COGNITIVE DEFICITS IN OBSESSIVE COMPULSIVE DISORDER IN TESTS WHICH ARE SENSITIVE TO FRONTAL LOBE DYSFUNCTION

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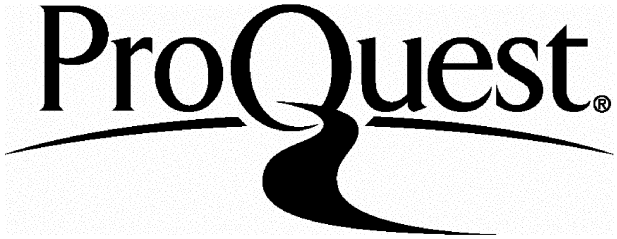

ABSTRACT

Forty patients with obsessive compulsive disorder (OCD) were compared to matched healthy controls on neuropsychological tests which are sensitive to frontal lobe dysfunction. On a computerised version of the Tower of London task of planning, OCD patients were no different to healthy controls in the accuracy of their solutions. There was no difference between the groups in the time spent thinking prior to making the first move or in the time spent thinking after the first move when "perfect move" solutions were considered. However, when the patients made a mistake, they spent more time than the controls generating alternative solutions or checking that the next move would be correct. The results suggest that OCD patients have a selective deficit in planning of generating alternative strategies when they make a mistake. In a separate attentional set-shifting task, OCD patients showed a continuous increase in terms of the number who failed at each stage of the task, including the crucial extra-dimensional set shifting stage. This suggests that OCD patients show deficits in both acquiring and maintaining cognitive sets. A sub-group of OCD patients who fail at or before the extra-dimensional shift stage also performed poorly on the Tower of London task. They are less accurate when solving problems and have a similar pattern of deficits to some neurosurgical patients with frontal lobe excisions. Both studies support the evidence of frontal-

striatal dysfunction in OCD and the pattern of results is compared to that found in other known fronto-striatal disorders. The results are discussed in terms of a functional absence of a Supervisory Attentional System (Norman and Shallice, 1980).

INDEX

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INTRODUCTION

In this review of the literature, I shall cover:

i) the clinical syndromes of Obsessive Compulsive Disorder (OCD) and Obsessive Compulsive Personality Disorder (OCPD) with particular attention to obsessional slowness

ii) the normal neuroanatomy and functional organization of the neural loops between the basal ganglia and frontal cortex

iii) the evidence for the possible dysfunction in the neural loops between the basal ganglia and frontal cortex in OCD

iv) the evidence for neuropsychological deficits in OCD from previous studies

v) the findings of computerised neuropsychological tests in patients with fronto-striatal dysfunction that have been used in this study.

Obsessive Compulsive Disorder

The prevalence of OCD is about 2% of the population and there is an equal sex ratio (Turns, 1985). The peak age of onset is adolescence or the early 20's, although OCD does occur in children. The onset of OCD may be precipitated by a life event although the average duration of the illness before presentation is about 10 years (Marks, 1987). OCD is primarily an anxiety disorder, characterised by the occurrence of recurrent and intrusive thoughts, images or

impulses to action that the patient finds repugnant or anxiety provoking. On calm reflection, obsessions are usually regarded as senseless or absurd. The degree of belief in the obsession varies: it may reach an overvalued idea and rarely a delusion. The content of the obsession is usually related to the possibility that the patient may be responsible for causing harm to himself or to others in the future. The most common obsessions are centred on fears of contamination; doubting; aggression or violence; blasphemy; accidents or injury; or sex (Rachman & Hodgson, 1980).

Obsessions are involuntary and are associated with anxiety and dysphoria. By comparison, rituals are partly voluntary acts that are compulsive. They decrease anxiety and are therefore reinforcing. Rituals are either repetitive acts or are performed according to certain stereotyped rules. The most common rituals involve cleaning, checking, repeating or reassurance seeking. OCD is characterised by extensive avoidance behaviour. Patients avoid touching or being close to a wide range of objects or activities either to prevent contamination by a feared object or to prevent the triggering of an obsessional thought or image and the anxiety that is thereby aroused.

Without treatment, the natural course of the disorder is chronic and unremitting, although a minority of patients have episodic remissions (Marks, 1987). OCD can lead to considerable psychological and social handicap as severe as

that in chronic schizophrenia. The current treatments of choice consist of behaviour therapy, namely exposure and response prevention (Marks, 1987), or serotonergic anti-depressant drugs (Zohar and Insel, 1987).

Obsessional slowness

Obsessional slowness is a more severe variant of OCD. Clinical definition of cases causes major difficulty as the patients are an extremely heterogenous group (Veale, 1993).

Rachman (1974) first used the term "Primary Obsessional Slowness" in a study of 10 cases. The main feature described was a meticulous concern for orderliness in which a patient would take hours to carry out daily tasks of self-care such as washing, shaving, brushing his teeth or getting dressed. A case history was provided of a man who spent hours shaving single hairs in a precise and ordered sequence. Similarly teeth brushing involved preparing the toothbrush and paste meticulously and placing it in a set position. Rachman has elaborated on the syndrome in a book chapter (Rachman & Hodgson, 1980). There remains some confusion as to the psychopathology of his 10 patients. He acknowledges that obsessional slowness can be secondary to rituals and care was taken to exclude patients in whom slowness was secondary to checking. However he later states that "all of the 10 patients were carrying out some checking behaviour". He proposed the term "Primary Obsessional Slowness" because the activities concerned were

not rituals as there was no reduction in anxiety or dysphoria prior to or after the activity. He noted in such patients the relative absence of obsessional thoughts and suggested that one possible purpose of the slowness was that it prevented the development of obsessions. All the cases had an obsessive compulsive personality and their estimate of objective time was normal.

Several similar cases have since been reported by Bilsbury & Morley (1979), Bennun (1980), Clark et al (1982), and Marks (1987). Marks (1987) also noted that obsessional slowness mainly affects self-initiated actions and does not affect automatic behaviour such as driving a car or playing squash in which a patient is continually responding to ongoing cues. Ratnasuriya et al (1991) report some evidence that most patients with obsessional slowness are male, possibly suggesting a genetic or biological predisposition to the condition (Comings & Comings, 1986).

The concept of "Primary Obsessional Slowness" seems to have been generally accepted in the literature although an unsigned editorial in the British Medical Journal (1974) questioned the existence of a separate syndrome. However, informal discussions amongst clinicians does not tend to lead to consensus on the classification and there is disappointment at the results of its treatment in the long-term. It is agreed that obsessional slowness is an uncommon but severely disabling variant of OCD. All the cases

reported usually have long histories, are often unemployable and are usually socially isolated.

Obsessional slowness however appears to be secondary to several different components of OCD that can be determined by a more detailed behavioural analysis (Veale, 1993). Another component is the neurological deficits and abnormal movements found in OCD which will be discussed later in this introduction. Slowness is thus viewed as an indication of the severity of the disorder and handicap suffered by the patient. The concept requires widening to include all the strategies adopted by the patient either to prevent anxiety or to reduce it as well as the neurological deficits.

Each of the main strategies used by patients with obsessional slowness will now be discussed. These strategies are used to a greater or lesser degree by all patients with OCD.

Avoidance strategies in OCD and obsessional slowness

In a standard behavioural analysis, avoidance prevents the occurrence of an obsession and the concomitant anxiety or dysphoria and is therefore reinforcing. Overt avoidance behaviour can easily be recognized: patients use many strategies to prevent touching or being close to a perceived contaminant or to prevent the transfer of a contaminant from one object to another. All these avoidance

strategies may contribute to the slowness. Another strategy is designed to avoid disorder, unmeticulousness, lack of cleanliness and untidiness where there are no overt contaminants. This is probably the group that Rachman (1974) has termed as having "Primary Slowness". He noted that the need for orderliness and meticulousness was not a ritual as it was not preceded or accompanied by any significant anxiety or dysphoria. The meticulousness and orderliness can be viewed as a form of avoidance behaviour as it prevents the concomitant anxiety or dysphoria and is used as a system to ensure that no part of the activity is left out. The behaviour of such patients merges with the perfectionism and meticulousness found in OCPD in the absence of OCD that will be discussed later.

Covert avoidance is more difficult to observe. It is sometimes described as compartmentalising unacceptable thoughts in one part of the mind. It is similar to physical avoidance of an external contaminant in which certain contaminated areas are cordoned off. These strategies may require intense concentration and therefore much time to maintain them.

Rituals in OCD and obsessional slowness

In a behavioural analysis, rituals are repetitive actions that reduce anxiety or dysphoria and are therefore reinforcing. An excessive length of time may be spent completing an activity because of an overt ritual such as

washing, checking or repeating - all may contribute to obsessional slowness.

Ruminations refer to the preoccupation with an obsessional thought or image and the associated covert avoidance and covert rituals. Covert rituals are more difficult to determine because they cannot be observed and are more difficult to treat. Patients may attempt to suppress or neutralise their obsessional thoughts (similar to an overt cleaning ritual) - this may require intense concentration and can lead to slowness in other activities.

Other covert rituals include mental checking as reported by Bennun (1980) in which a patient with obsessional slowness went over the previous performance of his overt rituals or ordinary actions in his mind. Alternatively a patient may be mentally planning a future ritual in minute detail. Patients may also be slow because they repeat in their mind or count an act a set number of times to erase or neutralise the obsession.

In a behavioural analysis, the characteristic avoidance behaviour and compulsions of OCD function by preventing or reducing anxiety or dysphoria (Rachman & Hodgson, 1980). These strategies may interfere in measuring latency times in neuropsychological testing. For example if the testing equipment is perceived as contaminated or if the patient was preoccupied by an obsessional thought at the time of

the testing then this would distract from or interfere with concentration on the task and therefore increase the latency times or the number of errors recorded in the test.

Neurological deficits in obsessional slowness

An alternative explanation for some compulsions is that they are complex motor tics to which a patient has subsequently attached a meaning (Holzer et al, 1994). It is sometimes difficult to distinguish between certain complex motor tics and some "tic-like" compulsions. Complex motor tics include facial gestures, grooming behaviour, jumping, touching, stamping and smelling an object. The presence of a tic would suggest neurological dysfunction in the basal ganglia.

Tic-like compulsions include touching, tapping, rubbing, stereotyped repetition of routine activities and evening-up behaviours. In the clinical setting, the patient's opinion regarding the motivation for his behaviour gives an indication as to whether the behaviour is a tic or a compulsion. Generally if the behaviour is performed for a specific reason (e.g. to prevent a disaster), it is called a compulsion. If however the patient has no idea why he is behaving as he is (apart from the fact that he would be anxious if he didn't) then it is referred to as a "tic". The distinction has some clinical relevance as dopamine antagonists in combination with a selective serotonin reuptake inhibitor (SSRI) appear to improve outcome in OCD

patients who are unresponsive to an SSRI alone especially in those who have a comorbid tic disorder (McDougle et al, 1990).

There is an increased frequency of neurological deficits in OCD patients which do not function in terms of regulating anxiety. These occur to a greater or lesser extent in all patients with OCD (Hollander et al, 1990) but may be more pronounced in patients with obsessional slowness (Hymas et al, 1991). The behaviours include difficulty in initiating movements; poverty of spontaneous movement; shifting between one set of movements and another; perseveration of unwanted movements and distraction to random visual stimuli. The motor deficits are similar to that found in basal ganglia disorders which are characterised by disinhibition of the frontal lobe and slowness in thinking, which are discussed later in this introduction. They are another component to our understanding of why some OCD patients are slow at completing everyday tasks such as dressing or bathing. Not only may they be adopting strategies which make them slow (eg avoiding certain contaminants or checking on feared dangers to reduce anxiety) but are biologically slowed down by unwanted movements, difficulty in initiating movements and are easily distracted. One of the aims of this study was therefore to determine whether OCD patients show any neuropsychological evidence for slowness in thinking.

In summary, obsessional slowness needs to be viewed as a severe variant of OCD in general. In a review, I have argued that it consists of many different components which are difficult to unravel in any given patient (Veale, 1993). Two of these components are avoidance and compulsive behaviours. The latter are partly voluntary or conscious strategies adopted by the patient. Another component to the slowness may be a neurological deficit. Each of these components may be more prominent in any given patient and might vary over time. A further component of obsessional slowness in some patients is Obsessive Compulsive Personality Disorder.

OBSESSIVE COMPULSIVE PERSONALITY DISORDER

Mention has already been made of Obsessive Compulsive Personality Disorder (OCPD) as defined in DSMIII-R (American Psychiatric Association, 1987) or anankastic personality disorder in ICD 9 (World Health Organization). The relationship between OCD and OCPD is controversial and complex. Some would regard OCD and OCPD as on the same continuum of psychopathology, but they are listed as separate disorders in DSMIII-R and ICD 9. Most clinicians would agree that the two disorders may coexist or occur separately.

DSMIII-R defines personality traits as enduring patterns of perceiving, relating to, and thinking about the environment and oneself, which are exhibited in a wide range of social

and personal contexts. When personality traits become inflexible and maladaptive and cause either functional impairment or subjective distress, they are termed "Personality Disorder". The clinical characteristics of OCD can be readily identified with a high level of reliability but there is no universally agreed operational definition of the criteria of OCPD. In a review of OCPD, Reed (1985) has collated 33 attributes of obsessional personality traits in the literature. They are accuracy; intolerance of ambiguity; high level of aspiration; concentration; conscientiousness; control; stress on trivial details; discipline; doubt; inconclusiveness; indecisiveness; meticulousness; obstinacy; orderliness; over-categorization; patterning; pedantry; perfectionism; perseveration; persistence; precision; propriety; punctiliousness; punctuality; rectitude; reliability; rigidity; routine; rules; scrupulousness; symmetry; thoroughness; and tidiness. Some of the attributes overlap and different diagnostic systems use different traits. Five out of ten selected traits are required for the diagnosis of OCPD in DSMIII-R (Appendix 1). This study has used the criteria from DSMIII-R as they are the most reliable criteria for diagnosing OCPD by a structured interview(Stangl et al, 1985). It does not of course mean that the DSMIII-R criteria are any more valid than any other definition.

Indecisiveness and procrastination are two criteria for

OCPD that can be discerned in several reported cases of obsessional slowness and could interfere with latency times in neuropsychological testing. In an extreme case, a man took five hours to bath in the morning - a significant component of this was the time he took to decide to have a bath (Marks 1987). Other attributes that could interfere with neuropsychological testing include the need for accuracy, perfectionism, persistence and rigidity. The diagnosis of OCPD should thus be controlled for in the measurement of latency times in any neuropsychological testing of patients with OCD.

NEUROANATOMICAL AND FUNCTIONAL ORGANISATION OF THE BASAL GANGLIA AND FRONTAL CORTEX

An emerging hypothesis is that the neuroanatomical basis of OCD may lie in one or more of the neural loops between the basal ganglia and the frontal cortex of the brain (Wise & Rapaport, 1989; Baxter, 1992). Before I consider this in more detail, I will discuss the normal anatomy and functional organisation of the basal ganglia and frontal cortex and the clinical manifestations of their dysfunction.

The basal ganglia are subcortical nuclei that consist of the caudate nucleus, putamen and globus pallidus (which together comprise the corpus striatum). Alexander et al (1986) have proposed the parallel organisation of functionally segregated circuits linking the basal ganglia and cortex. In brief, the inputs to the basal ganglia from the cortical areas appear to be anatomically and functionally segregated and regarded as "loops" or closed circuits. In the loops, the frontal lobe sends efferent fibres to the basal ganglia. Five distinctly separate, non-overlapping basal ganglia and thalamocortical circuits have been identified:

i) the motor;

ii) the oculomotor;

iii) the dorsolateral prefrontal;

iv) the lateral orbito-frontal; and

v) the anterior cingulate (limbic) circuits.

