The clinical differentiation of fronto-temporal dementia from psychiatric disease

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Objective: Frontal and/or temporal lobar atrophy (F/TA) is sometimes detected on neuroimaging in patients with psychiatric disease. This observation leads to difficulty in distinguishing whether patients have fronto-temporal dementia (FTD) or psychiatric illness. This paper sets out to develop clinical profiles that might be useful at first presentation to distinguish these two populations.

Methods: 29 patients were selected from a database of 250 current patients attending young onset dementia clinic. Control and experimental patient groups were established using DSM-5 criteria: (i) those without selective atrophy who had a psychiatric disorder (N = 5); (ii) patients who had FTD using consensus criteria (N = 13); and (iii) an experimental group of patients who had F/TA on neuroimaging, a psychiatric diagnosis and referral with possibility of a neurodegenerative disorder (N = 11). Profiles suggestive of FTD and psychiatric disease were established in the control groups utilising information from medical records, the neurological examination, the natural history and neuropsychometry to develop criteria to distinguish reliably FTD from psychiatric disease. These criteria were then applied to the experimental group. Patients were followed for five years.

Results: The developed criteria resulted in 3 patients being classified as FTD and 8 having psychiatric diagnoses in the experimental group. At follow-up, all the psychiatric patients remained functionally stable, whereas the FTD patients had deteriorated.

Conclusion: Characteristic profiles may prove useful in the diagnosis of patients with F/TA on imaging with a psychiatric illness and help to distinguish them from patients with FTD. At first presentation F/TA has been found in some patients with psychiatric disease who do not develop evidence of neurodegeneration. This suggests that F/TA on neuroimaging might be a feature of a subgroup of patients with psychiatric diseases.

Keywords: fronto-temporal dementia, frontal lobe atrophy, psychiatric disorders, diagnostic issues

Introduction

The difficulty of distinguishing psychiatric disorders from early neurodegenerative processes such as fronto-temporal dementia (FTD) relates to many factors, including comorbidity and the utility of consensus criteria and neuroimaging results.

While the presence of selective frontal and/or temporal atrophy is often associated with FTD, it can also exist in psychiatric conditions, and thus is of limited used diagnostically. A diagnosis of FTD is often based on behavioural changes (Pasquier et al 1998), however in the early stages, the paucity of obvious signs and symptoms may also hinder diagnosis (Mendez and Perryman 2002). Furthermore, psychiatric symptomatology often co-exists with FTD (Gregory 1999).

With the aim of assisting the clinician in distinguishing patients with early FTD from those with a psychiatric disorder, when frontal and/or temporal lobe atrophy is evident on imaging, this study outlines the development of comparative profiles of

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suggestive signs, symptoms and neuropsychometric results for patients with early FTD or psychiatric disorders.

Materials and methods

Participants

Twenty-nine participants were selected from a database of 250 patients currently attending or having previously attended the early onset dementia clinic at the Neurosciences Unit since its inception, 7 years prior. All individuals were referred to the senior author (PKP) for neurological examination from various general practitioners, neurologists, psychiatrists and other professional organisations. Two control groups and an experimental group were formed according to the following criteria. Inclusion in the psychiatric control group (CPsy) was dependent on (1) the presence of a psychiatric disorder conforming to the DSM-5 criteria, (2) the fact that FTD had been raised as possibility, leading to a neurology referral, and (3) no evidence of selective atrophy on neuroimaging. The FTD control group (CFtd) participants were required to have (1) a diagnosis of sporadic FTD based on the consensus criteria (Neary et al 1998), and (2) evidence of selective frontal and/or temporal lobar atrophy on imaging. Criteria for entry into the experimental group consisted of (1) atrophy on imaging suggestive of FTD and (2) referral to the Neurosciences Unit for elucidation of the diagnosis due to diagnostic uncertainty between FTD and psychiatric disorder. Demographic information for these groups is presented in Table 1.

Procedure

Patient files from the two control groups were reviewed, and the following information was extracted: patient demographics, details of clinical history provided at first presentation to the clinic, the results from presenting clinical examination, and neuropsychological data gathered at time of referral.

