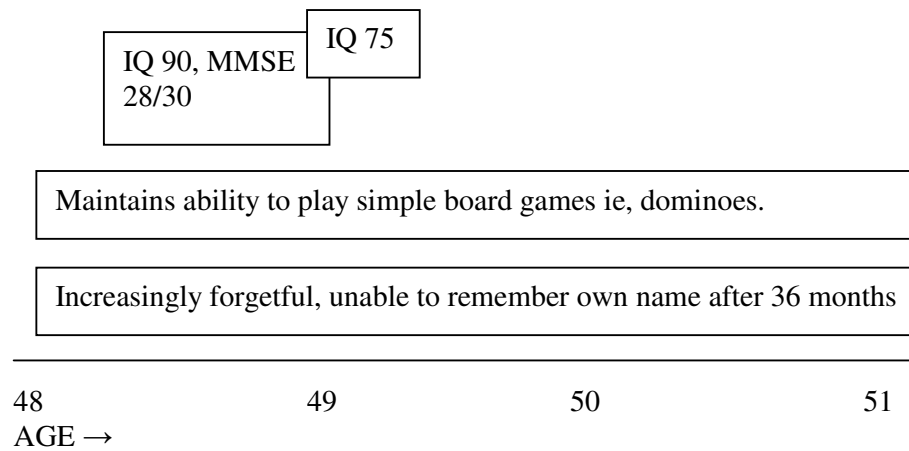
Timeline 6: Imaging results



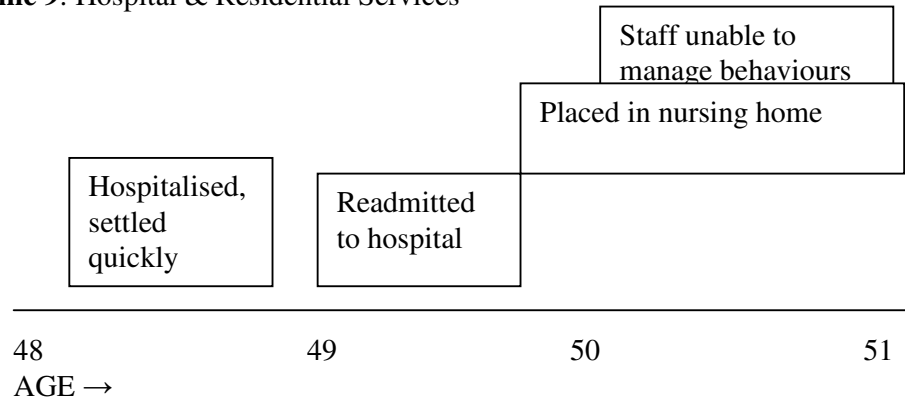
Timeline 7: Affective conditions



Timeline 8: IQ, memory & preserved skills.



Timeline 9: Hospital & Residential Services



6.2.4 Frontotemporal Dementia Case Study: “Julie” age 46

Age: 46 Years 5 months

“Julie”

Julie was initially referred to the hospital neurologist by her doctor who suspected dementia. She was initially seen with her husband who stated that her speech was “very poor”. Julie was cheerful during the interview, and denied any problems. Her husband stated that her memory had deteriorated rapidly over the past 18 months. She had become “stressed” at work, and had to stop working. She now required assistance to perform simple tasks, such as shopping, something she had previously loved doing alone. Her husband also noted some behavioural changes, such as walking around in the daytime in her underwear, something she previously would never do. He stated that his wife was generally happy, and had not noticed any major behavioural problems.

The results of the neurological investigations revealed a range of deficits:

CT: - shows some atrophy, no acute lesion.

SPECT: – symmetrical reduced perfusion to the frontal and temporal lobes

EEG: – Abnormal, slowing of the central rhythms as a result of structural abnormality or encephalopathy.

MRI: - Cortical atrophy present, particularly was affecting the frontal lobes.

Diagnosis: Frontotemporal Dementia/Parkinsonism

Age: 46 years 6 months.

Julie was seen for neurological assessment accompanied by her husband. He stated that her memory had continued to deteriorate, and that she had forgotten well-known prayers. She had difficulty naming objects, and recalling names of friends. He noted that her “personality had completely changed”. Julie had previously been outgoing and sociable, “a very confident person”. She was now withdrawn and uncertain, and completely dependent on her family. She was often tearful and anxious, and had frequent panic attacks, especially if taken out of her home. She frequently repeated herself during the assessment. Her speech was impoverished. Julie described herself as “very unhappy”.

The neuropsychological assessment was conducted over two days due to Julie’s slowness. She was easily distractible, had difficulties understanding the test instructions, and exhibited impaired memory. For example, she could not recall any details of the previous day. She was constantly distracted by objects in the room, and commented frequently on objects outside the window.

Age: 46 years 7 months

Julie was assessed by a speech pathologist. She was able to independently generate and employ a range of highly effective strategies to assist word retrieval and memory. However, she performed poorly on many tests sensitive to mild dementia. Julie reported that she had been prescribed an SSRI

antidepressant, and was now sleeping better, and was feeling less “panicky”.