All circuits share common structures - frontal lobe, corpus striatum, pallidum/substantia nigra and thalamus. Each circuit influences separate regions of the frontal lobe. The first two circuits are involved in the sensorimotor functions of the body and the eyes respectively; the third and fourth with cognitive processes; and the fifth with limbic mechanisms. One hypothesis is that obsessive compulsive symptoms in OCD results from a dysfunction in the loops which include the dorsolateral prefrontal or the lateral orbito-frontal circuits (Wise & Rapaport, 1989; Baxter, 1993).

The dorsolateral prefrontal circuit involves the following connections.

a) It originates from the dorsolateral prefrontal cortex, the posterior parietal cortex and the arcuate premotor area and connects to the dorso-lateral head of the caudate nucleus and a continuous rostrocaudal strip to the tail of the caudate.
b) from the caudate to dorsomedial globus pallidus and rostral substantia nigra,
c) from globus pallidus and substantia nigra to the ventral anterior and mediodorsal thalamic nuclei,
d) from the thalamic nuclei back to the dorsolateral prefrontal area of the cortex (thus closing the loop).

The lateral orbito-frontal circuit involves the following connections (Figure 1 overleaf).

a) It originates from the lateral orbito-frontal area of the cortex, the superior and inferior temporal gyri and the anterior cingulate area and connects to the ventromedial caudate,

b) from the ventromedial caudate to the dorsomedial globus pallidus and rostromedial substantia nigra,

c) from the substantia nigra to the medial portions of ventral anterior and mediodorsal thalamic nuclei,

d) from the thalamic nuclei back to the lateral orbito-frontal area of the cortex (thus completing the circuit).

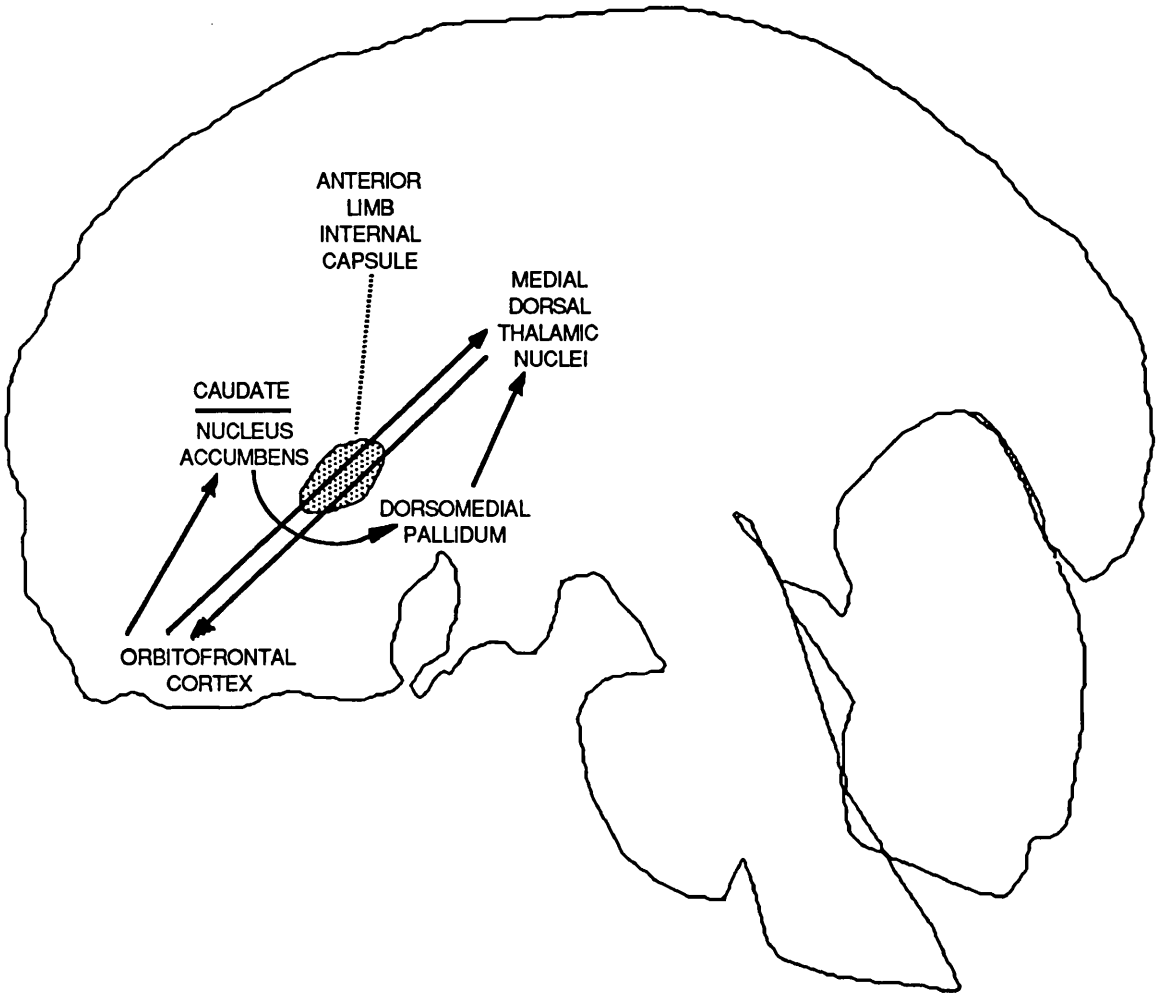


FIGURE 1: FRONTO-STRIATAL PATHWAY
(MID-SAGGITAL SECTION OF BRAIN)

Other pathways that may critically affect the functioning of the fronto-striatal pathway are the extensive interconnections between:

(i) the ventromedial caudate and the subjacent accumbens nuclei,

(ii) the substantia nigra and adjacent ventral tegmental area and

(iii) the extensive projections to the ventral striatum from the dorsal and median raphe nuclei of the midbrain.

These modulatory circuits have been included in Figure 2 (see overleaf). Numerous pathways from other brain regions also emanate from or impinge on the fronto-striatal pathway and may therefore serve additional modulatory or integrative functions.

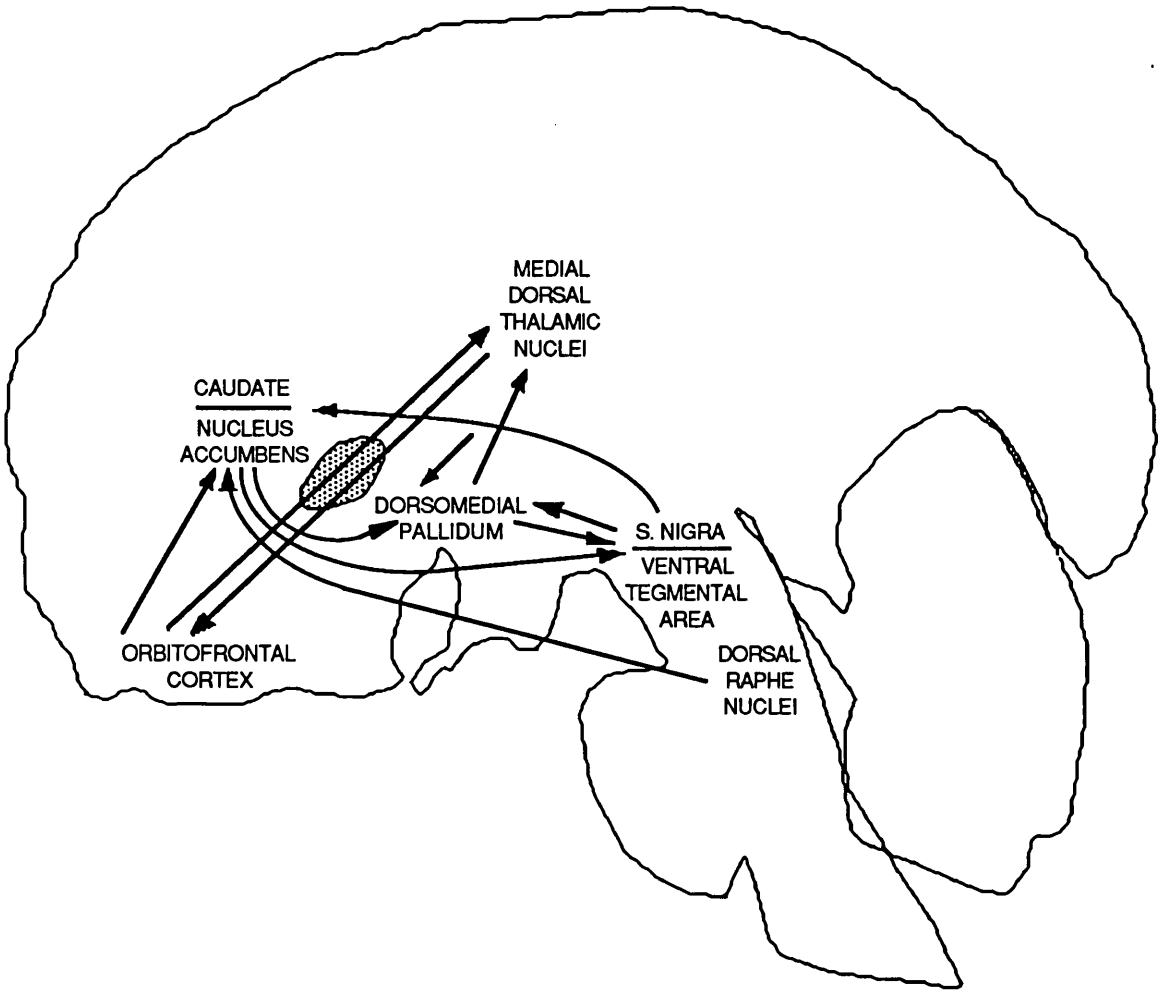


FIGURE 2: MODULATORY CIRCUIT AFFECTING FRONTO-STRIATAL PATHWAY

FUNCTIONS OF BASAL GANGLIA AND FRONTAL LOBES

The basal ganglia modulate cortico-spinal outflow or movement and are thought to be a repository of innate or learned motor programmes (Swedo, 1989b). The motor functions of the basal ganglia are carried out predominantly by the putamen, while the cognitive functions are thought to be carried out by the caudate nuclei (Cote & Crutcher, 1985). The caudate nuclei also serve as a sensory or information gating station for filtering behaviourally relevant from irrelevant stimuli (Schneider, 1984).

In animal studies bilateral lesions of the caudate nuclei are associated with perseveration, hyper-reactivity to certain sensory stimuli, stereotypy, and "compulsive approaching behaviour" (Villablanca et al, 1982). Mendez et al (1989) describe 12 patients with specific caudate nuclei lesions. Patients with lesions in the dorsolateral region of the caudate nuclei were apathetic and showed reduced spontaneity and initiative. Those with lesions in the ventromedial region were disinhibited, euphoric, disorganized and unkempt. On neuropsychological testing, both groups had short attention spans, impairment in executive function (planning, initiating or inhibiting behaviour) and decreased recall of episodic and semantic items with good recognition memory scores.

The primary pathology in Huntington's disease involves degeneration not only of the caudate nuclei but also of the putamen, thalamus and frontal cortex (Starkstein et al, 1988). They describe 34 patients with Huntington's disease and demonstrate an association between caudate atrophy and specific cognitive deficits in terms of conceptual tracking, psychomotor speed and set-shifting. Degeneration of the caudate nuclei are likely to interrupt the lateral orbito-frontal and dorsolateral prefrontal circuits thought to be responsible for cognitive processes but is difficult to prove because of the widespread cortical degeneration that frequently accompanies Huntington's disease.

In Parkinson's disease the most significant structural damage is in the substantia pars ~~nigra~~ compacta leading to degeneration of the nigro-striatal dopamine system and widespread loss of dopamine in the caudate and putamen. The symptoms are characterised by akinesia (difficulty in initiating movement), bradykinesia (slowness in movement), bradyphrenia, rigidity and tremor. It is thought that the cognitive symptoms may be due to the subsequent dopamine loss in the caudate nuclei and disruption of the lateral orbito-frontal and dorsolateral prefrontal circuits.

The term "bradyphrenia" was introduced by Naville (1922) to describe what he felt was a new psychiatric syndrome. It was the most frequent psychological sequelae of encephalitis lethargica, but had been noted earlier in some

patients with Parkinson's disease. The term refers to the clinical sign of slowness in thinking, impairment in concentration and apathy (Rogers, 1986). Comparisons have also been made with the overlap between bradyphrenia and the psychomotor retardation of depression and the possibility that they stem from a common neural substrate.

Bradyphrenia normally occurs in the presence of bradykinesia but it has been reported to occur in its absence (Laplane et al, 1984). They describe three patients with bradyphrenia without bradykinesia who were recovering from an encephalopathy. The patients also showed some features of OCD in terms of compulsive counting but without any anxiety or motivation (or "tic like" compulsions). In all their patients, computerised tomography showed bilateral lesions of the basal ganglia, mainly within the globus pallidus.

The slowing of cognitive function is regarded as the most important feature of bradyphrenia and may provide a distinction between a dementia of sub-cortical and of cortical origin. The term "sub-cortical dementia" (Wilson, 1912; Albert et al, 1974; Cummings 1986) describes the clinical syndrome of slowness of thinking and of initiating activities; poor attention; difficulty in making decisions; long term memory disturbances in which recall is facilitated by clues and recognition tasks; visuospatial impairments; poor abstraction and perseveration in tasks of

set-shifting; apathy, irritability and disturbances of mood. There are often abnormal movements (e.g. tremor, chorea, dystonia) or dysarthria. Sub-cortical dementias include those found in Parkinson's disease, Huntington's disease, and progressive supra-nuclear palsy. The term "subcortical dementia" is thus used to differentiate it from a dementia of neocortical origin which is characterised by focal signs such as aphasia, apraxia, and agnosia and memory deficits which are not aided by clues. Examples of cortical dementias include Alzheimer's diseases or Pick's disease. The cortical/sub-cortical dichotomy is probably useful to distinguish clusters of symptoms rather than having important neuroanatomical implications (Robbins, 1991). This is because pathology that affects, for example, the basal ganglia will affect the frontal cortex via the fronto-striatal loops described earlier.

The frontal lobe is essential for tasks that require anticipation, reasoning, goal establishment, planning, the organisation of behaviour in time and space, and monitoring of feedback - terms that are often subsumed under the heading "executive functions" (Baddeley, 1986). The executive function enables an individual to disengage from the immediate context in order to guide behaviour by reference to mental models or future goals. Deficits in executive function include such disparate phenomena as distractibility, perseveration, social irresponsibility, lack of initiative or planning skills, impulsiveness and

profound disinhibition extending even to the loss of control of primitive reflexes (Stuss & Benson, 1984). The exact deficits will depend upon the localisation of the lesion (Cummings, 1993). For example, lesions in the dorso-lateral prefrontal area of the cortex are characterised mainly by deficits in executive function. Lesions in the orbito-frontal area of the cortex result in disinhibition and mood changes such as anxiety, irritability or fatuous euphoria. Patients with anterior cingulate lesions usually present with severe apathy.

A critical component of executive function is the "attentional controller" or central executive (Baddeley, 1990) in Baddeley's (1986) model of "working memory". It supervises and coordinates the activities of at least two subsidiary slave systems (the "phonological" loop and the "visuospatial sketch-pad".) The phonological loop is assumed to be responsible for the manipulation of speech based information whilst the visuospatial sketch-pad is responsible for setting up and manipulating visual images for subsequent processing. The central executive integrates the information being held in working memory in order to determine a response appropriate to the situation. Baddeley (1986) has used Norman and Shallice's (1980) model of "The Supervisory Attentional System" (SAS) for the central executive.