All neuroimaging results had been evaluated by senior radiologists without prior knowledge of the nature of the study, and were performed using conventional computerised tomography (CT) or magnetic resonance imaging (MRI) techniques.

Selected results from exhaustive neuropsychological assessment were also reviewed. Choice of neuropsychometric measures to be addressed was driven by two factors: those tests used most extensively in neuropsychological assessments conducted at the unit, and those considered sensitive to frontal and temporal lobe dysfunction. Several memory and executive function measures were chosen on the basis of these criteria including the Rey Complex Figure Test (CFT) (Rey 1964), the Rey Auditory Verbal Learning Test (RAVLT) (Rey 1941) and the Controlled Oral Word Association Test (COWAT, or FAS; Benton and Hamsher 1989). Subtest and summary scores from the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) (Wechsler 1997) were used as a measure of overall intelligence. Results for the copy and 3-minute recall trials for the CFT were scored according to published norms (Boone et al 1993), as were scores from the RAVLT (Geffen 1995), and the FAS (Tombaugh et al 1999). A recently published meta-analysis of neuropsychological outcome of FTD listed the COWAT, WAIS measures, RCF and RAVLT as differentiating between controls and FTD patients with effect sizes ranging from moderate to extremely high (Zakzanis 1998).

Using normative data as a reference, the number of standard deviations from the age appropriate normal mean was calculated for each patient's result to render the findings comparable. These were then averaged within each control group. WAIS-III Performance, Verbal and Full Scale IQ summary scores as well as age-adjusted scaled subtest scores were averaged within groups for comparison. This method is not presented as being statistically rigorous. Data was assessed at the level of trends, rather than statistical significance. Therefore, descriptive terminology (based on that suggested in the WAIS-III manual; Wechsler 1997) is presented instead of numerical score values.

By reviewing the aforementioned information and data, profiles of characteristics were generated for both control groups. The resultant profiles were then used to classify individuals in the experimental group as having a diagnosis of psychiatric disorder or FTD.

The resultant profiles were then used to classify individual patients as having a diagnosis of psychiatric disorder or FTD. The details of the experimental group profile, the analysis in each patient and the conclusion in each patient are contained in the Results section. The more detailed clinical histories are contained in Appendix A.

Table 1 Demographic details for the experimental and control groups (Psychiatric and FTD)

Group	N	Mean age (years)	N male	N female
Control				
Psychiatric	5	50.2	3	2
FTD	13	58	7	6
Experimental	11	59.3	5	6

Independent verification of the experimental group was obtained after review by a psychiatrist who confirmed the psychiatric diagnoses in our patients labelled as psychiatric disorder in the experimental group and as FTD by a neurologist after five years of follow-up. Further verification was obtained by examination of the natural history in which patients with psychiatric diseases remain relatively stable at 5 years, whereas those with FTD had deteriorated.

Results

The following describes a summary of the presentation of both control groups on initial examination.

Referral source and reason for referral

As expected, CPsy participants were most often referred from psychiatry, whereas CFtd participants were more likely to be referred by their general practitioners. Both groups were most commonly referred due to suggestive neurology.

Presenting complaints

The most frequent presenting complaints of CPsy participants were found to be social withdrawal, poor short-term memory, whereas CFtd individuals were more often unable to provide a history, and reported problems with attention, concentration, memory and depression, but were less likely to complain of withdrawal. Reports of social withdrawal described by the patients were confirmed by informants such as the patient's spouse or carer. There seemed to be no differences insight between the psychiatric group and those with FTD as confirmed by interview of the patients, spouses or carers.

History of neurological/psychiatric symptoms

A large percentage of the CPsy group experienced onset of psychiatric symptoms prior to neurological problems. The CFtd group was more likely to have not experienced any preceding psychiatric symptomatology whereas individuals in CPsy reported the presence of a range of psychiatric factors.

History of neuroactive medication use

Antidepressant prescription was common in both groups (CPsy: 80%; CFtd: 46%), however, most CFtd individuals had no history of neuroactive medication use.

Medical/psychiatric history

Most CFtd participants (69%) reported no significant past medical or psychiatric history, while the majority of the CPsy group reported significant psychiatric histories, including depression in 80% of cases.