She showed some insight into the fact that her memory was failing.

Age: 46 years 8 months.

Julie was seen for neurological review. She complained of discomfort and aching in the top of her head, neck, chest, and limbs, and stated that sometimes she felt that her “head is going to blow up”.

Age: 46 Years 11 months

Julie was seen for neurological review. Her illness had progressed. Speech production was further reduced. She had developed significant tremors, more marked in the right upper limbs. She exhibited a resting tremor in her right hand. She complained of burning feet. She also exhibited jerks in her arms and legs.

These were described by the neurologist as “extra pyramidal features associated with Frontotemporal Dementia”. Her husband reported that Julie complained of “bad smells”, olfactory sensations of manure, sometimes overpowering. The neurologist suspected the smells were the result of olfactory seizures. Her husband stated that the “smells” occurred at the same time as her panic attacks. She often complained of feeling “cold and shaky”. Olfactory seizures are associated with progressive atrophy of the hippocampus and medial temporal lobe (Fried & Spencer et al. 1995; Pikkarainen & Pitkanen, 2001).

Age: 47 years 4 months

Julie was seen for her routine neurological review. The neurologist noted that she was more relaxed than at previous consultations. Her episodic memory, linguistic expression, and linguistic comprehension were all impaired. Her visuospatial construction skills remained within normal limits. Julie's Parkinsonism had become more profound, with her tremor now more exaggerated. She now experienced difficulty dressing. She complained of worsening depression and agoraphobia. Her husband reported increased episodes of crying. He also stated that she now had difficulty reading and writing, and was tearful at night, often waking from "bad dreams". She had lost her sex drive.

Julie had continued to experience panic attacks preceded by olfactory hallucinations. Her husband stated that the onset of these incidents were sudden, and their cessation swift. He reported these episodes occurred approximately twice per week.

Age: 47 years 11 months

Julie was visited at home by the author. She was fearful, and had only spoken when prompted. Her husband stated that she was scared when left alone. She had been attending respite care, and appeared to enjoy this. Her husband stated that Julie's memory had continued to deteriorate. She could no longer read or write, forgot people's names, and was unable to follow conversations.

Age: 48 years 6 months

Julie was seen by a speech pathologist. Julie spoke in slow, halting utterances, with frequent semantic errors. She was able to accurately copy a geometric design. All other assessment tasks were impaired. She was experiencing increasing swallowing difficulties, and was placed on a soft diet.

Age: 48 years 8 months.

Julie was assessed as requiring “high level hostel care”, and placed in permanent care.

Age: 49 years

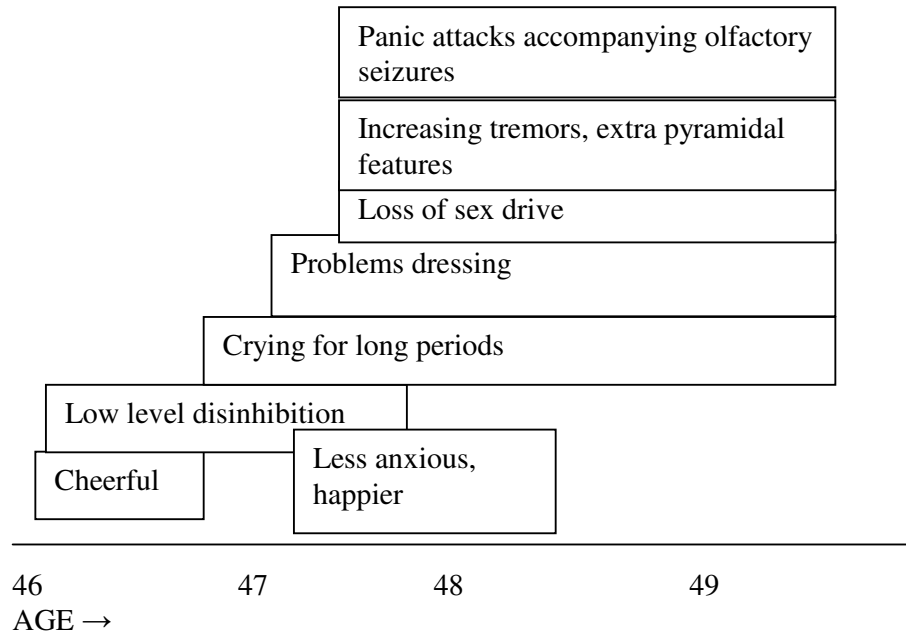
Staff at the nursing home reported that Julie was deteriorating rapidly, and had developed generalized tonic clonic seizures.

Age: 49 years 2 months.