According to their model there are "schemas" which consist

of highly specialised routines and may represent either actions or thoughts. These ensure the correct sequencing of response elements, including the specification of goals and subgoals. Schemas may control a specific overlearned action such as making breakfast, doing long division or normal driving. For example, most people have had the experience of driving while thinking about something totally different. Suddenly they realise that they have no recollection of having driven the last few miles, despite perhaps having negotiated a difficult bend.

A schema is selected if it exceeds its threshold of activation and may be influenced by motivational state and the SAS. It allocates attentional resources when planning is required or for responding to novelty. It is required for efficient response selection in certain situations and to bias a decision towards one response (e.g. an action) or another. Normally action schemas that represent the performance of particular responses are triggered by perceptions of external stimuli. The choice between different responses is hypothesised to be controlled by a process of "contention scheduling". This is a relatively automatic and autonomous process (e.g. lateral inhibition of a competing response). The SAS is required when there is no automatic response to be selected (eg coping with novelty in new learning situations) or when there is a conflict between two or more dominant responses (for example in decision making during distraction) or in

dealing with danger. For example, if in the previous example, a driver needs to avoid a pedestrian, he or she is able to concentrate immediately on driving and stop thinking about any other issue. Norman and Shallice liken the SAS to the operation of a conscious "will".

The model predicts both increased distractibility and increased perseveration depending on the precise situation. If there is no current activity, then in the absence of a functional SAS, the system will remain inert or tend to be captured by whatever stimulus the environment happens to present. Thus irrelevant environmental features trigger action schemas which cannot be suppressed and the subject is easily distracted.

When a schema has been adopted, and a response is no longer rewarded (extinction), the previously dominant but now ineffective response will continue unabated (leading to perseveration and difficulty in shifting mental set). The activity will thus continue to run, since in the absence of a functional SAS, a subject has lost the capacity to interrupt and change ongoing activity.

There is evidence that the SAS, or central executive, is located in the frontal cortex and that working memory is dependent upon efficient frontal lobe functioning (Baddeley, 1986). Robbins & Sahakian (1983) have suggested that the repository of schemas are in the basal ganglia

where interaction between the SAS and response selection occurs. The SAS may also be modulated by the activating influence of the ascending striatal dopamine innervation.

The theory predicts that a cardinal feature of fronto-striatal dysfunction is cognitive deficits in initiation and planning which can result in aimless, perseverative behaviour in the face of changing environmental stimuli. Perseveration in behaviour has been demonstrated in animals, such as rats, cats, dogs and monkeys, with frontal lobe excisions (especially the orbito-frontal cortex). For example, if an animal is trained to find food under a foodwell located to its left, and the food is then shifted to a location under another foodwell to the animal's right, an animal with a frontal lobe lesion persists in looking for food under the original foodwell (Kolb & Whishaw, 1980).

One of the aims in this study was therefore to determine whether OCD patients demonstrate dysfunction in the SAS. This would predict increased distractibility and perseveration in tests of executive function from the theory of Norman and Shallice (1980).

DOES BRADYPHRENIA OCCUR IN OCD?

Some OCD patients (especially those with obsessional slowness) appear clinically at times to exhibit bradyphrenia. I have argued previously that the apparent slowness in thought and movement is usually selective and occurs only when a patient is engaged in a compulsive ritual or rumination (Veale, 1993). In this case, the slowness in thought is secondary to the obsessive compulsive symptoms and occurs only when the individual is distressed by an obsession or has an urge to ritualise. On clinical grounds therefore, OCD patients should not show any neuropsychological evidence of slowness in thinking unless they were distracted by an obsessional thought or ritual. However, some OCD patients show evidence of neurological deficits which may contribute to their slowness in goal-directed behaviours and difficulty in suppressing perseverative behaviour (Hymas et al, 1991; Hollander et al 1990). In addition, the functional neuroanatomical theories and results of neuroimaging studies in OCD (discussed later in this introduction) point to a lesion in the caudate nuclei and fronto-striatal dysfunction. These findings would therefore predict that OCD patients will show evidence of slowness in thinking in tests of executive function. One aim of this study was therefore to determine whether OCD patients show any neuropsychological evidence of slowness in thinking similar to that found in other basal ganglia and fronto-striatal disorders or whether any deficits are secondary to

obsessive compulsive symptoms.

EVIDENCE FOR FRONTO-STRIATAL DYSFUNCTION IN OCD

I have made several references to a proposed fronto-striatal dysfunction in OCD and I will now describe the evidence:

i) OCD is associated with Tourette's syndrome and other basal ganglia disorders

There is a high incidence of OCD in specific basal ganglia disorders such as Tourette's syndrome (Cummings & Frankel, 1985). Between 20%-90% of patients with Tourette's syndrome have at least some symptoms of OCD depending on the population studied (Pauls et al, 1986; Karno et al 1988). Other basal ganglia or fronto-striatal disorders associated with an increased incidence of OCD include encephalitis lethargica (Kettl & Marks, 1986); Sydenham's Chorea (Swedo et al, 1989a); Huntington's disease (Cummings & Cunningham, 1992); idiopathic spasmodic torticollis (Bihari et al, 1992); and lesions of the basal ganglia (Laplane et al, 1989) or frontal lobes (Eslinger & Damasio, 1985).

ii Basal ganglia and frontal lobe dysfunction in neuroimaging studies

The most influential evidence for fronto-striatal dysfunction has come from neuroimaging studies.

Structural abnormalities in the brain were first reported by Luxenberg et al (1988). They found that the volume of the caudate nuclei as measured by computed tomography (CT) was significantly smaller bilaterally in 10 male patients with childhood onset OCD compared to 10 healthy matched controls. None of the patients was suffering from a depressive disorder and all had normal neurological examinations. The volume of the lenticular nuclei, thalami and ventricular brain ratio as measured by the CT scan did not differ in the two groups. The findings of smaller caudate nuclei in OCD patients on CT scan has been replicated in the UK in 12 OCD patients with matched controls by Freeman et al (personal communication).

Stein et al (1993) also compared 8 OCD patients with high scores on a soft neurological sign examination against ~~a patient~~ against 8 OCD patients with low soft sign scores and 8 control subjects on computed tomography. (A discussion on soft neurological signs is on page 46 of this introduction). Those OCD patients with high soft sign scores had significantly increased ventricular volumes compared with OCD patients with low soft sign scores and the control subjects. In this study the caudate and lenticular nucleus volume did not differ between groups. A criticism of this study is the small number of subjects (leading to a possible Type 2 error) and a

low reliability on the measures of caudate volume by two different raters. The study also did not match for other variables such as intelligence, alcohol and drug abuse or handedness.

In the only other study using CT scans, Behar et al (1984) reported that 16 adolescents with OCD had a significantly higher mean ventricular-brain ratio (VBR) than 16 matched controls. The control subjects did not display any change in consciousness, psychiatric symptoms or "hard neurological signs" but were suspected of having brain pathology as the reason for a CT scan. Their CT scans were described as not "questionable clinically" but the nature of the controls for this study is not ideal. Several of the OCD patients had "secondary" depression. The measures did not correlate with any of the measures of demography, symptom severity, or neuropsychological tests. Those with compulsions tended to have higher VBRs than those with obsessions only.

Studies using Magnetic Resonance Imaging (MRI) (Garber et al, 1989; Kellner et al, 1991) have not however found any structural abnormality in the caudate nuclei. The difference in the findings between CT (2 studies) and the MRI studies might have occurred because MRI may not be as good at viewing the encapsulated structures in the basal ganglia. The

technique for measuring the caudate nuclei also differs as the CT images calculate the volume, whereas on the MRI study by Garner, it is visually inspected from the scan. Alternatively the differences may be accounted for by different populations. For example, a population with more chronic symptoms might have a greater degree of atrophy in the caudate nuclei. The MRI study by Garber et al (1989) did however report prolonged T1 values (an estimate of cell density) in the right orbital frontal cortex, frontal white matter, the cingulate ~~nucleus~~ gyrus and lenticular nuclei in 36 OCD patients compared to matched controls. (A shorter T1 value putatively denotes either (i) a reduction in neuronal density, or (ii) a demyelinating condition, or (iii) decreased blood flow.) The findings of a prolonged T1 value in the orbital frontal cortex (a possible increase in blood flow) in Garber's study are however consistent with the results of studies using Positive Emission Tomography (PET) described below. The findings of a prolonged T1 value in the right orbital frontal cortex were not replicated in an MRI study by Kellner et al (1991) who found no differences between 12 OCD patients and 12 healthy controls in the measurement of the head of the caudate nucleus, cingulate gyrus thickness, intracaudate/frontal horn ratio or area of corpus callosum. Differences in populations studied may have accounted for the results.

A number of Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) scan studies have been published in patients with OCD. PET or SPECT are high-resolution imaging techniques in which tracer amounts of biochemicals of interest are labelled with unstable atoms that emit positrons (PET) or a single photon (SPECT), injected and subsequently localised in the brain. The main advantage of PET is that is has higher resolution than SPECT.

Baxter et al (1987) first used 18F fluorodeoxyglucose PET to study the local cerebral glucose metabolic rates of 14 OCD patients. When compared with a group of depressed patients and healthy controls, OCD patients had significantly increased local glucose metabolic rates in the whole supra-tentorial hemispheres, the left orbital frontal cortex and the heads of the caudate nuclei bilaterally. Since several of the original patients also met diagnostic criteria for depression or were taking anti-depressant medication and there was an unequal sex ratio across experimental groups, Baxter et al (1988) attempted to replicate their findings in 10 OCD matched patients who were not depressed. The results were similar to the previous study, as OCD patients had significantly increased glucose metabolic rates for the whole cerebral hemispheres, the orbital frontal cortex and heads of the caudate nuclei bilaterally compared to

healthy controls.

Nordahl et al (1989) studied a matched group of 8 non-depressed OCD patients and 30 controls during a continuous auditory discrimination task and found a bilateral increase in cerebral glucose metabolism in the orbital frontal cortex but not in either caudate nucleus. Small and unexplained reductions in metabolism occurred in the right parietal and left parieto-occipital regions.

Swedo et al (1989b) found that local cerebral glucose metabolic rates were significantly higher in the left orbito-frontal cortex, the prefrontal areas bilaterally, the left premotor area and the anterior cingulate bilaterally in 18 adults with childhood onset OCD compared to healthy controls. They had no concurrent depression or other anxiety disorders. The values for the caudate nuclei were no different to those of the controls. Patients who attempted to resist their obsessions and compulsions during the PET scanning showed a higher right prefrontal metabolic rate than those who did not and than those in the control group.

Martinot et al (1990) studied 16 OCD patients and 8 matched healthy controls. OCD patients had <u>reduced</u> cerebral glucose metabolism of global grey matter in

the whole cortex and in the prefrontal lateral cortex. However, the cerebral glucose metabolism values in the control group were higher compared to previous studies. There are also important differences in the populations studied. The patients in the study by Martinot et al:

a) were older and had a mean duration of illness of 18 years. They may therefore have been more chronically ill than subjects in previous studies.

b) may have been more depressed than the patients in other studies (the mean Montgomery Asberg Depression Rating score was 10.1). Depressed mood may decrease glucose metabolism values in the prefrontal lateral cortex although the results of cerebral blood flow in patients with a major depressive disorder are often variable.

Sawle et al (1991) studied 6 OCD patients with obsessional slowness and found an increased metabolism in orbital frontal, premotor and mid-frontal cortex. The Dopa uptake into the caudate, putamen and medial frontal cortex was normal. The premotor areas include the supplementary motor area, which is related to self-initiated movements. The area is strongly activated when healthy subjects are required to generate a motor sequence at will. This area is also less strongly activated in patients with Parkinson's

disease and classical bradykinesia (Passingham, 1987). It was previously noted that patients with obsessional slowness are often unable to move at normal speed when left alone yet may do so with an external pacer.

Two longitudinal treatment studies with PET and one with SPECT scans have been conducted. Hoehn-Saric et al (1991) studied 6 OCD patients before and after 4 months of treatment with fluoxetine. The treatment was associated with significant reductions in obsessive compulsive symptoms and in cerebral blood flow on SPECT in the medial frontal cortex (but not in the orbital frontal cortex).

Baxter et al (1992) report a decrease in cerebral glucose metabolism in the right head of the caudate nucleus (but not in the left orbito-frontal cortex) after 10 weeks treatment with either fluoxetine or behaviour therapy but only in those who improved. There was also evidence for significant correlations between the orbito-frontal cortex activity and both the caudate nucleus and the thalamus before treatment in treatment responders.

Swedo et al (1992) restudied 13 of their OCD patients from their 1989 study. They found that treatment with either clomipramine or fluoxetine had decreased the cerebral glucose metabolism in orbital frontal cortex

in OCD patients rescanned after treatment for at least 1 year. The decrease in orbito-frontal cortex was twice as great in the treatment responders (n=7) compared to those who had a poor response.

The treatment studies provide evidence for fronto-striatal dysfunction in OCD and suggest that:
a) the increase in cerebral glucose metabolic rates in the orbito-frontal cortex and caudate nuclei is state dependent, and
b) that changes in orbito-frontal cortex may only occur after more than 10 weeks of treatment.

McGuire et al (1994) have investigated the relationship between obsessive compulsive symptoms and regional brain activity in OCD by measuring cerebral blood flow while patients were experiencing the urge to ritualise. They studied 4 patients who were scanned on 12 occasions in the same session with each scan paired with brief exposure to one of a hierarchy of contaminants that elicited increasingly intense urges to ritualise by handwashing.

The patients showed significant positive correlations between symptom intensity and blood flow in the right inferior frontal gyrus, caudate nucleus, putamen, globus pallidus, and thalamus, and the left hippocampus and the posterior cingulate gyrus. They

proposed that the positive correlations in the orbito-frontal cortex, neostriatum, globus pallidus and thalamus are related to the urges to ritualise while those in the posterior cingulate cortex and the hippocampus may correspond to the anxiety that accompanies them. This is discussed in more detail later. They also reported negative correlations between the tempero-parietal junction and right superior prefrontal cortex. The region around the tempero-parietal junction is associated with attention to extra-personal space and lesions in this area are associated with visuo-spatial neglect. The authors speculate that decreased activity in these regions during an urge to ritualise might reflect a shift in attention from extra-personal space consequent upon the subject's preoccupation with an essentially internal experience and anxiety. They may also be related to the visuo-spatial deficits identified in neuropsychological testing discussed later in this introduction.

In summary, five of the seven PET scan studies with control subjects have reported an increased neuronal activity in the orbito-frontal cortex (Baxter et al, 1987; Baxter et al 1988; Swedo et al, 1989b; Nordahl et al, 1989; Sawle et al, 1991). One study has found a decreased metabolism in the orbital frontal cortex (Martinot et al, 1990). Two of the studies suggest an

additional abnormality in the premotor and mid-frontal cortex (Swedo et al, 1989b; Sawle et al, 1991). Two of the studies have found an increased metabolism in the caudate nuclei (Baxter et al, 1987; Baxter et al, 1988) and one in the cingulate cortex (Swedo et al, 1989b). The studies with longitudinal data suggest that the abnormalities are state dependent.

The differences in the results of the PET scans might be accounted for by differences in:

a) Scanner resolution. For example, Baxter et al (1987, 1988) used a camera with lower resolution than the one used by Sawle et al (1991). Swedo et al (1989) reconstructed their images to a higher transaxial resolution which reduces the signal to noise ratio and might have contributed to scattered areas of hypermetabolism through both hemispheres.

b) Scanning technique and methods of analysis. For example in Swedo's (1989b) study, the patients had their eyes blindfolded and their ears plugged, whereas the patients in Martinot et al (1990) were blindfolded but their ears were not plugged. Deprivation of audio-visual stimuli can significantly decrease hemispheric and regional cortical glucose metabolism (Mazziotta et al, 1982).

c) Populations studied. The differences in some of the studies may be accounted for by the heterogeneity of the disorder - for example patients with comorbid tic disorders may be more likely to show abnormalities in the basal ganglia. The duration of illness also varies between populations studied.