Family history

The families of the CPsy patients were found to have histories of depression, alcoholism, and bipolar affective disorder, in contrast to the CFtd group, where significant family history of dementia in both first and second-degree relatives was noted. These families were also more likely to have motor neurone disease in their lineage or no relevant family history than to have a positive psychiatric history.

Forensic/compensation issues

There were no positive forensic histories or workers compensation claims in the CFtd group. In the CPsy group, 40% were claiming worker's compensation.

Family report on patient status on presentation

The families of CPsy participants were most likely to complain of excessive anger, whereas those of CFtd participants more commonly noted poor memory, disinhibition, and social withdrawal among numerous other symptoms in their relatives.

Professional's report on patient status on presentation

Professional reports of patients' behaviours revealed a similar pattern, with poor memory, depression, and evidence of frontal lobe syndrome most commonly present in both groups. However, unlike those in the CFtd group, CPsy patients were more frequently considered to display communicative difficulties in terms of impaired comprehension or aphasia.

Results of neurological examination

With the exception of complaints of poor working and semantic memory, the individuals in the CPsy group did not demonstrate positive signs on neurological examination. In contrast, the signs noted on examination of the CFtd group were wide ranging. The CFtd individuals demonstrated eye movement abnormalities, abnormal reflexes, posture, gait and involuntary movements, frontal lobe release signs, abnormal executive functions and a poorer performance than the CPsy group on bedside memory tests of autobiographical and semantic memory (but not for working memory). None of the CPsy group were found to have extrapyramidal signs or signs of motor neurone disease at presentation or at subsequent reviews, whereas one patient in the CFtd group developed

signs consistent with anterior horn disease, and three displayed extrapyramidal signs. Rigidity was tested at rest and with contralateral augmentation. There was no evidence of oppositional or facilitatory paratonia in our patients.

Natural history

None of our patients died during the study and neuropathological examination was therefore not possible. Twenty-nine patients in total within the control and experimental groups in this study were followed for 5 years and the results of those patients only are included. No patients were lost to follow-up in the study and in general patients in the CPsy group had a fluctuation course and some showed improvement. In the CFtd group the patients deteriorated.

Neuropsychometry

Neuropsychometric test results at presentation revealed a pattern of general impairment in the CFtd group in contrast to the CPsy group. The results of the CPsy group were generally within normal limits. On all measures, there was a trend that the CPsy group outperformed the CFtd group. There was a trend that Full Scale, Verbal, and Performance IQ scores were lower in the CFtd group than the CPsy group. The largest difference on average was in terms of the PIQ, which was 20 scale points lower for the CFtd group. At a subtest level, the largest between-group discrepancy (of over 6 scaled score points) was on the Comprehension subtest. The CFtd group showed relatively preserved performance on the recognition trial of the RAVLT, however their performance on the learning trials of this task was impaired.

Clinical profiles for FTD and psychiatric disorder

The above trends are summarised as patient profiles suggestive of FTD and psychiatric disorder in Table 2.

Details regarding all factors from these clinical profiles were then obtained for the experimental group in order to generate putative diagnoses for the individual patients. Below is a summary of the experimental group details. More detailed clinical descriptions of each patient are presented in the Appendix.

Experimental group profile

In terms of presenting complaints, these individuals reported a range of behavioural disturbances (eg, anger, confusion, avolition, social withdrawal), neurological signs (eg, seizure activity, pain, incontinence, sleeping difficulties), cognitive difficulties (eg, visuospatial, memory, attention, decision making, reduced reading ability), psychological symptoms (eg, depression, psychosis) and some were unable to provide a clear case history. The mean age at onset of neurological disease (M = 54.5) was higher than age at onset of psychiatric disease (M = 35.6). The majority of these individuals were medicated at presentation with prescriptions including anticonvulsants, anxiolytics, antidepressants, and neuroleptics. In terms of forensic issues, charges had been laid against two individuals (theft and murder), and one was involved in litigation.

Neurological examination of these individuals revealed a range of features across the 11 individuals including bradykinesia (N = 1), frontal release signs (eg, grasp reflex; N = 3), and abnormal pout reflex (N = 1). In terms of bedside testing, poor performances were apparent in some cases on the "Go-No-Go" test (N = 2), the Luria "fist, palm, edge" test (N = 3), proverb interpretation (N = 1) and the alternating hands test (N = 3). In terms of memory, autobiographical memory was judged to be intact in this group, while a small number of individuals demonstrated difficulties with semantic (N = 1) and working (N = 2) memory on bedside testing.