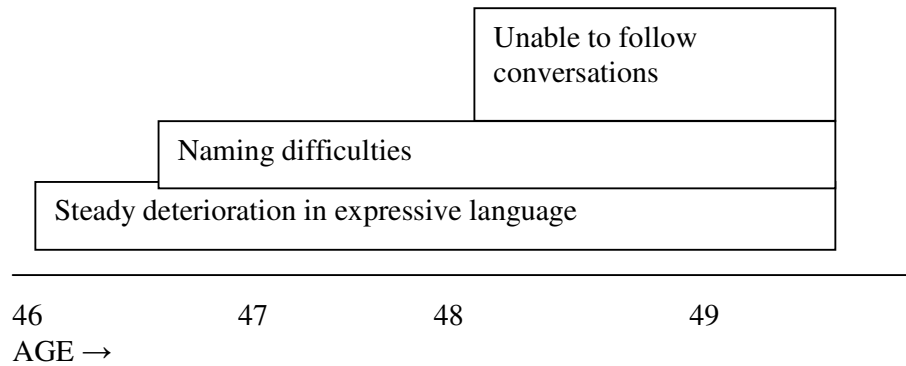
Julie died in the nursing hostel. Staff reported seizures continued until her death.

Julie's Timelines: Each bar indicates the length of time (years) each event occurred.

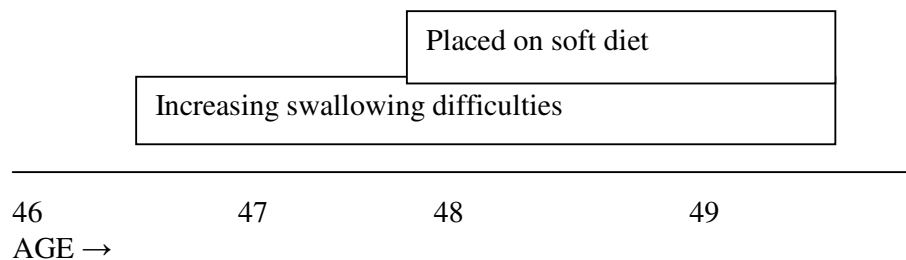
Timeline 1: Behaviours



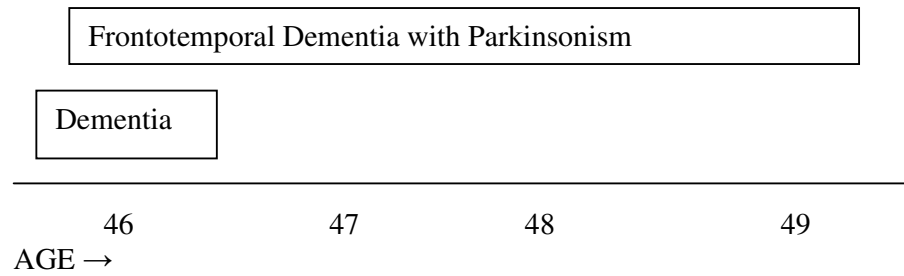
Timeline 2: Speech



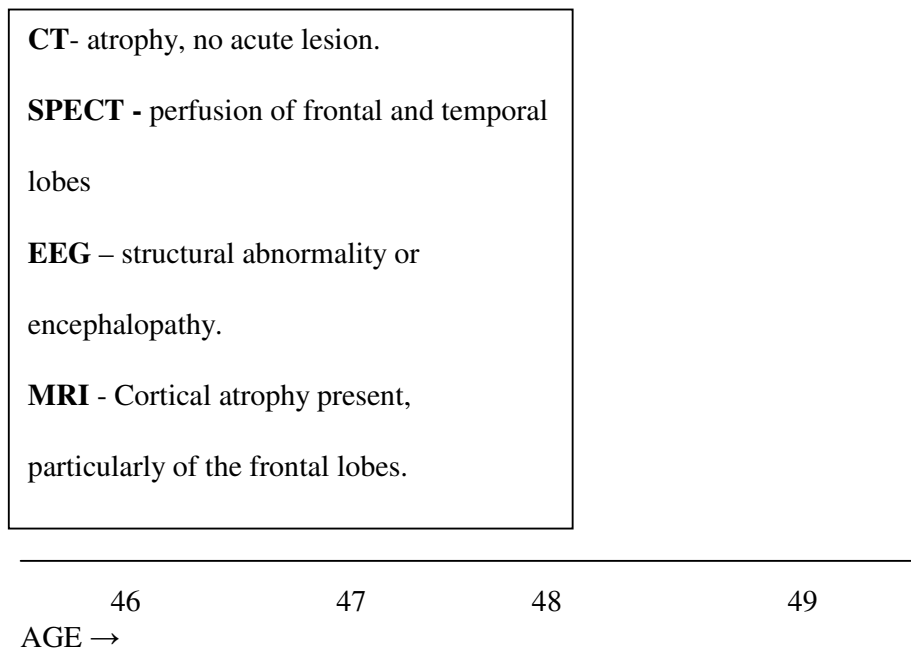
Timeline 3: Eating & Swallowing.



Timeline 4: Diagnosis.