The neuroimaging findings may also be non-specific as symptoms of general anxiety might account for an increase in cerebral glucose metabolic rates in the orbital frontal cortex and further studies are required to compare OCD with other anxiety disorders. Future studies will need to detect changes in specific receptors (such as serotonin and dopamine) as imaging in glucose metabolism may not be sufficiently sensitive. There is however a degree of consistency throughout all the studies that some OCD patients have a smaller volume in the caudate nuclei and increased metabolism in the orbito-frontal cortex and in the caudate nuclei.

iii) Effect of psychosurgery

Psychosurgery can reduce the symptoms of OCD (Kettle & Marks, 1986). There are no controlled trials but the rates of improvement are between 60-80% in patients who have been unresponsive to other treatments. The

preferred operation is anterior capsulotomy or cingulotomy, which interrupts the connections between the anterior cingulate and the corpus striatum. Hassler (1981) reported that stereotactic lesions in the medio-dorsal and anterior nuclei of the thalamus, and their projections to the frontal cortex, may reduce the symptoms of both Tourette's syndrome and OCD. The results of psychosurgery are therefore consistent with fronto-striatal dysfunction as it directly interrupts the loop.

iv) Neuropharmacology of OCD

Evidence for involvement of serotonin receptors in the pathophysiology of OCD is based upon:

a) the modest improvement in symptoms (average 50% reduction) with the potent serotonergic reuptake anti-depressant (clomipramine) in about 50% of OCD patients compared to less than 5% with a placebo (Zohar & Insel, 1987). This compares with a placebo response rate of between 30 and 50% for studies in depression (Fineberg et al, 1992). Response rates of 50% have been also reported in patients taking a selective serotonergic reuptake inhibitors (fluvoxamine) compared to about 10% of OCD patients treated with a selective noradrenergic reuptake inhibitors (desipramine) (Goodman et al, 1990). The response may take up to 12 weeks to occur and there is a high rate of

relapse on discontinuation of the drug.

b) the use of serotonergic probes in OCD to study the behavioural and neuroendocrine response of serotonin agonists and antagonists. 1-[3-chlorophenyll]-piperazine (mCPP) is a serotonin agonist which has been used in a double blind placebo controlled study. m-CPP produced no noticeable effect in healthy controls while OCD patients became more anxious and had an acute transient exacerbation of their obsessive compulsive symptoms (Hollander et al, 1988). Pre-treatment with metregoline (a serotonin antagonist) one hour prior to m-CPP administration will abolish the behavioural response of OCD patients to m-CPP (Piggott et al, 1991).

Multiple types and sub-types of serotonin receptors and pathways make the notion of hyper or hyposerotonergic state too simplistic. There is however a high concentration of serotonergic neurons in:

(i) the basal ganglia (Steinbusch, 1981; Stuart et al, 1986) especially in the ventral-medial region of the caudate nucleus and the nucleus accumbens

(ii) in the dorsal raphe nuclei which innervate the prefrontal cortex and striatum

(iii) in the median raphe nuclei which innervate mainly the hippocampus and septum.

Down-regulation of the serotonergic receptors in the caudate nucleus may improve the sensory gating mechanism which is hypothesised as defective.

In Tourette's syndrome and Sydenham's Chorea, the dopamine receptors are thought to be hypersensitive with consequent hyperactivity of the basal ganglia and limbic dopaminergic systems. Treatment involves dopamine antagonists, such as haloperidol. Dopamine agonists (amphetamine or L-Dopa) have been reported to induce obsessional symptoms in healthy subjects (Jenike, 1984) and to improve them transiently in OCD patients (Insel, 1983). Dopamine antagonists alone are ineffective in OCD and there were no significant differences in dopa uptake between patients with obsessional slowness and healthy controls on PET scanning (Sawle et al, 1991). Dopamine antagonists in combination with a selective serotonin reuptake inhibitor (SSRI) appear to improve outcome in OCD patients who were unresponsive to an SSRI (fluvoxamine) alone especially in those who had a co-morbid tic disorder (McDougle et al, 1990).

v) OCD is associated with "soft" neurological signs.

Soft neurological signs are non-localising signs of an abnormal motor or sensory test in the absence of any focal neurological disorder which are thought to be related to disinhibition of the frontal lobe.

Hollander et al (1990) reported that patients with OCD have significantly more neurological soft signs compared to a matched control group. Similar findings have been documented in adolescents by Denkla (1988). If patients with obsessional slowness are a more severe variant of OCD then the neurological signs are more likely to be detected in sufferers. Using a questionnaire, Hymas et al (1991) (also discussed by Lees (1989)) selected twelve adult in-patients with OCD who were excessively slow in their self-care and daily activities. They all had several soft neurological signs including delay in initiating some voluntary movements; difficulty in switching from one motor programme to another; difficulty in carrying out two motor acts simultaneously; and general clumsiness and distractibility. The presence of neurological soft signs are consistent with the hypothesis of fronto-striatal dysfunction in OCD and disinhibition of the frontal lobe.

FUNCTIONAL NEUR0ANATOMICAL THEORIES OF OBSESSIVE COMPULSIVE DISORDER

I have discussed the normal neuroanatomical connections between the orbito-frontal cortex with the basal ganglia and the evidence for dysfunction in OCD patients. These findings have generated a number of theories about the anatomical localisation of OCD.

The posterior cingulate cortex and the hippocampus (identified in the PET scan studies by McGuire et al, 1994 and Swedo et al 1989b) are regarded as part of the "limbic" system and animal studies implicate these in the expression of anxiety (Gray, 1982). State anxiety and agitation in depressed patients correlates positively with cerebral blood flow in the posterior cingulate cortex (Bench et al 1993). McGuire et al (1994) have therefore proposed that the posterior cingulate cortex and hippocampus are associated with the anxiety that accompanies OCD when a patient is exposed to perceived contaminants. This hypothesis will require further testing in patients with other anxiety disorders without the urge to ritualise or in OCD patients who have no anxiety when they ritualise.

Gray (1982) was the first to propose a comparator model of OCD which has some similarities to that of the Supervisory Attentional System of Norman and Shallice (1980). He postulated that the septo-hippocampal system and associated

limbic areas function as a "behavioural inhibition system". This system has the task of predicting sensory events and checking whether they actually occur. The behavioural inhibition system is activated if there is a mismatch between the predicted and actual events (novelty) or if the predicted event is aversive or non-rewarding. Gray concluded that the role of the ascending serotonergic projections to the septo-hippocampal system from the dorsal and medial raphe nuclei is to add information that a stimulus is associated with punishment and to bias the operation of the septo-hippocampal system in favour of inhibition of motor behaviour. This would inhibit normal function, create anxiety and selectively focus attention on the potential danger. Obsessions and compulsions would be behaviours which have been activated by the behavioural inhibition system while normal functioning is inhibited. Gray believes that the perception of external signals is matched to predictions, rather than goals or intentions.

By comparison, Pitman (1987) suggested that obsessive compulsive symptoms resulted from an exaggerated, unsuccessful attempt to match a perceptual signal to an internal goal or plan. He proposed that the core problem in OCD is persistence of high error signals, or a mismatch that cannot be reduced to zero through behavioural output. There is a number of similarities between Gray's model of OCD and that of Norman and Shallice's Supervisory Attentional System (SAS)(1980). The SAS would be responsible for matching perceptual signals to the internal

goal in the frontal cortex and the response selection would occur at the level of the basal ganglia. According to Pitman (1987), the mismatch between perception and goals in OCD is subjectively manifested by pervasive doubt or incompleteness. The behavioural output stems from the basal ganglia leading to stereotyped behaviour as the innate motor programmes are repeatedly executed in a vain effort to reduce error signals. In Gray's view, septo-hippocampal (limbic) generated compulsions are a symptom of OCD whereas in Pitman's theory, the compulsions represent a potential but failed cure.

Wise & Rapaport (1989) have also proposed a model for OCD based on the basal ganglia being a repository of innate motor programmes and a gating mechanism for sensory input. They speculate that if specific sensory inputs (eg the perception of dirtiness) are sent from the orbito-frontal cortex (or anterior cingulate cortex or other cortical "association" areas involved in the perception of objects or sounds), they are transmitted to a cell in the caudate nucleus to inhibit a pallidal cell. This, in turn, would inhibit the thalamic cells and lead to disinhibition or release of the cortex and excitation of the motor systems. If the output of the circuit was blocked or dysfunctional then there would be a build up of basal ganglia activity and "sparking over" to collateral motor circuits into a ritual. This theory is similar to Gray's view and is simplistic but it has been developed by others. Some CT

scan studies (Luxenberg et al, 1988; Freeman et al, personal communication) suggest that the primary pathology may be in the caudate nuclei and that this could result in a secondary increase in fronto-orbital activity. The defective caudate may have to increase its activity in the remaining undamaged region to compensate. Modell et al (1989) and Baxter et al (1992) propose that defective caudate nuclei lead to inadequate filtering of "worry" outputs from the orbito-frontal region (see Figure 3 overleaf). The inadequate filtering at the caudate might include impulses such as aggression, hygiene, danger, sex - the content of obsessions that are normally inhibited by the caudate nucleus. This defect increases the inhibitory output to the globus pallidus. This in turn reduces inhibition to the thalamus thus making it vulnerable to being driven by the orbito-frontal cortex. The excitatory connections between the orbito-frontal cortex and the thalamus make it a potentially reverberating circuit and thus difficult to break. Orbital outputs may have an undue influence on the thalamus to other brain regions mediating other OCD symptoms that are not localized to the orbito-frontal cortex. Compulsions would be viewed as behavioural responses executed by the striatum in response to the sensations or impulses not being inhibited by the frontal lobe. Thus OCD patients cannot concentrate and pursue goal directed behaviour without these distractions. Conscious efforts to combat these impulses (e.g. superstitious thinking, consciously executed rituals, avoidance of

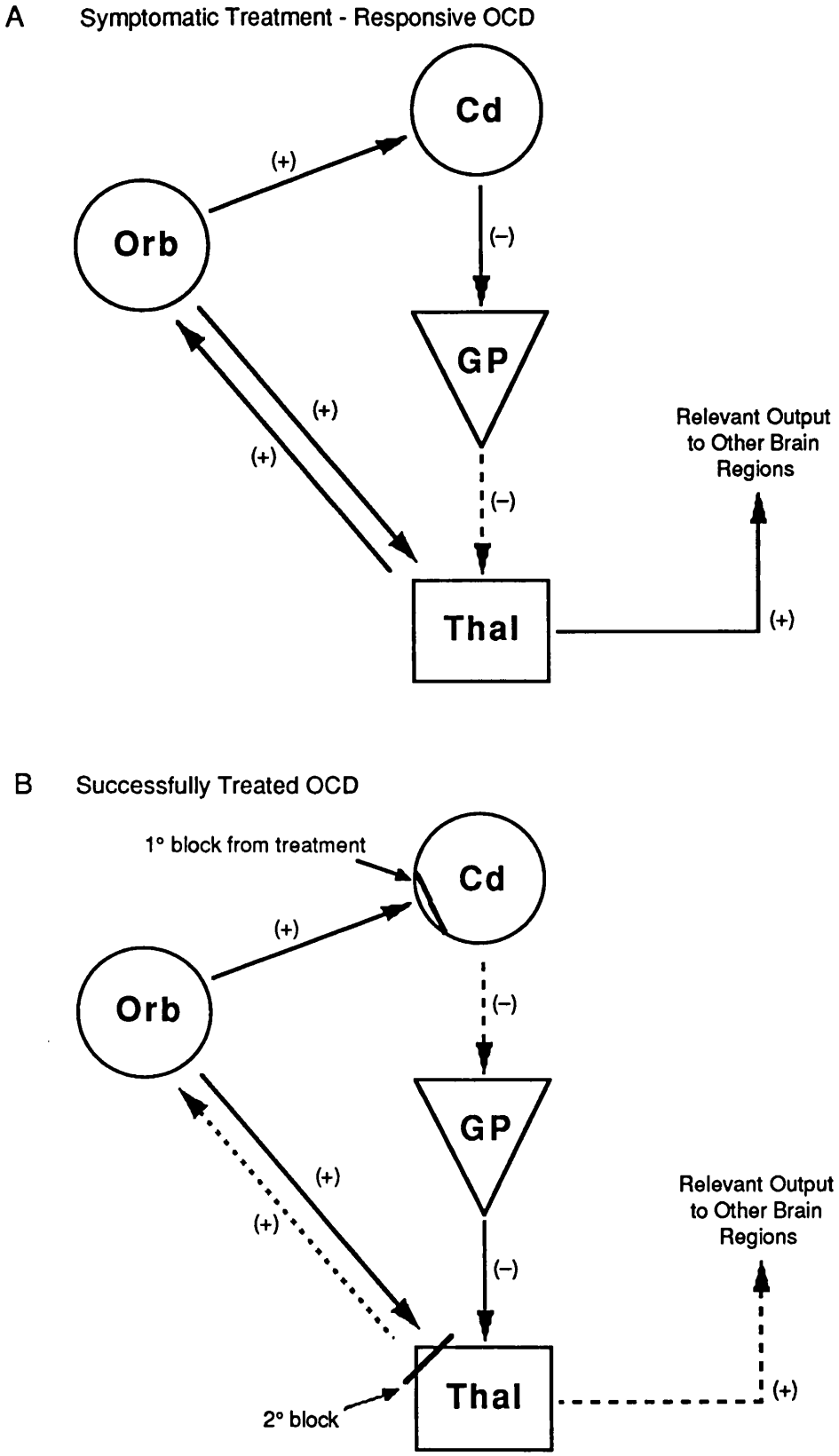


Figure 3: Arrows indicate the effect of stimulating one brain region at the rate of neuronal firing. (+) = excitatory; (–) = inhibitory. Broken lines represent reduced effect. Cd = head of caudate nucleus; GP = globus pallidus; Orb = orbital frontal cortex; Thal = thalamus.

triggers) are viewed as cortical responses to reduce the unwanted impulses and thoughts and are manifested by increased neuronal activity in the orbito-frontal cortex. OCD patients are therefore typically over-responsible, over-controlled in their proneness to violence or excessively clean. Of interest is that damage and reduced neuronal activity in this area can lead an individual to be disinhibited - displaying sexually inappropriate behaviour, being prone to violence and lacking concern for hygiene (Stuss & Benson, 1984).

Treatment would increase the "filtering" function in the caudate and reduce the inhibitory output to the globus pallidus, which in turn would increase inhibitory output to the thalamus. This would result in "uncoupling" of the "worry circuit" and allow a patient to terminate a compulsion more easily. The decrease in orbito-frontal activity with treatment might represent the subject's reduced effort or resistance to control intrusive thoughts.

Lastly, the striatum has a well described topographical organization that has been used to hypothesise the association between OCD, Tourette's syndrome (TS) and simple motor tics (SMT). According to a hypothesis proposed by Baxter et al (1991), striatal pathology would result in symptoms of OCD, TS, or SMT depending on which regions of the striatum are defective above a critical threshold value beyond which the system cannot compensate. (An analogy is

in Parkinson's disease in which the threshold of damage is approximately 70% of the dopamine system.) Pure obsessions (without compulsions or other motor abnormalities) are expected to show pathology over the critical threshold primarily in the ventral medial region of the caudate (which interacts with limbic cortex and limbic system.) Typical OCD would be expected to affect the ventral medial and the dorsal lateral region of the caudate. GMT patients would be expected to show above threshold pathology confined to the putamen. Patients with TS alone would be affected in the dorsal lateral caudate and putamen. Patients with mixed TS and OCD would show suprathreshold pathology throughout the striatum and overactivation in the various appropriate areas of the frontal cortex when attempting to suppress tics or compulsions. Such theories are attractive and may be susceptible to test with more detailed neuroimaging studies in the future.