Diagnosis of individual patients using clinical profiles

Best-fit analysis of the individual experimental patient records was conducted in comparison with the profiles displayed in Table 2, thus yielding putative diagnoses for the experimental group. Three individuals were considered to have FTD and eight to have psychiatric disorders.

Patient 1 (P1)

Scores on the clinical criteria suggested FTD. This patient had not undergone neuropsychological assessment due to poor comprehension of the English language leading to pragmatic difficulties with testing. In the absence of this data, we surmised P1 was more likely to have FTD.

Patient 2 (P2)

This individual scored highly on the psychiatric criteria for clinical information, and neuropsychological impairments were thought reflective of her complicated history, as opposed to the presence of FTD. P2 was classified as having a psychiatric disorder.

Patient 3 (P3)

This patient's clinical results were consistent with psychiatric disorder whilst the neuropsychometry is inconclusive. Therefore it was concluded that P3 was more likely to have a psychiatric disease.

Table 2 Characteristic profiles of FTD and psychiatric diseases at first presentation

	FTD	Psychiatric disease
Clinical history	Referred by GP	Referred by psychiatry
	Patient unable to provide history	Patient complaint of social withdrawal
	Neurological predate psychiatric symptoms (or no psychiatric symptoms)	Psychiatric predate neurological symptoms
	No history of neuro-active medication use	Patient takes/has previously taken neuroleptics, lithium, anxiolytics or hypnotics
	No relevant past medical history	Medical history includes depression, head injury or ECT
	Family history of dementia, motor neurone disease or no relevant family medical history	Family history of psychiatric disorder
	No forensic or compensation issues	Positive history of forensic or compensation issues
	Family report poor memory or disinhibition	Family reports of increased anger
	Professional report of communication problems	Professional reports of no abnormalities
Neurological examination	Abnormal gait and CNS and PNS examination. Frontal release signs present, poor performance on bedside tests of executive functioning, autobiograhical and semantic memory. May display extrapyramidal or motor neurone disease symptoms.	Essentially normal but with poor working memory on bedside testing
Natural history	History of functional decline with/without a preceding period of stability	Fluctuating course or no follow-up
Neuropsychometry	Poor verbal learning, with intact recognition. Low average Intelligence. Poor verbal reasoning.	Generally, within normal limits in all areas

Patients 4 and 5 (P4 and 5)

These patients both rated higher on the psychiatric scale for both clinical information and neuropsychometry. Both were concluded to have psychiatric disorders.

Patient 6 (P6)

The clinical score was equivocal in this case, but neuropsychometry suggested neurological disorder. On balance of results, this client was considered more likely to have FTD.

Patient 7 (P7)

Results on the clinical scale suggested psychiatric disease whilst the neuropsychometry was inconclusive, leading to a premise of psychiatric disorder.

Patient 8 (P8)

This patient scored highly on the psychiatric scale for clinical data and the neuropsychometry data and was therefore concluded to have a psychiatric condition.

Patient 9 (P9)

This individual rated highly on the psychiatric scale for clinical information and weakly on the neurological scale for neuropsychometry. Therefore, it was considered that P9 was more likely to fall into the psychiatric group.

Patient 10 (P10)

In this case, the clinical results were consistent with neurological disorder. Again, due to language barrier, no neuropsychological assessment was conducted. P10 was suggested to have FTD.

Patient 11 (P11)

This patient scored more highly on the psychiatric scale for clinical information and neuropsychometry. We concluded that P11 was more likely to have a psychiatric disease.

In summary, according to the criteria derived from analysis of the control groups, P1, P6, and P10 were considered to have FTD, whilst P2, P3, P4, P5, P7, P8, P9, and P11 were more likely to be psychiatric cases. At follow-up after 5 years, the psychiatric patients were functionally stable, whereas the FTD group had deteriorated.