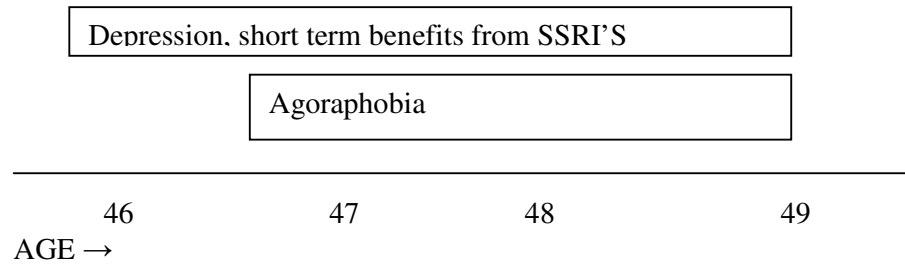


Timeline 5: Imaging results

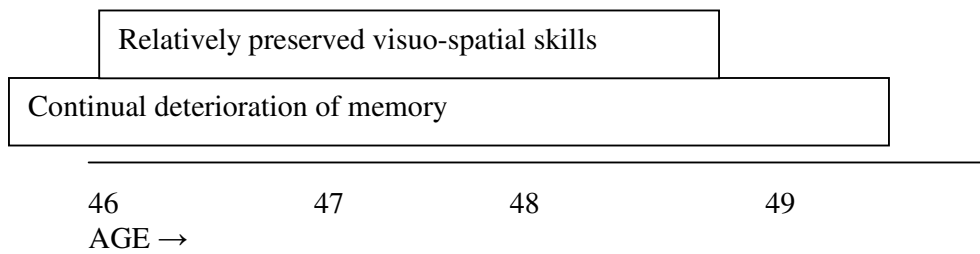


Diagnosis: Frontotemporal Dementia/Parkinsonism

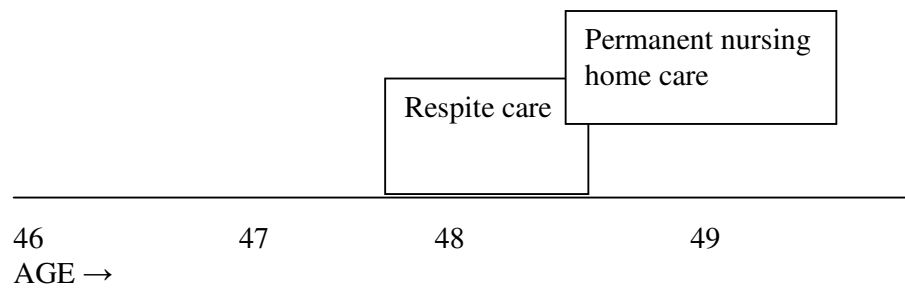
Timeline 6: Affective conditions



Timeline 8: Memory & preserved skills.



Timeline 9: Hospital & Residential Services



CHAPTER 7

CONCLUSIONS AND IMPLICATIONS OF

THE STUDY FOR THE CARE OF PATIENTS

WITH EARLY-ONSET DEMENTIA

“It is our responsibility to treat patients and teach others to care for patients in the least restrictive environment possible, while maintaining a choice of options, promoting optimal functioning, and fostering independence in the patient”

Richards, 1990

7.1 CONCLUSIONS

7.1.1 Study Objectives

- This evaluation of Frontotemporal Dementia found that this relatively new diagnostic category is valid and useful, and can be reliably differentiated from Alzheimer’s Disease.
- Behavioural, neurological, and neuropsychological assessment were found to be important in the early and accurate diagnosis of early-onset dementia.

- This study provides practical information to care-providers regarding the needs of people who receive a diagnosis of early-onset dementia.

7.1.2 Hypotheses

1. This study found that the clinical criteria developed by Neary & Snowden et al. (1998) differentially diagnosed early-onset Frontotemporal Dementia patients from early-onset Alzheimer's Disease patients.
2. The analysis of this group of patients provides information that can assist in the formulation of care and treatment plans for patients with differing forms of early-onset dementia.
3. This study found that the Frontotemporal Dementia patient group had significantly increased behavioural disturbances throughout the course of the illness in comparison with Alzheimer's Disease patient group. Evaluation of behavioural profiles assisted with the differential diagnosis of Frontotemporal Dementia patients from Alzheimer's Disease patients, supporting previous research (Levy & Miller et al. 1996; Duara & Barker et al. 1999; Pasquier 1999; Tanabe & Ikeda et al. 1999; Cummings & McPherson, 2001; Kertesz & Davidson et al. 2003; Mourik & Rosso et al. 2004; Engelborghs & Maertens et al. 2005; Thompson & Stopford et al. 2005).

4. This study found that Frontotemporal Dementia and Alzheimer's Disease patients showed significant differences on visuospatial neuropsychological tests. The Frontotemporal Dementia patients had relatively preserved visuo-spatial abilities compared to Alzheimer's Disease patients, supporting previous research (Elfgren & Passant et al. 1993; Stuss, 1993; Gregory & Orrell et al. 1997; Duara & Barker et al. 1999; Pasquier, 1999; Ikeda & Tanabe, 2000; Storey & Slavin et al. 2002; Kramer & Jurik et al. 2003; Harciarek Jodzio, 2005).