NEUROPSYCHOLOGICAL TESTING IN OCD PATIENTS

There are twelve published studies that have conducted controlled neuropsychological testing of OCD patients. Patients are mostly matched for age and IQ with control subjects. Before discussing each study, I shall consider the interpretation of the results in general.

A reported cognitive deficit could either provide evidence for the neural substrate of the disorder (e.g. an impairment in set shifting used as evidence of fronto-striatal dysfunction) or it could occur as secondary to the disorder. For example, latency times on some tests may be delayed because of the occurrence of obsessional thoughts or fears of contamination that interfere with the procedure. These factors should be controlled for as far as possible. Alternatively, an impairment on a neuropsychological test may represent a strategy that has been adopted by the patient to deal with obsessions. For example, a patient may repeatedly check his performance in a test before he is satisfied that it is "right" and this may affect the latency time (as part of an obsessive compulsive personality disorder). Again these findings would be secondary to the disorder and could not be used as evidence of a neural substrate. The validity of using neuropsychological tests in this population is therefore questionable. There is however some consistency in the results which suggest that OCD patients are not uniformly

impaired on all tests, which would be expected if their performance simply reflected their obsessional symptoms (Head et al, 1989).

Conversely, a negative finding on a neuropsychological test is also not incongruent with an abnormal neural substrate. It may mean that the dysfunction is not sufficient to disrupt significantly the tasks mediated by the structures or that the test is not sufficiently sensitive. The neuropsychological findings may also give rise to theories of information processing as a primary cause of OCD.

In the first study, Flor-Henry et al (1979) administered a battery of neuropsychological tests based on the Halstead Reitan battery, to a series of 11 OCD patients who were matched for age and for IQ to 11 healthy control subjects. The mean of the control group was however 10 points higher on the WAIS full-scale IQ. 6 of the 11 patients had secondary depression and this may have influenced the results. The patients showed poorer performance on the Category test of the Halstead Reitan battery and on two sub-tests of the Wechsler Adult Intelligent Scale (WAIS), namely the Digit Span and Digit Symbol. The authors interpreted the results as suggesting bilateral frontal impairment with the <u>left</u> hemisphere showing greater impairment than the right. They suggested that this may account for obsessions: an inability to inhibit verbal representations. However the two sub-tests of the WAIS

(Digit Span and Digit Symbol) are not regarded as good tests of frontal lobe function. The one established measure on the WAIS of frontal lobe function (Verbal Fluency) did not show any differences and there was no correlation with findings on the EEG.

Insel et al (1983) were unable to replicate the findings of Flor-Henry et al (1979) in a sample of 18 OCD patients (11 males and 7 females) and no control group. They excluded patients with a "primary affective disorder". The OCD patients were compared to the tests' normative data. In only 1 test out of the 11 in the Halstead Reitan battery used in Flor-Henry's study, the Tactile Performance sub-test were abnormal. They noted that the mean verbal minus performance IQ on the WAIS was 12.7 (SD 9.1) from low scores on the Picture Arrangement, Block Design and Object Assembly sub-tests of the WAIS. These results may reflect impairment in visuospatial skills (and therefore right hemisphere dysfunction compared to Flor-Henry's interpretation of left hemisphere dysfunction). They suggested that the impairment in visuospatial skills could lead to the development of compulsive symptoms such as excessive vigilance and checking and that verbal strategies evolve as a coping mechanism to deal with spatial difficulties.

Behar et al (1984) compared 17 adolescents suffering from OCD with a matched control group of 16 subjects. The

patients had a mean full scale IQ of 108.2 (SD 13.5). The control group had a full scale IQ of 117.8 (SD 11.2) or 9.6 points higher compared to the patients and this was accounted for by sub-tests of visuospatial functioning. 16 of the 17 patients had a past history of major depressive disorder (MDD) and 3 out of the 17 patients had a MDD at the time of the testing. Both of these factors may have influenced the results. Patients had higher rates of errors and more frequent rule breaks on the Stylus Maze Learning test (Milner, 1964) (a test sensitive to frontal and temporal lobe impairment) and more errors on the Money Road Map test. Both tests measure visuo-spatial and set shifting ability. 6 of the patients showed an abnormal result in the Rey-Osterrieth Figure Copying test (which is a measure of delayed visual memory and visuo-spatial skills). Patients tended to use a disorganised and inefficient strategy when completing the task. There was no difference on the Rey Word Learning test (for delayed verbal memory), Dihaptic (tactual) testing (a measure of attention), and reaction time. The authors interpreted their findings as evidence of right hemisphere dysfunction and an impairment in visuo-spatial memory and rule following skills, namely an inability to rotate oneself mentally in space and to discern and follow rules and patterns during maze learning. The Stylus Maze Learning test and Money Road Map tests may be impaired in patients with frontal lobe lesions (Milner, 1964) or fronto-striatal dysfunction because of the demand for flexibility in following rules. They can also be failed

because of inability to attend to rules, visuo-spatial memory impairment (in parietal lobe lesions) or deficits in motor functioning. The tests for memory, reaction time and decision time were all normal in OCD patients compared to controls. There was no correlation with symptom severity or with neuroanatomical measure (on the ventricular-brain ratio).

Cox et al (1989) describe an extension to the study by Behar et al (1984). They compared 42 OCD adolescent patients and 35 matched controls according to age, sex, handedness and IQ ("within 15 points"). Patients with primary major depressive disorder were excluded but patients with secondary symptoms were included. OCD patients took significantly longer to reproduce the figure on the Rey-Osterrieth Complex Figures test (a measure of delayed visual memory and visuo-spatial skills). They scored significantly fewer card sorts on the Wisconsin Card Sort test (WCST) than control subjects but the number of perseverative and non-perseverative errors were no different to controls. The WCST is a classic frontal lobe test that is sensitive to frontal lobe pathology particularly when the damage is on the left side (Milner, 1964). (The interpretation of the WCST is discussed in more detail later in the introduction.) OCD patients were impaired on the Stylus Maze test and made more route-finding errors than controls. Symptom severity did not correlate with any of the measures on the Rey Osterrieth

Complex Figures test or the WCST.

Harvey (1986, original reference unobtainable but cited in Hollander et al, 1991) studied 19 OCD patients with no matched control group. They were impaired on the Modified Wisconsin Card Sort test (Nelson, 1976) with a tendency to perseverate which was related to the severity score on the Lepton Obsessional Inventory. No other details are given in the citation.

Head et al (1989) attempted to test the spatial skills and the ability to switch set in 15 OCD patients and 15 normal controls. They were matched for age, verbal IQ, years in education, and sex. The patients were drug free at the time of testing. There is no data on depression scores or diagnosis of comorbidity. They tested their visuo-spatial skills with the Line Orientation test (Benton et al, 1978) and the Block Design sub-test of the WAIS. They tested their set switching ability with the Modified Wisconsin Card Sort test (MWCST) (Nelson, 1976) and the Verbal Fluency test. The Verbal Fluency test is not usually regarded as a good measure of rule switching but is used as a test of frontal lobe dysfunction. Both spatial and rule switching ability were measured on the Money Road Map test (Butters et al, 1972), the Semmes Personal Orientation test (SPOT) (Semmes et al, 1963) and the Stylus Maze test (Milner, 1964). The results provided some evidence for a deficit in spatial skills and rule switching. The patients

made significantly more errors compared to the controls on one of the two spatial tests (WAIS Block design); and perseverative errors on one of the two rule shifting tests (MWCST). They scored normally on the Verbal Fluency and on one of the three spatial plus rule shifting tests (Money Road Map test). These results were with one tailed t tests at the 0.05 level and so were presumably insignificant with a two tailed t test (except on the MWCST for number of total errors which was significant at the 0.005 level). No data were provided on the relationship between symptom severity and neuropsychological measures.

Rosen et al (1988) (an abstract but cited with limited detail by Hollander et al (1991) studied 34 OCD patients and 14 normal controls. They were drug free for at least two weeks at the time of the study. The full-scale IQ in the control group was higher than the OCD group and the sex distribution was different and this may have confounded some of the findings. There was no concurrent diagnosis of major depressive disorder. They were matched for age and handedness. OCD patients were impaired on the Benton Visual retention test (a measure of visual delayed memory) and this correlated with the total number of neurological soft signs (r=0.49). There was no impairment on the Matching Familiar Figures test (a test of visual recognition and matching). OCD patients were slower on measures of interference on the Stroop Colour Word Interference test. This involves identifying the colour of the ink that a word

is printed on (e.g. green) while the word itself is a different colour name (e.g. red). This indicates difficulties in maintaining attention to the relevant stimulus.

Boone et al (1991) compared 20 non-depressed OCD patients and 16 matched control subjects for age and years in education (and not formal IQ testing). They were drug free for at least four weeks prior to testing. Women were however over-represented in the control group (9 female and 7 male) and men were over-represented in the patient group (11 male, 7 female). Patients were excluded if they had a Hamilton Depression score above 14. There were no differences in performance scores between unmedicated and medicated patients. OCD patients compared to controls did worse on some of the measures of visuo-spatial functioning. They had a lower performance IQ and lower scores on the Hooper Visual Organisation test (HVOT). Several items on this measure are thought to be sensitive to right frontal lobe lesions. OCD patients were also impaired on the copy measure of the Rey-Osterrieth Complex Figure test. There was no significant difference on other tests of visual delayed memory (Visual Reproduction sub-tests) or verbal immediate and delayed memory (WAIS Digit Span, or Wechsler Logical Memory). There were no differences on the Stroop Colour Word Interference test, Rey Tangled Lines, Wisconsin Card Sorting test, Auditory Consonant Trigrams, or Design Fluency. There was no significant correlation between

symptom severity and neuropsychological measures except a compulsion scale score and a visual memory measure. Patients with a family history of OCD were significantly worse on the tests of visuo-spatial functioning.

Zielinski et al (1991) compared 21 patients with OCD against 21 healthy controls. They were matched for age, sex, race, educational background and handedness. Patients with a major depressive disorder were excluded. The OCD patient group was unexpectedly significantly different on the Raven's Progressive Matrices with the patients making more errors but the distribution of errors appearing to be linked to a deficit in visuo-spatial functioning. They found no significant differences on measures of attention, verbal memory and learning (California Verbal Learning test (a measure of immediate verbal memory); fluency (Controlled Oral Word Association test; Design Fluency test) or on frontal lobe tests for rule shifting (Wisconsin Card Sort test). Tests of visuo-spatial functioning or visual memory were impaired on some measures of Kimura's Recurring Figures test (a visual memory task using geometric and nonsense drawings) with respect to false positives reported in immediate and delayed trials. There were also deficits on the Corsi Block Tapping test on measures of visuo-spatial sequences. This is a wooden board in which nine blocks are randomly arranged. The subject copies the examiner's tapping pattern which becomes increasingly complex. It was originally devised to test memory

impairment in patients with temporal lobe resections. It is considered as a test of immediate recall of sequences and visuo-spatial memory. OCD patients were impaired on spatial span and had difficulties learning a recurring visual sequence. There was no relationship between symptom severity and neuropsychological indices.

Christensen et al (1992) compared 18 patients with OCD and 18 controls matched according to age, sex and education. Patients were drug free for at least two weeks prior to participating in the study. Exclusion criteria included another DSM-III Axis I diagnosis. OCD patients were significantly impaired on the Wechsler Memory Scale Visual Reproduction tests (30 minute recall) but not on the design component of the Continuous Paired Associates test (a test of immediate non-verbal memory). OCD patients were impaired on one of the visuo-spatial tests (WAIS Block design) but not on the WAIS Object Assembly. No differences were found in tests of executive function (Category test, Controlled Oral Word Association test, the Design Fluency test or the Wisconsin Card Sort test) or on Verbal sub-tests of the WAIS.

Hollander et al (1993) studied 37 OCD patients and 35 patients with Parkinson's disease (PD). Because of the age difference, they were matched with their own group of healthy controls. There was no co-morbid depressive disorder or other anxiety disorder. OCD and PD patients

performed significantly worse than healthy controls on Block Design. There was no differences on the Digit span of the WAIS or the Stroop Colour Word Interference test in OCD or PD patients compared to their own controls.

Lastly Martin et al (1993), compared 17 OCD patients, 11 patients with trichotillomania, and 11 healthy controls. They were matched for age, sex and verbal WAIS IQ. Patients were medication free for 6 weeks at the time of testing. Martin et al found no differences on the WAIS Block Design (visuo-spatial and constructional ability), the California Verbal Learning test (verbal memory), the Money Road Map test (visuo-spatial and set-shifting ability), verbal fluency tests (set-shifting), simple and choice reaction times (motor speed and decision time), or visual search tests (visual processing speed).

The conflicting results in the studies may be accounted for by:

i) a failure to distinguish between subjects with OCD alone and those with OCD and OCPD (all studies). The presence of OCPD may contribute to the indecisiveness, procrastination and meticulousness in the execution of a neuropsychological test.

ii) a failure to exclude patients with concurrent depression (Flor-Henry et al, 1979; Insel et al, 1983; Behar et al, 1984).

iii) not using a control group which is well matched for IQ (Cox et al, 1989; Flor-Henry et al, 1979).

iv) not using a control group but comparing results against the test's data for a normal population (Insel et al, 1983; Harvey, 1986).

v) not controlling for fears of contamination from the equipment (all studies).

vi) not excluding patients who are dominated by obsessional ruminations that may interfere with the task (all studies).

vii) the heterogeneity in OCD patients. Some studies might contain a higher proportion of OCD patients with neurological deficits or more severe pathology in the fronto-striatal pathway.

None of the previous studies have attempted to compare sub-groups of OCD patients (eg checkers or washers). Few studies have examined chronicity of symptoms as a factor or sub-divided patients according to the presence of neurological soft signs or tics. Each of these sub-groups may have a different pattern of cognitive deficits which will lead to different results according to the population studied. Of particular interest would be the pattern of cognitive deficits in OCD (for example patients with obsessions only compared to obsessions and compulsions, Tourette's syndrome, or simple motor tics.) Lastly none of the studies have compared OCD patients with a control group of patients suffering from an anxiety disorder of

comparable severity which may be interfering with some tasks.

Summary of neuropsychological evidence in OCD

This section will summarise the existing neuropsychological evidence in patients with OCD under the following headings:

i) Learning and memory

ii) Visuo-spatial/constructional functioning

iii) Attentional ability

iv) Thinking time

v) Frontal lobe or executive functions

i) Learning and memory

Although there are, of course, many forms of memory, there is no consistent evidence to date of deficits in OCD on any verbal memory tests (immediate or delayed). The many tests which have been found to be normal include the California Verbal Learning test and the Controlled Oral Word Association test (Zielinski et al, 1991; Martin et al, 1993); the Rey Word List Learning test (Behar et al, 1984); the WAIS Digit Span, and the Wechsler Logical Memory (Boone et al, 1991, Insel et al, 1983). Only one study has found deficits on the WAIS Digit Span (Flor-Henry et al, 1979) whilst it was normal in all other studies.