Discussion

Our results suggest that the majority of patients with frontal and/or temporal lobe atrophy on imaging suggestive of FTD who are referred to neurological services are more likely to have psychiatric diagnoses. As mentioned earlier, criteria for entry into the experimental group included evidence of selective atrophy on imaging, yet we have demonstrated that a large proportion of these patients were likely to have psychiatric disorders. What then is the significance of the imaging data?

Recent research suggests that progressive brain structural changes may occur as a result of prolonged neuroleptic therapy (Madsen et al 1998) that may mimic the changes seen in FTD. It has also been suggested that the brains of schizophrenic patients show various microanatomical abnormalities as a result of factors including oxidative stress and loss of trophic factors (Smythies 1998). Obviously, the relationship between psychiatric disease, neuroactive medications and structural brain changes has yet to be fully elucidated. Indeed, all of these factors may be operative in this group of patients, including previous treatments like electroconvulsive therapy (ECT). This would lead us to emphasise the importance of interpreting neuroimaging data in the light of clinical and neuropsychometric findings, eschewing sole reliance on evidence of structural brain changes as evidence of FTD. Indeed, the consensus criteria (Neary et al 1998) do not consider the absence of selective atrophy as an exclusion factor, nor do they consider the presence of atrophy a core diagnostic feature.

Unfortunately, no biological marker exists to assist in the differentiation of these two classes of disorder. The diagnosis of FTD may be obvious in those families with a strong pedigree of dementia occurring in the presenium, but FTD is more likely to occur with sporadic aetiology. FTD is second only to Alzheimer's disease (AD) in causes of dementia with onset in the presenium (Panegyres et al 2000; Hokoishi et al 2002; Panegyres and Frencham 2007). At post-mortem, up to one-fifth of dementia deaths are retrospectively attributed to FTD (Lebert et al 1998).

Common characteristics of FTD include onset of behavioural changes predating cognitive decline (Pasquier et al 1998), dietary changes, hypersexuality and bizarre compulsions (Miller et al 1995). Differing predominant symptom spectrums have been found to be associated with FTD affecting one hemisphere to a greater extent, with language changes associated with left-sided disease and aggression and antisocial behaviours associated with a preponderance of disease on the right (Mychack et al 2001). Despite the commonality of this condition, FTD remains under-diagnosed due to confusion with other forms of dementia and with psychiatric disorders. The subtypes of FTD have been found to be indistinguishable by neuropsychological examination, behavioural abnormalities and psychiatric symptoms as assessed by the Neuropsychiatric Inventory with the exception of aphasia in primary progressive aphasia (Ikeda and Tanabe 2000).

Evidence from the literature suggests FTD may be differentiated from AD on the basis of the presenting symptoms with disinhibition, social awkwardness, passivity and loss of executive function seen in the former and memory loss more commonly found in the latter (Lindau et al 2000). In the later stages of FTD, stereotypic eating behaviour and further loss of social graces have been found to be discriminatory factors, regardless of disease severity (Bozeat et al 2000).

While various modalities of neuroimaging have been found to be of merit in the distinction between other neurological pathologies and depression (Olazartan et al 2002) one should be wary of excessive reliance on these techniques, and imaging data does not play a role in the consensus criteria for FTD (Neary et al 1998).

Diagnosis of FTD is traditionally reliant upon the development of characteristic behaviours over time (Kertesz et al 2000). This focus on behavioural features may partially explain the trend of FTD being misdiagnosed as a psychiatric condition in the early stages of the disease (Olazaran et al 2002).

While we propose that it is possible to distinguish psychiatric disorders from FTD on the basis of clinical information gathered at first presentation irrespective of imaging results, there are several potential limitations to this study. The sample sizes of the control and experimental groups were small. While we have not conducted statistical analysis, and have reported on trends and patterns of symptoms, our conclusions would be strengthened by increased sample size and replication of findings. Relating to the frequency of signs

and symptoms, and more specifically to neuropsychometric results, future research (incorporating larger sample sizes) could analyse the data statistically, and generate effect sizes associated to the characteristics in the profiles generated. Finally, while many of the patients previously described underwent comprehensive speech and language assessments, the results were not incorporated into this study. In light of the communicative dysfunction that has been reported to be associated with FTD in particular, it would be clinically useful to add this information to the characteristic profiles.