5. This study found that the course of the illnesses differed significantly between the early-onset Frontotemporal Dementia and Alzheimer's Disease groups. Frontotemporal Dementia patients experienced rapid progression of disease symptoms, with all but one of the Alzheimer's Disease patients showing a more gradual deterioration. These findings are consistent with previous research (Barber, Snowden & Caufurd, 1995; Pasquier & Richard et al. 2004; Kertesz & McMonagle et al. 2005; Roberson & Hesse et al. 2005; Pasquier & Lebert et al. 2005).

7.2 CARE OF PATIENTS WITH EARLY ONSET DEMENTIA

This research has shown that over a 3-year time period Frontotemporal Dementia patients' care needs are more complex and difficult to manage than that of all but a few Alzheimer's Disease patients. Care programs need to be capable of adapting to the patients' (and families') rapidly changing requirements.

This study found that families, health service providers, and residential care facilities were commonly overwhelmed by the ever-changing needs of some early-onset Alzheimer's Disease patients, and nearly all the Frontotemporal Dementia patients. The rapid onset of complex behavioural problems, often combined with marked physical decline, posed significant challenges to all those involved in the care of this often overlooked group of dementia sufferers. These findings support previous research which has highlighted the difficulty in caring for patients with early-onset dementia (Harvey, 1998; Tanabe, Ikeda, & Komori, 1999; Tune & Bowie, 2000; Mourik & Rossi et al. 2004; Passant & Elfgren et al. 2005; Chapman & Williams et al. 2006; Yokota & Fujisawa et al. 2006).

A major obstacle to the provision of quality services for this group has been that generic dementia services have been designed to cater for patients fitting the traditional profile of Alzheimer's Disease. These services work with the underlying assumption that there will be adequate time to tailor services, and that there will be suitable accommodation options. Generic services also assume

that patients fall into the broad framework of Alzheimer's Disease (Harvey, 1998). Common assumptions are that patients have relatively preserved social skills, impaired memory, impaired visuospatial functioning, and decline slowly. The results of this study support previous research (e.g. Neary, Snowden, & Mann, 2005; Passant & Elfgren et al. 2005) which has found that Frontotemporal Dementia patients do not fall into this framework. Frontotemporal Dementia patients have relatively preserved visuo-spatial skills, decline rapidly, exhibit extremely challenging behaviours, and undergo a rapid change of personality (Chapman & Williams et al. 2006; Roberson & Hesse et al. 2006).

This research indicates that for most Frontotemporal Dementia patients and some early-onset Alzheimer's Disease patients the generic model of dementia care does not adequately meet the needs of patients and their families.

7.3 SUGGESTIONS FOR THE IMPROVEMENT OF SERVICES FOR EARLY ONSET DEMENTIA

7.3.1 Rapid Service Response

Due to the rapid onset of Frontotemporal Dementia, and the high level care and respite requirements early in the course of the illness, special funding should be allocated to patients immediately a diagnosis of Frontotemporal Dementia is given. Most current dementia services are funded for the over 65 age group. This mode of funding has resulted in early-onset dementia patients being inappropriately hospitalised in psychiatric units and nursing homes.

The current services, although providing much needed relief for families, are often seen as degrading by families and the patients. This research indicates that Frontotemporal Dementia patients often require 24-hour supervision early in the course of their illness. If this supervision was implemented with specialist back-up, many of the behavioural problems outlined above may be minimised, and the quality of life for patients and their families greatly increased (see below for details).

7.3.2 Nursing Homes and Hospitals

Staff in nursing homes are often untrained in the management of severe behavioural problems such as those exhibited by many of the Frontotemporal Dementia patients in this study. This lack of training inevitably leads to behavioural disturbances that could be avoided if an adequately resourced management plan was in place. Several recent studies have shown that modification of the nursing home or hospital environment can significantly improve the quality of life for patients with Frontotemporal Dementia (e.g. Robinson, 2001; Testad & Aasland et al. 2005; Yokota & Fujisawa et al. 2006).

7.3.3 Palliative Care

This study produced results consistent with previous research which has shown that patients diagnosed with Frontotemporal Dementia frequently die 2-3 years after diagnosis (Pasquier & Richard et al. 2004; Roberson & Hesse, 2005).

These findings have important implications for the care of this population.

Frontotemporal Dementia patients deteriorate rapidly, experiencing severe behavioural changes accompanied by increasing medical problems such as gait disturbance and swallowing difficulties. In the context of crisis responses to challenging behaviours, palliative care issues can easily be overlooked.

Providing palliative care for this group of patients requires significant skills and resources. The provision of quality palliative care services may assist families through their grief processes, and allow patients to feel secure during their last days. All the Frontotemporal Dementia patients in this study remained aware of their immediate environment, and continued to recognise and respond positively to family members. This preserved orientation to environment holds open the opportunity to provide a pleasant environment that patients can enjoy, and a peaceful space for family members to spend their last hours with their loved ones.

Although behavioural problems can persist to the end of the illness, the episodes of problematic behaviours described in this study were generally of short duration, and patients continued to enjoy activities such as playing cards and drives with relatives. If the focus of care is solely on behavioural and medical management, rich opportunities for enhancing not only the early stages but also the last stages of life can be lost.