Regarding visual memory, one study has found impairments on spatial span for the Corsi Block test

and Kimura's Recurring Figures test regarding the number of false positives for nonsense figures in both immediate and delayed recall (Zielinski et al, 1991). One study reported a delayed recall on the Rey-Osterrieth Complex Figures test (Boone et al, 1991) and another on the Benton Visual Memory test (Rosen et al, 1988). However, Boone et al (1991) found no differences on the Visual reproduction sub-test of the Wechsler Memory Scale. Christensen (1992) reported impairments on the delayed recall of the same test and no impairment on a test of immediate visual memory. It is however impossible to determine whether the deficits are due to limitations in visual memory or difficulties in visuo-spatial skills. For example, the Rey Osterreith test is based on a highly complex pattern that makes substantial demands on the perceptual and copying skills of a patient, as well as those of memory. The visual reproduction sub-test of the Wechsler Memory Scale almost certainly encourages verbal encoding and fail to allow the possibility of problems in spatial skills and drawing rather than memory (Baddeley et al, 1994).

ii) Visuo-spatial functioning

The most consistent findings are that patients with OCD have deficits in visuo-spatial skills compared to controls. There is evidence of lower scores on visuo-spatial tasks in OCD patients in the Hooper Visual

Organisation test, the Rey-Osterrieth Complex Figure test and Block Design sub-test of the WAIS (Boone et al, 1991; Behar et al, 1984; Cox et al, 1989; Hollander et al, 1990; Head et al, 1989; Zielinski et al, 1991; Hollander et al, 1993; Christensen et al, 1991); on Raven's Matrices (Zielinski et al, 1991) and on the Halstead Reitan Battery (Flor Henry et al, 1979). The impairment in visuo-spatial skills is reflected in a lower performance than verbal IQ amongst OCD patients (Insel et al, 1983; Swedo et al, 1989; Boone et al 1991). Only two studies found no impairment on some visuo-spatial skills on the WAIS Block Design (Martin et al, (1993) or the Line Orientation test (Head et al, 1989).

Overall, these results indicate either right hemisphere (parietal or frontal lobe) or basal ganglia dysfunction as visuo-spatial defects may be associated with lesions in the basal ganglia (Boller et al, 1984). Visuo-spatial deficits have also been reported in non-demented patients with Parkinson's disease (Pirozollo et al, 1982) and Tourette's syndrome (Golden, 1984) - both disorders of fronto-striatal dysfunction.

iii) Attentional ability

There are three main forms of attention. The first of these is selective attention - the ability to

selectively attend to one stimulus whilst simultaneously ignoring another. Sustained attention is the ability to maintain attention on a particular stimulus for a prolonged period of time. Lastly divided attention is the ability to divide attention equally between more than stimulus at a time.

OCD has been considered as a disorder of selective attention in which the focus is excessively narrow and intense (Reed, 1985). There is evidence that attention is excessively focused on threat and responsibility for the prevention of harm in OCD. For example, Foa et al (1993) used a modified Stroop Processing task which incorporated a semantic manipulation in OCD patients and matched controls. Subjects were asked to colour name contamination words, general threat words, neutral words and non-words. OCD washers had longer latencies to contamination words than to neutral words. This indicated that OCD patients process fear related words differently and maintain longer attention on them.

Performance on the Stroop Colour Interference task was abnormal in OCD patients compared to controls in one study by Rosen et al (1988) but normal in studies by Boone et al (1991) & Hollander et al (1993). Sustained attention has been found to be normal in OCD patients. On a continuous performance task, patients with OCD

were no different from their controls (Zielinski et al, 1991).

iv) Thinking time

None of the previous studies in patients with OCD has determined whether there is any slowness in thinking time. One study found no difference in reaction time on the two-flash threshold in patients with OCD (Behar et al, 1984). Simple and choice reaction time (which is a measure of motor and thinking time) or a visual search task was normal in the study by Christensen et al (1993) and Martin et al (1993).

v) Frontal lobe or "executive" functions

As I have already discussed, the frontal lobe is essential for tasks that require anticipation, reasoning, goal establishment, planning, the organisation of behaviour in time and space, and monitoring of feedback - terms that are subsumed under the heading "executive functions" (Baddeley, 1986). An inability to shift sets or to plan ahead are therefore characteristic of frontal lobe dysfunction (Shallice, 1982). Most of the evidence for impairment in frontal lobe or executive function has been derived from the Wisconsin Card Sorting test (WCST) (Grant & Berg, 1948) (to be discussed later) and a test of verbal fluency (Jones-Gottman and Milner, 1977). This involves a subject attempting to produce as many words

as possible from a given category such as animals or words beginning with F. Patients with frontal lesions, irrespective of laterality tend to have lower scores on the Verbal Fluency test; however patients with left frontal lesions appear to have more severe deficits than right. Patients may produce only three or four words in a minute, whereas a normal subject might expect to produce at least a dozen. The Verbal Fluency test is difficult for patients with frontal lobe lesions probably because there is no standard overlearned programme (or schema in the Norman and Shallice model (1980) for generating sequences of items from a category, with the result that the subject must set up and run his own retrieval strategies, at the same time monitoring that the items come from the correct category and are not repetitions (Baddeley, 1990).

Four studies have found no impairment for perseverative errors on the Wisconsin Card Sorting test in OCD (Cox et al 1989; Boone et al, 1991; Zielinski et al, 1991; Christensen et al, 1992) and on Verbal Fluency (Zielinski et al, 1991) One study has reported a significant difference of perseverative errors on the WCST by a one tailed t test but not on Verbal Fluency (Head et al, 1989). The WCST was also abnormal in one uncontrolled study (Harvey, 1986).

No differences between OCD patients and controls have been found on the following tests that are often abnormal in frontal lobe dysfunction:

(i) the Stroop test in two studies (Boone et al, 1991; Hollander et al, 1993) but abnormal in one (Rosen et al, 1989)

(ii) Auditory Consonant Trigrams (Boone et al, 1991);

(iii) Design Fluency test (Boone et al, 1991; Zielinski et al, 1991)

(iv) Verbal Fluency (Flor Henry et al 1979, Head et al, 1989; Martin et al, 1993).

(v) the Controlled Oral Word Association (Zielinski et al 1991) although this was impaired in the study by Head et al, (1989).

Several studies have found deficits in OCD patients compared to controls on a range of other tests that may be impaired in frontal lobe dysfunction. However patients will also fail these tests when there is impaired visuo-spatial functioning. These include:

(i) the Money Road Map test which was impaired in OCD patients in studies by Behar et al (1984), Cox et al (1989) and Head et al (1989) but not in the study by Martin et al (1993). Poor performance may reflect the visuo-spatial demand of making mental

rotations and a general difficulty in shifting mental set will also depress scores.

(ii) the Stylus Maze Learning test which was impaired in OCD patients in studies by Behar et al, (1984) and Cox et al (1989) but not in that by Head et al, (1989). In this test, the subject has to learn a spatial arrangement. Poor performance may be attributed to set-shifting difficulties, an inability to attend to rules, an impairment in visuo-spatial memory or motor functioning.

The results of neuropsychological testing of frontal lobe functioning in OCD are still congruent with the neuroimaging studies that have shown hyper-metabolism of the frontal lobes.

In summary, to date the results from tests of frontal lobe function in OCD have been inconsistent and difficult to interpret. The WCST is one of the most widely used tests of frontal lobe function but is criticised as involving many different cognitive processes (Downes et al, 1989). In the WCST, the subject is asked to sort correctly a deck of cards, according to one dimension (eg colour). Each card simultaneously varies in three dimensions (number,

shape and colour) and as each card is presented, the subject matches it to a set of reference cards based on one specified dimension. Once the subject has achieved a specified number of consecutive correct matches, he is asked to change the sorting principle without warning to one or the other previously irrelevant dimensions.

Categories of sorts received and the number of perseverative errors in sorting the cards are the two key measures on the WCST. Neurosurgical patients with frontal lobe excisions achieve fewer categories and make a greater number of perseverative errors than normal control subjects. The patients continue to sort cards according to a previous rule after they have been informed that the rule is no longer applicable. Successful performance on the task requires an ability to sort and form concepts; to shift sets; and to perform a matching to sample procedure. Failure may result from an inability to coordinate these different requirements or from a deficit in one of these components. The WCST also requires a strong visuo-spatial component that is known to be impaired in OCD (Boone et al, 1991). The WCST is now recognized not to be specific to frontal lobe dysfunction as patients with right temporal lobe and generalised brain damage have also been reported to be impaired (Robinson et al, 1980). Some "executive" functions may be impaired

after damage to the basal ganglia (Laplane et al, 1989). Lastly some patients with gross frontal lesions and behavioural abnormalities can function normally on the WCST (Shallice & Burgess, 1991).

The Tower of London task

In recent years, a number of new tests have been developed to investigate more precisely the role of the frontal lobes in normal cognitive functioning. Shallice & McCarthy (Shallice, 1982) have developed the Tower of London task which consists of a series of problems thought to depend more heavily on planning than on spatial processing abilities. The other advantage is that it can be broken down into several components. This is vital for a better understanding of the neuroanatomical loops between the basal ganglia and frontal cortex as it is presumed that the functioning of the loops will be impaired in different ways depending on the site of the pathology.

In the Tower of London task, the subjects are required to move equally sized coloured beads between three vertical rods to match a goal arrangement. Performance was rated according to the proportion of problems solved at the first attempt in less than 60 seconds. Patients with left anterior frontal lobe lesions were impaired compared to matched healthy controls. The deficit could not be explained regarding visuo-spatial factors. This was because the results were unchanged when the Tower of London task

performance was covaried with performance on the Block Design test (a sub-set of the Wechsler Adult Intelligence Scale that measures visuo-spatial functioning).

The Tower of London task has been computerised on CANTAB and used in patients with Parkinson's disease (Morris et al, 1988); neurosurgical patients with frontal lobe lesions, temporal lobe lesions, and amygdalo-hippocampectomy (Owen et al, 1990); autism (Hughes et al, 1994) and Dementia of Alzheimer's type (Sahakian et al, 1990). Patients with mild Parkinson's disease are unimpaired regarding the number of moves taken to solve a problem, but take significantly longer to think about the solution, prior to making the first move (Morris et al, 1988). This impairment in "Initial Thinking Time" may reflect one component of the clinical sign of bradyphrenia. By contrast, patients with frontal lobe lesions are less accurate in solving a problem and take more time thinking after the first move (Owen et al, 1990). This is termed the "Subsequent Thinking Time" and may reflect a different component of bradyphrenia. Similar impairments in accuracy or thinking time are not evident in either patients with temporal lobe lesions or amygdalo-hippocampectomy (Owen, 1992).

An impaired executive function has been investigated in several neurological or psychiatric disorders apart from frontal lobe lesions. These include schizophrenia

(Goldberg et al, 1987) and conduct disorders (Mattes, 1980) for which the Tower of London task is being applied. The contrast in the pattern of the deficits for these different disorders may help to determine the underlying neuropathology. The Tower of London task was therefore chosen in this study to determine whether patients suffering from OCD have a deficit in a specific component of their ability to plan and in their thinking time that is related to fronto-striatal dysfunction. More importantly, previous studies now make it possible to contrast the pattern of results in OCD with patients with Parkinson's disease, frontal lobe lesions, temporal lobe lesions, autism, and multiple systems atrophy (a condition involving diffuse sub-cortical damage that includes the basal ganglia).

Various deficits in planning have been linked to dysfunction in the fronto-striatal pathways or in the frontal cortex (Robbins & Sahakian, 1983). Unfortunately, it is not yet possible to link the results of the Tower of London task to specific neural pathways in animal studies as has been attempted with the attentional set shifting task. A PET scan has however been done in a single healthy subject in which areas 10 and 45 of the frontal cortex bilaterally were activated during the completion of the Tower of London task (Robbins, personal communication).

Attentional set shifting task

The Wisconsin Card Sort test measures the ability to shift set and maintain attention. Pure "set-shifting" ability may be more accurately assessed using a paradigm based on theories of intra- and extra-dimensional shifting (Downes et al, 1989). It is based on animal learning literature whereby if one dimension (eg colour or shape) of a compound stimulus is reinforced and the other is not, then humans and primates are able to attend to the reinforced dimension. An intra-dimensional shift (IDS) occurs when a subject is required to transfer to a new stimulus (eg from the colour "blue" to "red") but the dimension relevant to reinforcement continues to be relevant (eg the colour but not the shape). An extra-dimensional shift (EDS) occurs when the relevant dimension (eg the colour) is switched to the previously irrelevant dimension (eg the shape).

The WCST can be used to assess extra-dimensional shifting but it is less suitable for experimental analyses. Milner (1964) favoured the dorsolateral prefrontal cortex as the major focus for set shifting but Passingham (1972) found that "non-reversal" shifts were sensitive to damage in the orbito-frontal cortex, though using a flawed method for measuring the shifts, as pointed out by the author.

A computerised attentional set shifting task is available on the Cambridge Neuropsychological Test Automated Battery

(CANTAB) that is suitable for experimental analyses. It has been used in patients with Parkinson's disease (Morris et al, 1988); frontal lobe lesions, temporal lobe lesions, and amygdalo-hippocampectomy (Owen et al, 1990); and autism (Hughes et al (1994). In the CANTAB test, the subject learns a set of discrimination tasks in which one of two stimuli is correct and the other is not, based on feedback provided by the computer. It is designed to be a "purer" test of set shifting ability and removes the need to perform the matching to sample element that complicates the WCST. Because the test is presented in several stages, it enables more precise information on the locus of difficulty. The earlier stages of the test are a measure of simple discrimination learning and provide training for the subject before the intra-dimensional and extra-dimensional shift stage. Patients with frontal lobe lesions are impaired at the extra-dimensional shift stage but not at any other stage. By contrast patients with temporal lobectomy or amygdalo-hippocampectomy have an intact extra-dimensional shift stage (Owen et al, 1991). Patients with Huntington's disease are impaired only at the extra-dimensional set shifting stage (Sahakian, personal communication). The results in patients with Parkinson's disease are dependent on the stage of the disease - for example medicated (severe) Parkinson patients have similar deficits to neurosurgical patients with frontal lobe excisions. They are significantly more impaired at the extra-dimensional shift stage than a medicated (mild) group

and a non-medicated group (Downes et al, 1989; Owen, 1992). A significant proportion of non-medicated patients fail at the intra-dimensional shift and earlier stages of the test in which the patients are required to shift response set to new stimuli of the previously relevant dimension. This represents a more general attentional failure in which subjects are easily distracted. This might have occurred as a result of a diminished supervisory frontal lobe influence (Robbins & Sahakian, 1983). It is predicted from the model of the Supervisory Attentional System by Norman & Shallice (1980). Patients with early Dementia of Alzheimer's type (DAT) are unimpaired at either the IDS or EDS stage despite impairments in short-term visual memory. However patients at a later stage of DAT typically fail before reaching the Extra-Dimensional Shift stage (Sahakian et al, 1990). A successful Extra-Dimensional Shifting performance is assumed to depend on the integrity of the fronto-striatal pathways (Downes et al, 1989; Sahakian et al, 1990) and this has been formally tested in studies on non-human primates (Roberts et al, 1991).

The attentional set shifting task was therefore chosen in this study to determine whether patients with OCD show a deficit in set shifting ability that is independent of the ability to plan ahead and is related to fronto-striatal dysfunction. Again, the results will be contrasted with the pattern of deficit found in patients with Parkinson's disease, frontal lobe lesions, autism, multiple system

atrophy and in dementia.

COMPUTERISED NEUROPSYCHOLOGICAL TESTING

Mention has been made of two tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB). CANTAB is a series of computerised paradigms developed by Dr Barbara Sahakian, Dr Trevor Robbins, and colleagues at the Department of Experimental Psychology, University of Cambridge. These tests measure aspects of visuo-spatial memory, learning, attention and planning.

Computerised neuropsychological testing has several advantages over paper and pencil tests.

1) The presentation and feedback of the tests are uniform across subjects.
2) There is greater precision, reliability and speed of presentation of the test material and greater accuracy in recording responses.
3) Both response accuracy and reaction speed can be measured reliably.
4) There is an accurate running score as the test progresses. It allows progression onto the next stage following a certain level of performance.