In this paper we have attempted to provide the clinician with profiles of data that can be collected at first presentation in order to differentiate between two difficult groups of patients. We suggest that with further experience and research, these profiles should be further refined to achieve better representation of the patient population, and will be augmented by the future development of biological markers including genomic analysis (Panegyres and Zafiris-Toufexis 2002). Functional brain imaging in the form of SPECT and PET scanning might be additional aids in the differential diagnosis of FTD from psychiatric disease. Unfortunately not all clinicians have access.

The results also suggest a subgroup of patients with psychiatric disease who have frontal and/or temporal lobe atrophy on neuroimaging.

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Appendix A

Patient 1

This woman was referred by psychiatry and neurology. While she was unable to provide a history, it was possible to ascertain that onset of psychiatric symptoms was 59 years and of neurological symptoms was 62 years. She had been prescribed neuroleptic medication for 3 years and had a history of depression and psychosis. Her family reported personality changes and incontinence, while professional reports noted decreased motivation and speech output. On neurological examination she displayed bradykinesia, bilateral grasp reflex and extrapyramidal symptoms were present. Neuropsychological assessment was not possible due to language constraints. Symptomatology had been stable for 3 years.

Patient 2

This woman was referred by psychiatry due to atrophy on imaging. She reported increased anger, with onset of psychiatric symptoms at age 29, and onset of neurological symptoms at age 56. She reported having been prescribed neuroleptic, antidepressant and anxiolytic medication, but could not specify how long she had taken these medications for. There was a family history of personality disorder and learning disability. Professionals report indicated anger, reduced libido and generalised affective changes. Her neurological examination was normal except for poor performance on the go-no-go and alternating hands sequences tests. On neuropsychological assessment, she demonstrated poor verbal fluency and verbal learning, with intact recognition. Her Full Scale IQ was in the Extremely Low range. Symptoms had been stable for 2 years but had subsequently deteriorated over a 2 year period.

Patient 3

This woman was referred by neurology due to atrophy on imaging. Her presenting complaints included increased anger, confusion, seizure activity, poor memory and visuospatial difficulties. The onset of psychiatric symptoms was 28 years, and of neurological symptoms was 52 years. While she had no history of psychoactive medication, her relevant medical history included that she had undergone ECT and had required hospitalisation and had incurred two mild head injuries. There was a positive family history of depression in a first degree relative. Her family reported that she had become more socially withdrawn and that her sleeping patterns had been interrupted. No abnormalities were noted on neurological examination. Her neuropsychological profile was generally within normal limits, apart from a poor performance on a visual recall task. Symptoms were stable for 2 years, but subsequently deteriorated over a 2-year period.

Patient 4

This man was referred by psychiatry and neurology. His presenting complaints included depression, pain and poor short-term memory. Ages at onset of psychiatric and neurological symptoms were similar, being 51 and 52 years respectively. He had been taking antidepressant medication for one year and anxiolytic medication for 6 months. He had a history of depression requiring hospitalisation and his family reported increased depression, poor memory and social withdrawal. Professional reports noted depression, disinhibition and abulia. There were no abnormalities on neurological examination, however neuropsychological examination demonstrated impaired verbal learning and recognition and poor verbal fluency. In terms of the history of symptoms, a previous 2 year period of deterioration in functioning was followed by a 2 year period of stability.

Patient 5

This man was referred by psychiatry and neurology. His presenting complaints included depression, decreased attention and concentration, incontinence, psychosis, ECT and changes in sleeping pattern. The age of onset of neurological symptoms was 49 years, while the age of psychiatric symptoms was 51 years. He had taken neuroleptic, antidepressant and anxiolytic medication for a period of six months. Relevant past medical history included depression, psychosis (requiring hospitalisation) and ECT. There was a history of psychiatric disorder (nature unknown) in one first-degree family member. Professional report noted abulia, impaired frontal or executive functioning and frontal lobe syndrome. Neurological examination revealed poor performance on the Luria "fist, palm, edge" test and the alternating hands test. On neuropsychological examination, he demonstrated intellectual functioning in the Extremely Low range. Symptomatology had been stable for 3 years.