There is currently no published research on the provision of palliative care to

Frontotemporal Dementia patients. This is an important area for future research, not only in assisting the dying, but also for their families. Due to the strong hereditary component of the condition it is important that family members see that their loved ones are cared for in the best possible way. Families caring for relatives who have a long family history of Frontotemporal Dementia know that they may develop the illness. Seeing that relatives are well cared for may reduce their anxiety about their own future.

7.3.4 Behavioural Care

This study found high levels of ritualistic and environmentally dependent behaviours in the Frontotemporal Dementia patients, and a complete absence of these behaviours in the Alzheimer's Disease patients. This finding suggests that behavioural care strategies for the two groups of patients may need to be significantly different. Recent research has shown that individualised behavioural care programs can successfully improve the quality of life for dementia patients who display challenging behaviours (e.g. Moniz-Cook & Woods et al. 2001).

Using Preserved Skills

Utilising the preserved skills of Alzheimer's Disease patients has successfully been used to enhance their quality of life. For example, patients are encouraged to recall pleasant memories from their past (e.g. Rentz, 1995; Cotelli & Calabria et al. 2006; Yokoto & Fujisawa et al. 2006). A similar strengths-based approach

shows promise with Frontotemporal Dementia patients. Several researchers (Ikeda & Tanabe et al. 1995; Tanabe & Ikeda et al. 1999; Robinson, 2001) have successfully used the preserved skills associated with Frontotemporal Dementia to enhance the quality of patient care.

Recommendations

Assess all Frontotemporal Dementia patients' histories to find out non-verbal procedures that the patients carried out before developing their illnesses. This information can provide a rich source of information for structuring care plans. Utilising activities that the patients are familiar with may assist with creating least-restrictive environments and reduce behavioural problems.

7.3.5 Promising New Therapies

Routinizing Therapy

One new therapy that has shown promise for use with Frontotemporal Dementia patients has been developed by Tanabe, Ikeda and colleagues (Ikeda & Tanabe et al. 1995; Tanabe & Ikeda et al. 1999). These researchers have outlined a form of behavioural care which they have labelled "routinizing therapy". Routinizing therapy uses patients' environmental dependency syndrome and stereotypical behaviours (see table 43 above) to improve their quality of life, and to reduce the burden on caregivers. They present 5 case studies where patients with previously unmanageable behaviours were encouraged to perform visuospatial tasks they had performed frequently before they became affected by

Frontotemporal Dementia. The tasks used included knitting, board games, and assisting nurses to measure blood pressure. All these tasks were procedures that the patients had performed routinely before they developed Frontotemporal Dementia. For example, the patient who assisted the nurses measuring blood pressure had been a doctor. Although this patient had been difficult to manage, once assigned a task that he was familiar with, his behavioural problems rapidly decreased.

In the current study many of the Frontotemporal Dementia patients exhibited similarly preserved procedural memory, and enjoyed outings, board games, television and sometimes performing ritualistic behaviours throughout the course of their illness (see Chapter 6 above).

Harnessing environmental dependency and preserved visuo-spatial skills.

If adequate resources are available to implement behavioural management programs Frontotemporal Dementia patients can be engaged in a range of activities such as going for drives, playing card and board games, walking, playing pool, and gardening. Focusing on such positive activities can provide patients with opportunities to engage in behaviours that are enjoyable, and divert them away from engaging in socially inappropriate behaviours.

Recommendations

Given these findings, future applied research could explore the efficacy of utilising visuospatial tasks to enhance the quality of life for Frontotemporal Dementia patients.

7.3.6 Flexible Care Plans

A major issue in the behavioural management of early-onset Frontotemporal Dementia patients and some early-onset Alzheimer's Disease patients is the rapid deterioration in their functioning. If behavioural care programs are to have any chance of success they need to be constantly updated to meet the changing needs of the patients. For example, in the early stages of the illness a walking partner may be suitable. As the patient deteriorates, drives or walks in a wheelchair may be appropriate.

7.3.7 Ethical Issues – Creating “Least Restrictive Environments”

Early-onset dementia patients, regardless of their diagnosis, deserve to be cared for in the least restrictive environment possible. That is, in an environment that is as close to home-like as possible, and maximizes independence and functioning.

Providing “appropriate” services to young Frontotemporal Dementia patients is an ethically difficult task. Many Frontotemporal Dementia patients in this study became childlike, and enjoyed activities such as playing with dolls, colouring-in

children's books, and watching children's television programs. To ensure that dementia-care programs enhance patients' quality of life, and are acceptable to families, it is essential that a clear framework of service delivery is developed (e.g. Kalis & van Delden et al. 2004).

Early-onset dementia patients are one of the most vulnerable groups in our society, and have specific requirements. Providing safety and meeting the basic needs of FTD patients in as normal a setting as possible is a special challenge. There are no easy answers to providing appropriate care. Care-plans should always attempt to meet the sometimes competing needs of the individual (for example, if an adult patient wants to play with dolls) and the ideals of the "least restrictive environment".