The tests incorporate levels of difficulty that allow training and avoid ceiling/floor effects. Because of this they can assess a broad range of abilities and are not demoralising. In studies to date, including groups of

patients with Alzheimer's disease, there has been very good compliance.

The CANTAB tests have a strong theoretical basis. First, as argued cogently by David (1992), it is essential to be able to carry out a componential analysis of the processes comprising particular forms of cognitive function. Second, four of the CANTAB tests have been modified for humans from tests developed in rodent and non-human primate studies (delayed matching to sample test; spatial working memory; conditional associative learning; simple and choice reaction time). These considerations allow the results to be interpreted using concepts derived from human cognitive psychology and to be related to specific neural systems already implicated from animal lesion paradigms.

The tests have been used to study many groups of neurological and psychiatric patients. These include patients with Alzheimer's disease (Sahakian et al, 1988; Saghal et al 1991); Korsakoff and non-Korsakoff alcoholics (Joyce and Robbins, 1991); Parkinson's disease (Morris et al, 1988; Downes et al, 1989); frontal lobe excisions (Owen et al, 1990; Owen et al, 1991); depression in the elderly (Abas et al, 1990; Beats et al, 1994); supra-nuclear palsy and multiple system atrophy (Robbins et al, 1994). In addition studies are underway with, for example, patients with schizophrenia (Pantelis et al, unpublished), HIV (Green et al, unpublished) and undergoing kidney dialysis

(Saghal et al, unpublished). In many of these studies individual and group patterns of impairment have been shown, including double dissociations of cognitive deficits mediated by different neural substrates. This has allowed comparisons and inferences to be made in other groups of patients where the pathophysiological process is unknown.

In this study, two of the sub-tests on CANTAB were selected:

a) the Tower of London task which tests spatial planning

b) the attentional set shifting task that tests the ability to attend to specific dimensions of compound stimuli and to shift attention when required.

I have previously discussed the evidence that these tests are sensitive to fronto-striatal dysfunction. They were therefore chosen specifically:

(i) to determine whether OCD patients show deficits in spatial planning on the Tower of London task, and increased distractibility and perseveration on the attentional set shifting task as would be predicted by the functional neuroanatomical theories of OCD, and

(ii) to determine whether OCD patients show evidence of slowness in thinking similar to that found in basal ganglia disorders and fronto-striatal

dysfunction.

Previous studies have also not excluded the influence of Obsessive Compulsive Personality Disorder (OCPD) in neuropsychological testing. Patients with OCPD and OCD may have increased latency times compared to those with OCD alone because of their increased meticulousness and perfectionism. One of the aims of this study was therefore to determine the influence of OCPD in neuropsychological testing.

HYPOTHESES

The hypotheses in this study were that:

i) Patients with OCD would be slower but as accurate as healthy controls in completing the Tower of London task of planning compared to matched controls

ii) Patients with OCD would be impaired at the extra-dimensional set shifting stage and would be more easily distracted at the earlier stages compared to controls on the attentional set shifting task.

iii) Patients with OCD and OCPD would be slower and more accurate compared to patients with OCD alone on both the Tower of London task and the attentional set shifting task.

METHOD

POPULATION

About 80% of the subjects tested by the author were consecutive cases admitted under Professor Marks as in-patients in the behaviour therapy unit at the Bethlem Royal Hospital. About 20% of the subjects were random out-patients receiving behaviour therapy at the Maudsley Hospital. The unit is a secondary and tertiary referral centre and the sample is likely to be biased towards more severe cases of OCD. Data for the control group of healthy volunteers was obtained from medical and ancillary staff at the Maudsley Hospital. Subjects in both groups had to be aged between 18 years and 65 years but could be of either sex.

INCLUSION CRITERIA

All patients had to fulfil the diagnostic criteria for the DSMIII-R diagnosis of Obsessive Compulsive Disorder (American Psychiatric Association, 1987) (see Appendix 2).

EXCLUSION CRITERIA

Subjects were excluded from the study if they reported either:

i) fears of contamination (such as dust or radiation) from the computer screen, or

ii) obsessional thoughts or ruminations that interfere

with their concentration on the neuropsychological testing.

Concurrent psychiatric diagnoses from DSMIII-R that excluded the subject were:

a. Organic Mental Disorder
b. Mental disorders due to psychoactive substance use
c. Schizophrenia and delusional disorders
d. Major depressive disorder
e. Eating disorder
f. Learning disability or an IQ less than 85.

An additional diagnosis of another anxiety disorder, such as agoraphobia, was permissible.

CONSENT FORM

All subjects completed a consent form before the test that complied with the Ethical Committee of the Maudsley and Royal Bethlem Hospitals (Appendix 3).

PROCEDURE

Each subject was specifically asked at the beginning and after the procedure whether:

i) he or she had any fears of contamination by radiation, dust or dirt from the computer screen that might interfere with him or her touching the computer screen,
ii) he or she experienced any obsessional thoughts or

ruminations that was sufficient to interfere with his or her concentration on the task on the screen.

Both of these exclusions were based upon the patient's self-report. Each patient was then screened by a clinical interview to exclude a major depressive disorder or other psychiatric disorder according to DSMIII-R criteria.

ASSESSMENT MEASURES

The following data were recorded in respect of each patient at assessment:

1. Demographic data

The age and sex of each patient was recorded.

2. Drugs

The use of any psychotropic medication and alcohol. Eight patients were being treated with anti-depressant medication for their OCD before being admitted to the unit and being tested by the author.

3. Compulsive Activity Checklist

All patients completed the Compulsive Activity Checklist (CAC) (Marks, 1986). The check list is routinely used on the unit as an indicator of the severity of the disorder and as an outcome measure after behaviour therapy. Patients are asked to rate the severity of their handicap on a 4 point scale according to the time spent or the frequency of

behavioural repetitions or the degree of avoidance related to 37 everyday life situations. The CAC has been validated in patients with Obsessive Compulsive Disorder (Freund et al, 1987). It was found to be sensitive to change after treatment and to have satisfactory convergent validity with other measures. The questionnaire has also been used in a French population and found to be valid and sensitive to change although only moderately reliable (Cottraux et al, 1988).

4. Obsessive Compulsive Personality

All patients were interviewed with the relevant questions for the diagnosis of Obsessive Compulsive Personality Disorder from the Structured Interview for DSMIII-R Personality Disorders. The criteria for OCPD are listed in Appendix 1. Criteria related to other personality traits were not rated.

5. Intelligence Quotient

Estimates of premorbid and current verbal IQ were made.

i) Pre-morbid verbal IQ was estimated from the National Adult Reading Test (NART) (Nelson, 1982).

ii) The current verbal IQ of each patient was pro-rated from the Vocabulary and Comprehension sub-tests of the revised version of the Wechsler Adult Intelligence Scale (WAIS-R).

6. Cambridge Neuropsychological Test Automated Battery

All subjects were then assessed on two tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB).

i) the Tower of London Task which tests spatial planning

ii) the attentional set shifting task that tests the ability to attend to specific dimensions of compound stimuli and to shift attention when required.

The software was run on an Acorn BBC microcomputer fitted with a high resolution 14" colour monitor with a Microvictec (Touchtec 501) touch sensitive screen. The latter was used to monitor the speed and accuracy of the subject's responses to the stimuli appearing on the screen. At the start of each session, the subject was seated about 0.5 metres in front of the screen so that he or she could comfortably point to all areas. The subject was introduced to the touch screen by a simple pointing exercise. He or she was asked to respond to a series of flashing crosses on the screen by placing the index finger of the preferred hand on the centre point of each cross. The finger had to be held on the screen for 6 seconds, when the next cross appeared. Following a short demonstration by the author in which three consecutive crosses were touched, the subject was presented with a series of 10 crosses to touch at 6 second intervals. He or she then commenced the Tower of London task of planning.

a) Tower of London task

Two sets of three coloured balls are presented, one in the top half of the screen and one in the bottom half. These were described to the subject as snooker balls since they appeared to be hanging in "pockets" (Figure 4 overleaf).

There were three pockets in each half of the screen:

i) one that could clearly hold three balls,

ii) one that could hold two balls, and

iii) one that would be completely filled by just one ball.

On each trial, a red ball, a blue ball and green ball were placed by the computer in predetermined positions in the pockets of each of the two displays. The subject was asked to rearrange the balls in the bottom display, such that their positions matched the pattern in the top half of the screen. The subject was informed how many moves were required to complete the match (i.e. the subject was told that it was either a 2, 3, 4 or 5 move problem). This reflects the graded levels of difficulty within the task. The subject was told to plan the solution before making the first move. A ball could be moved by first touching it and then touching an empty position in one other pocket. Once selected a tone sounded and the rim of the ball began to flash, indicating that the ball was ready to move. At any time, the subject could cancel a selected

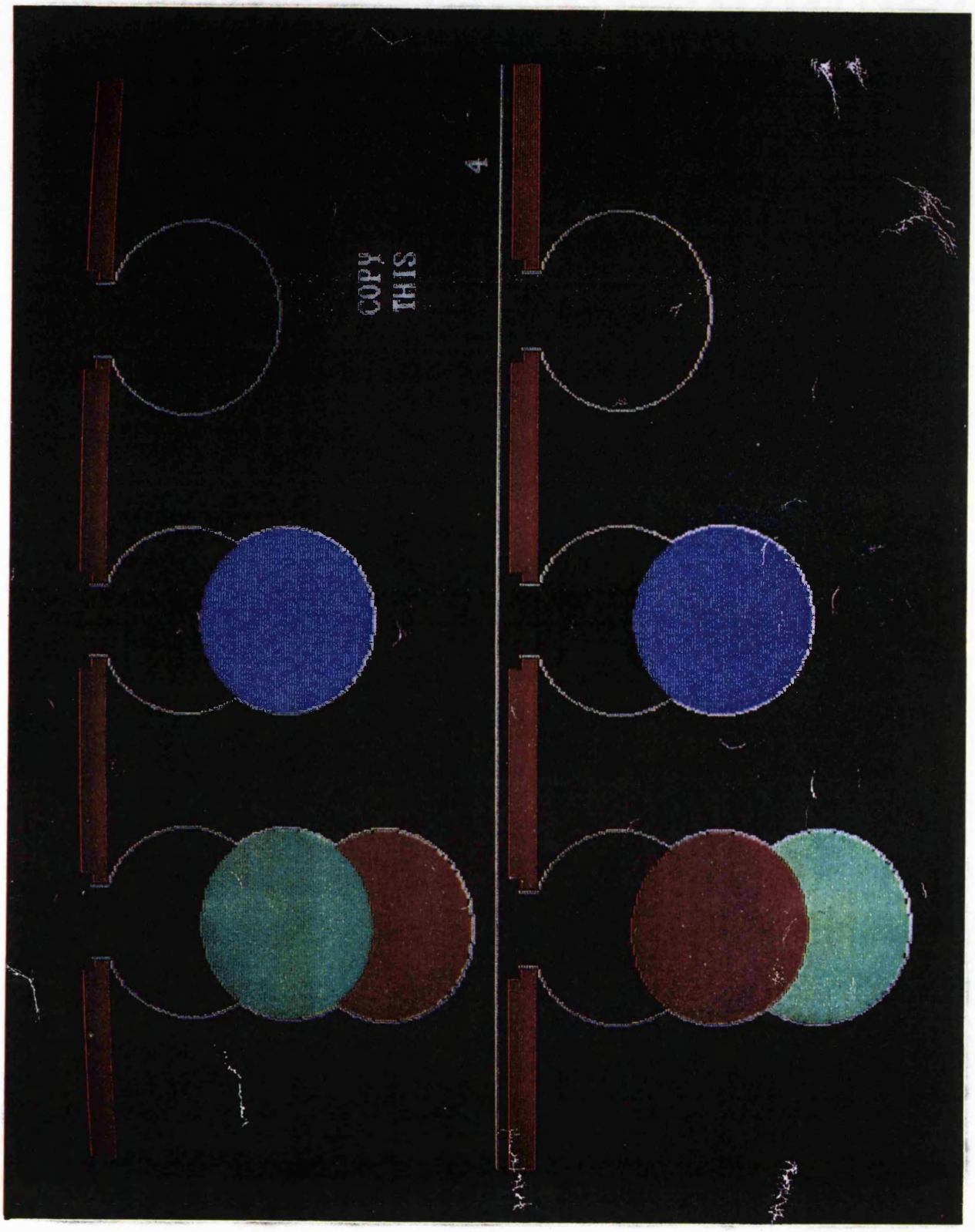


Fig. 4

ball by touching it a second time. "Illegal" moves, such as trying to place a ball high in a pocket when there was no other ball beneath it, or trying to remove a ball while there was another sitting above it in the same pocket, were carefully explained to the subject. If an illegal move was attempted they were registered, but evoked no response from the computer. The aims of the test were to copy the pattern correctly in the minimum number of moves necessary (as rapidly as possible). After six practice trials with one and two move problems, the subject was given two each of two and three move problems and four each of four and five move problems (making a total of 12 trials).

In a yoked control condition, the computer "plays back" the solution to each problem using the sequence of moves actually used by the subject, one move at a time. The number of trials in the yoked condition is the same as in the original condition (12 trials). The subject simply has to copy each individual move, without of course having to plan them as part of a sequence. This derives the measure for the "Initial" and "Subsequent Movement Time". Subtraction of the latencies to move the balls in this yoked control condition from the overall latency provides a measure of "Initial" and "Subsequent Thinking Time".

The main dependent variables for the statistical analyses were:

i) The mean number of moves taken to solve the problems, which provides a general measure of accuracy at each level of difficulty

ii) The proportion of problems solved in the minimum number of moves possible (or "perfect solutions"), which provides more specific information about accuracy of the solution

iii) The proportion of problems solved in the maximum allowed number of moves, which provides an index of the ability to solve the problem, irrespective of the quality of performance. This is the crudest measure of accuracy.

iv) The Initial Thinking Time. (The time taken between the presentation of the problem and the first touch, minus the corresponding motor initiation time, as calculated from the "yoked control" tests.)

v) The Initial Thinking Time for perfect solutions only. (This is the same calculation as the initial thinking time but only for those solutions where the problem is correctly solved in the minimum number of moves possible.)

vi) The Initial Movement Time. (This represented the mean time between the onset of each problem and the completion of the first selection, that is, a correct touch of the required ball. The

movements are yoked to test problems, which results in an average movement time per move.)

vii) The Subsequent Thinking Time. (The average time taken between the selection of the first ball and the completion of the problem minus the total motor execution time derived from the corresponding control problem.)

viii) The Subsequent Thinking Time for perfect solutions only. (The same calculation as for the subsequent thinking time but only for those solutions where the problem is correctly solved in the minimum number of moves possible.)

ix) The Subsequent Movement Time. (The average time taken between touching the first ball and completing the sequence of single moves that comprise the whole problem. The movements are yoked to the test problems, so that the total time was divided by the number of moves to give an average movement time to make each subsequent move.)

Any negative values from the subtraction of time from the movement time in the yoked control task were corrected to zero (assuming minimal thinking time) although this was not a common occurrence.

After completing the Tower of London task, subjects performed the attentional set shifting task on the same computer equipment.

b) Attentional set-shifting task

This test examines the patient's ability to attend to specific dimensions of compound stimuli and to shift attention when required. Four rectangular boxes, to the top and bottom and to the right and left of centre appeared on the screen (Figure 5 overleaf). Two of these contained the test stimuli and the boxes used changed from trial to trial.