Patient 6

This man was referred by psychiatry and neurology due to atrophy on imaging. His presenting complaints were depression, decreased motivation and psychosis. His psychiatric symptoms were longstanding (onset at 16 years). He was 52 years old at the time of onset of neurological symptoms. He had been on antidepressant and neuroleptic mediation for 10 years. He reported a history of psychosis (requiring hospitalisation), ECT and alcohol dependency. Professional

report noted poor short-term memory and a frontal lobe syndrome. On neurological examination, bilateral grasp and pout reflexes were present. Performance on the go-no-go test, Luria "fist, palm, edge" test and proverb interpretation was found to be poor. On neuropsychological examination, his copy and recall of a geometric figure was impaired, as was his verbal learning and memory, while his recognition was intact. Verbal fluency was markedly poor, in the context of a Low Average Full Scale IQ. His condition had remained stable for 3 years.

Patient 7

This woman was referred by her general practitioner due to signs suggestive of a neurodegenerative process. She complained of poor short-term memory, reduced decision making ability and social withdrawal. The age of onset of neurological symptoms was 66 years. She had been on antidepressant medication for an unknown period of time, and had a history of depression. There was a family history of alcohol dependency in a first-degree relative. The professional report noted fronto-temporal dysfunction. Neurological examination was normal, except for poor working memory on bedside testing. Neuropsychological assessment revealed markedly impaired recall of visual and verbal information, and poor verbal recognition. While summary scores were not available, her performance on WAIS-III subtests tended to fall in the average range. There was a 2 year history of decline in her status.

Patient 8

This man was referred by psychiatry and neurology. His was unable to provide a history. Onset of psychiatric symptoms was 31 years, and 55 years for neurological symptoms. He had taken neuroleptic and lithium medication for an unknown time period. He had been diagnosed with bipolar affective disorder. Professional report noted the presence of a frontal lobe syndrome, however neurological examination was normal. His neuropsychological profile was essentially within normal limits, apart from a poor performance on a task of verbal fluency. He had a 2 year history of decline in status.

Patient 9

This woman was referred by psychiatry and neurology due to atrophy on imaging. Her main complaint was of depression. She was 33 years old at onset of psychiatric symptoms, and 52 years at onset of neurological symptoms. She had taken anticonvulsant, neuroleptic and antidepressant medication for an undefined time period. She had a complex background including bipolar affective disorder, psychosis, alcohol dependency requiring hospitalisation and ECT. There was a history of alcohol dependency in a first-degree family member. Her family reported poor memory, and professional report commented on changed in affect and frontal lobe syndrome. Her neurological examination was normal, however neuropsychological assessment revealed poor delayed visual and verbal recall, in the context of intact verbal recognition. Her status was stable for 3 years.

Patient 10

This woman was referred by psychiatry and neurology with presenting complaints of poor memory and difficulty reading. She had been 35 years old at onset of psychiatric symptoms and 62 at onset of neurological symptoms. She had taken neuroleptic and lithium medication for 2 years and antidepressant medication for an unspecified time. She had a history of depression requiring hospitalisation and ECT. There was a history of motor neurone disease in five family members and of depression and bipolar in two others. Her family reported confusion, incontinence, delusions, poor short-term memory, disinhibition, decreased motivation and wandering behaviour. Professional report noted poor memory, abulia, confusion, depression and decreased verbal fluency. One neurological examination, the bilateral grasp reflex was present and the performed poorly on the Luria "fist, palm, edge" test, and bedside tests of working and semantic memory. She did not undergo neuropsychological assessment due to language difficulties. She had a 2 year stable history.

Patient 11

This man was referred by psychiatry due to atrophy on imaging. His presenting complaints included poor short-term memory, social withdrawal, decreased attention and concentration and depression. The onset of psychiatric symptoms was 25 years, and 34 for neurological symptoms. He had taken antidepressant, neuroleptic and anxiolytic medication for one year. He had a history of mild had injury, post traumatic stress disorder and personality disorder along with anxiety, requiring hospitalisation. Relevant forensic history included a charge of theft. His family reported poor hygiene, depression and difficulty following instructions. Professional report noted personality disorder. Neurological examination was normal, and neuropsychological examination revealed intellectual functioning in the Average range. He had a tonth stable history of symptoms.