7.3.8 Pharmacological Interventions

Recent research has indicated that pharmaceutical treatments can assist with the management of the behavioural disorders accompanying Frontotemporal Dementia (Lebert & Stekke et al. 2004; Morretti & Torre et al. 2004; Ishikawa & Shimomura et al. 2006). medications for treating dementia are designed to treat abnormalities in the cholinergic and serotonigenic systems (Snowden & Neary et al. 2002; Chow, 2005).

Cholinergic Medications

There is limited evidence that cholinergic medications have any clinical effect with Frontotemporal Dementia patients as there is no clear evidence that this group has any disruption of the cholinergic system (Snowden & Neary et al. 2002; Chow, 2005). One study using a cholinergic medication, Rivastigmine, indicated that the medication significantly reduced the frequency and intensity of behavioural disturbances, and subsequently reduced caregiver distress (Moretti & Torre et al. 2004).

Selective Serotonin Reuptake Inhibitors

There is some limited evidence indicating that selective serotonin reuptake inhibitors (SSRI's) may reduce ritualistic behaviours, disinhibition, and compulsive eating in a minority of Frontotemporal Dementia patients (Swartz & Miller et al. 1997). The SSRI Trazodone, in a randomized placebo-controlled study of 26 Frontotemporal Dementia patients, was shown to significantly decrease patients' irritability, agitation, depression, and eating abnormalities (Lebert & Stekke et al. 2004). The SSRI fluvoxamine malate was found to significantly reduce stereotyped behaviours in 16 Frontotemporal Dementia patients over a 16 week period (Ikeda & Shigenobu, 2004). Paroxetine has been found ineffective in reducing behavioural problems in 10 Frontotemporal Dementia patients (Deakin & Rahman et al. 2004). The caregivers of 8 Frontotemporal Dementia patients treated with Paroxetine reported a decrease in their levels of stress (Moretti & Torre et al. 2003).

Neuroleptics

Neuroleptic medications may not be suitable for use with Frontotemporal Dementia patients. A study of 24 Frontotemporal Dementia patients medicated with neuroleptics found significant extrapyramidal side effects in 33% of the patients. The study recommended that if neuroleptics are used with Frontotemporal Dementia patients, caution should be used as this group appears to be particularly susceptible to the adverse side-effects associated with this class of drugs (Pijnenburg & Sampson et al. 2003).

Other Agents

Several medications have shown promise for controlling behavioural disturbances associated with Frontotemporal Dementia. valproic acid has been found useful in some patients for agitation, anxiety, and repetitive/ritualistic behaviours. Donepezil has not been shown to have any clinical efficacy (Chow & Mendez, 2002).

Recommendations

There is evidence that pharmacological interventions may assist with managing some of the symptoms associated with Frontotemporal Dementia. Symptoms that have shown response to medications include aggression, stereotypical behaviours, disinhibition, impulsivity, and abnormal eating behaviours. Further research is required to determine the long-term effects of medications, and to evaluate the impact of the medications on the quality of life of both patients and their carers.

7.3.9 Neuropsychological and Behavioural Assessment

The results of the current study indicate that neuropsychological assessment of patients with Frontotemporal Dementia provides useful information that can be used in clinical management (see Chapter 4 for details). Much of the useful information obtained was from the observation of the patients' behaviours during the extended time intervals spent with the patients. It is possible that the use of a behavioural rating scale during assessment could assist in quantifying behaviours. Rating scales that have been shown to have clinical utility are the Stereotypy Rating Inventory (SRI, Shigenobu & Ikeda et al. 2002), the Frontotemporal Behavioral Scale (Lebert & Pasquier et al. 1998), the Frontal Behavioural Inventory (Kertesz & Davidson et al. 1997), and the Neuropsychiatry Inventory (NPI, Srikanth, Nagaraja, & Ratnavalli, 2005). These scales have the advantage of being brief, and are effective in differentially diagnosing Frontotemporal Dementia from other conditions such as vascular dementia and Alzheimer's Disease.

Drawbacks of Using Neuropsychological Tests

Verbal Tests of Limited Use

This study has shown that the vast majority of the neuropsychological tests were sensitive to neurological dysfunction. However, only one verbal test (the immediate recall condition of the Wechsler Memory Scale Logical Memory test) was found to differentiate between the two groups. Non-verbal tests were found

to be useful in discriminating between the groups (WAIS-111 Block Design and Picture completion subtests; Purdue Pegboard Test; Tactile Finger Recognition Test; Rey-Osterrieth Complex Figure Test; Freehand Clock Drawing test; Written component of the Symbol Digit Modalities Test; Wechsler Memory Scale Visual Recall Test). The results are consistent with previous research that has shown that the majority of neuropsychological tests are not useful in the differential diagnosis of Frontotemporal Dementia from other conditions (e.g. Siri & Benaglio et al. 2002).

Time and Cost

Neuropsychological assessment is costly and time-consuming. Testing places patients in situations where their deficits are exposed. If not managed tactfully, the assessment can be disturbing for the patient (Lezak, 1995).

Recommendations

To minimise patient distress assessments should be kept to a minimum.

Neuropsychological assessment should only be conducted if there is a clear clinical purpose (i.e. to assist with differential diagnosis from other neurological conditions).

The Mini Mental State Exam (MMSE, see Chapter 4) and a behavioural inventory such as the Neuropsychiatry Inventory (NPI, see section 7.2.7) can be

used in conjunction with brief neuropsychological instruments such as the Tactile Finger Recognition Test and the Freehand Clock Drawing test. If results of this brief battery were found to be abnormal patients should be given a comprehensive neurological imaging work-up.

7.3.10 Limitations of the current study

Within this study neuropsychological tests were administered in a non-standardised way (see Chapter 4). The tests were used to assist with the clinical management of the patients rather than primarily for research purposes. Therefore, the neuropsychological test results reported above need to be treated with caution.

Neurological imaging investigations (CT, MRI, EEG, SPECT) occurred at different times during the course of patients' illnesses. As neurological imaging assessments were not conducted at the same point in their illness for each patient, direct comparison between the different imaging modalities was not possible. A standardised approach to neurological imaging studies may assist in the exploration of early-onset dementia patients.

Some of the "difficult behaviours" reported in this study may have been the result of the failure of care and support services to adequately respond to the rapidly changing needs of early-onset dementia patients.

7.3.11 Directions for future research

Future research in the area of early-onset dementia care is required to develop services that have the capacity to combine high-quality medical care with behavioural care. This study has highlighted the individualised and ever-changing needs of many early-onset dementia patients. The provision of palliative care to this group has not been researched. Future research could assist in the development of palliative care services for this population. Specific issues that could be examined by future research are the provision of age-appropriate services, and developing individualised care-plans that focus on patients' strengths, rather than on their deficits.

APPENDICIES

APENDIX 1: CONSENT FORM

MURDOCH UNIVERSITY LETTERHEAD

CONSENT FORM FOR CARER

I am a Doctor of Psychology student at Murdoch University. I am investigating if people diagnosed with Alzheimer's Disease perform differently to people diagnosed with Frontotemporal Dementia on commonly used neuropsychological tests. I am also investigating the sorts of behavioural and memory difficulties people with Frontotemporal Dementia and Alzheimer's Disease experience.

The purpose of this study is to look for factors that may help with the diagnosis of frontotemporal dementia and Alzheimer's disease. New treatments are becoming available, so correct diagnosis may help people diagnosed with either Frontotemporal Dementia or Alzheimer's Disease get the best treatment available.

You can help in this study by consenting to the information obtained during the assessment from the person for whom you are the authorised representative being used for this proposed research.

You can decide to withdraw your consent at any time. All information given during the assessment is confidential and no names or other information that might identify the person for whom you are the authorised representative will be used in any publication arising from the research.

If you are willing for the person for whom you are the authorised representative to participate in this study, could you please complete the details below? If you have any questions about this project please feel free to contact either myself, John Rudge, on 9347 6464 or my supervisor, Dr Peter Drummond on 9360 2415

My supervisor and I are happy to discuss with you any concerns you may have on how this study has been conducted, or alternatively you can contact Murdoch University's Human Research Ethics Committee on 9360 6677.

I have read the information above. Any questions I have asked have been answered to my satisfaction. I agree for the person for whom I am the authorised representative to take part in this activity. However, I know that I may change my mind and stop the participation at any time without prejudice to the future medical treatment of the person I am signing on behalf of.

I understand that all information provided is treated as confidential and will not be released by the investigator unless required to do so by law.

I agree that research data gathered for this study may be published provided the name of the person for whom I am the authorised representative or other information which might identify the person for whom I am the authorised representative is not used.

Authorised Representative:

Date:

Investigator:

Date:

Investigator's Name:

APPENDIX 2: FRONTOTEMPORAL DEMENTIA (FTD) – ALTERNATIVE LABELS

- DISINHIBITION-DEMENTIA-PARKINSONISM-AMYOTROPHY COMPLEX (DDPAC)
- FRONTAL VARIANT OF FRONTOEMPORAL DEMENTIA (fv-FTD)
- FRONTOTEMPORAL DEMENTIA WITH MOTOR NEURONE DISEASE (FTD/MND)
- FRONTOTEMPORAL DEMENTIA WITH PARKINSONISM
- FRONTOTEMPORAL DEMENTIA-AMYOTROPHIC LATERAL SCLEROSIS (FTD-ALS)
- FRONTOTEMPORAL LOBAR DEGENERATION (FTLD)
- FRONTOTEMPORAL LOBE DEMENTIA (FLDEM)
- FRONTOTEMPORAL LOBE DEMENTIA ASSOCIATED WITH MUTATIONS ON THE TAU GENE (FTDP17)
- MULTIPLE SYSTEM TAUOPATHY WITH PRESENILE DEMENTIA (MSTD)
- PICK COMPLEX
- PRIMARY PROGRESSIVE APHASIA (PPA)
- SEMANTIC DEMENTIA (SD)
- TEMPORAL VARIANT OF FRONTOTEMPORAL DEMETIA (tv-FTD)
- WILHELMSSEN-LYNCH DISEASE (WLD)

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