Subjects were instructed by the author in the following way: "Now you can see patterns. One pattern is correct and the other is wrong. What you have to do, is point to the one you think is correct. There is a rule that you can learn and follow, to make sure you make the correct choice each time. When the computer is sure you know the rule, because you keep on getting it right, then the computer will change the rule, but this will not happen very often. When the rule is changed you will have to think of a different rule to go on doing well. This first time, you'll have to guess, of course, so just have a go." If necessary the instructions were repeated or clarified to ensure that the subject had a clear idea of what was required.
The test then proceeded with a series of stages, each with a different contingency, up to a maximum of 9 (Figure 6, overleaf). For each, continuation to

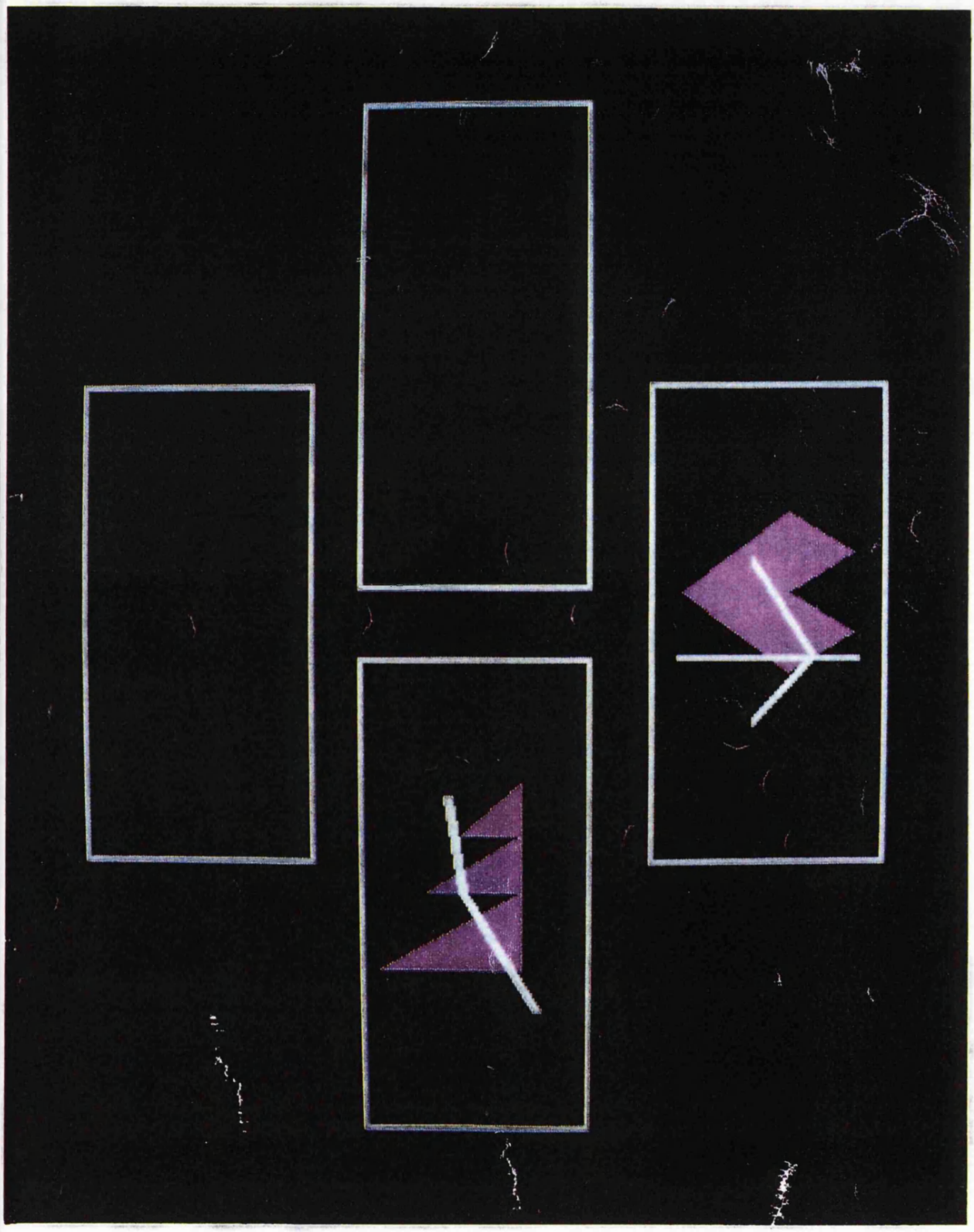
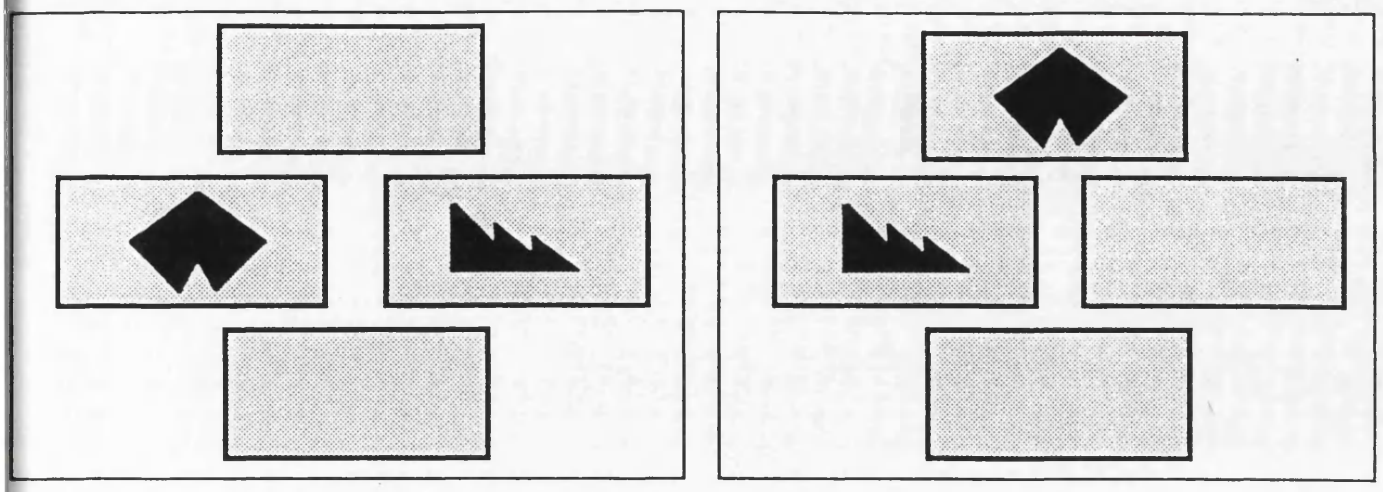
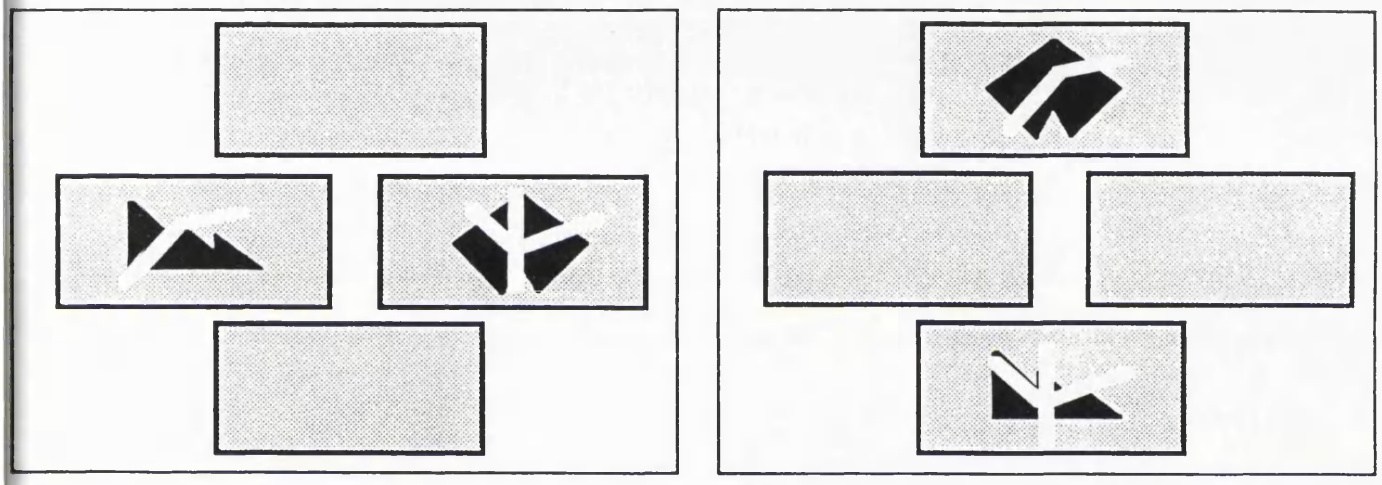


Figure 5

Simple discrimination and reversal



Compound discrimination and reversal



Intra-dimensional or Extra-dimensional shift and reversal

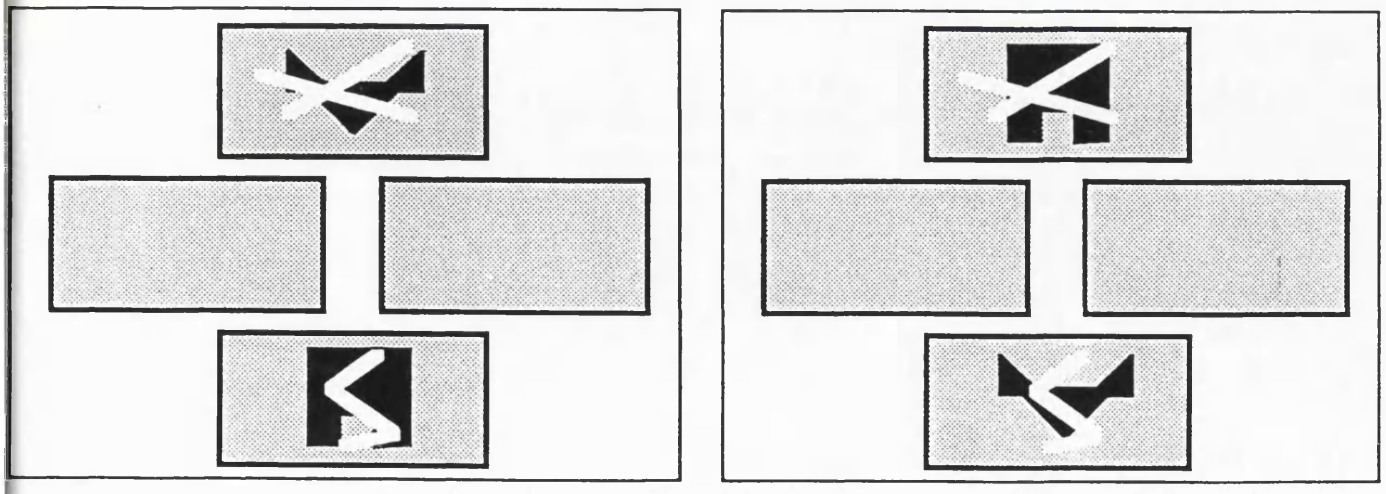


Figure 6

the next trial was dependent upon a criterion of six successive correct discriminations being reached. If the criterion was not reached at the fiftieth trial of a stage then the test was stopped automatically by the computer at that stage and subjects did not go to the subsequent, more difficult stages.

Initially, subjects were given a simple simultaneous discrimination (SD) in which the stimuli varied along only one "dimension" to derive the stimuli. These dimensions were purple-filled shapes or white lines. The starting dimension was balanced across subjects and groups so each subject commenced the test with either the purple shapes or the white lines. A response to one of two boxes containing the stimuli resulted in an auditory tone, with visual feedback which told the subjects the correctness of their response. This was as the words "correct" or "wrong" presented respectively in green and red lettering above the middle two boxes. After 1.5 seconds the screen cleared and an inter-trial interval of 1 second was begun.

Following the initial simple discrimination (SD), the remaining eight stages were as follows. For the second stage (SR), the dimension remained the same, but the previously incorrect choice became the correct one, that is the contingencies were reversed.

At the third stage (C_D), the second dimension was introduced as an irrelevant distractor with one exemplar of each dimension paired together to give a compound stimulus in two of the response boxes. To succeed, subjects had to continue responding to the correct exemplar of the previous stage. For this and all subsequent stages, exemplars of the different dimensions were paired in a pseudo-random fashion with the constraint that runs of no more than 3 trials with the same pairings were allowed. The stimuli for the fourth stage (CD) and subsequent stages were also compound but the two exemplars from the different dimensions were superimposed with the white line always in the foreground. The contingencies again remained unchanged from those for the previous two stages. A reversal then occurred at the fifth stage (CDR). New exemplars for both dimensions were introduced at the sixth stage, the intra-dimensional Shift (IDS), but the relevant dimension was unchanged from the original (by using a different patterned purple shape or white line). This was succeeded by a further reversal at the seventh stage (IDR). For the penultimate stage, the extra-dimensional Shift (EDS), new exemplars were again introduced, but success at this point was dependent on the subject shifting response set to the exemplars of the previously irrelevant dimension. Finally contingencies were reversed to the now correct (but previously incorrect)

exemplar of the new dimension (EDR). The order of discrimination was fixed, so that the extra-dimensional Shift (EDS) always followed the intra-dimensional Shift (IDS).

The main dependent variables for the statistical analyses are:

i) the number of stages that the subject successfully completed,

ii) the number of trials the subject had to make before reaching the criterion of six consecutive correct choices at both the intra-dimensional Shift stage (IDS) and the extra-dimensional Shift stage (EDS). (If the subject did not successfully complete either the IDS or the EDS stage then the number of trials was coded as the maximum number of trials permissible (50).

iii) the response latency (in seconds), which is the mean choice time for both the correct and incorrect choices at both the intra-dimensional shift stage (IDS) and at the extra-dimensional shift stage (EDS).

STATISTICAL ANALYSES

The data were analyzed using the Statistical Package for Social Sciences (SPSS-PC) on an IBM-PC compatible computer. The age and verbal IQ of the two groups was compared by a one way analysis of variance (ANOVA). The sex distribution

was analyzed by a Chi-square test. Data from the Tower of London task were compared by analysis of variance (ANOVA) with repeated measures for a two factor design - a ~~within~~ between subjects factor (group) and a ~~between~~ within subjects factor (difficulty level). There was no transformation of the data. The likelihood ratio method of contingency tables (sometimes called "the information statistic") (Kullback, 1968; Robbins, 1977) was used for the small cell frequency in the rule following task. The Pearson product moment correlation coefficient (Winer, 1971) and the Spearman rank order correlation coefficient was calculated for correlations between the severity of the symptoms of OCD and the data from the Tower of London task.

RESULTS

Forty-nine patients were recruited to the study of which nine patients were excluded. One patient was excluded because she reported a fear of contamination from the radiation of the computer screen; two because of a fear of contamination from dust on the computer screen; six because they suffered a major depressive disorder. These subjects did not participate further and no data were recorded for them. Clinical descriptions of the patients are recorded in Appendix 4. These were collected retrospectively from the medical notes. The data were regrettably not recorded systematically and no standardised clinical interview or physical examination was used.

1) Tower of London task of planning

There were 40 patients with OCD and 22 healthy controls for comparison. One way analysis of variance confirmed that the two groups were well matched regarding mean age (Table 1, overleaf) and mean NART verbal IQ (Table 2, overleaf). There was no significant difference between the estimated Verbal IQ from the NART or the WAIS Verbal IQ. Although the sex distribution appears slightly biased in favour of males in the control group (Table 3, overleaf), a Chi-Square test confirmed the two groups were matched (Chi-Square = 2.79, $P < 0.10$). Sex differences have also not been found to be significant on the Tower of London planning test in previous studies (Robbins, personal communication).

The mean score on the Compulsive Activity Checklist was 35.1 (SE = 2.55) which suggests that the OCD patients were significantly handicapped.

TABLE 1: MEAN AGE OF PATIENTS AND CONTROLS IN TOWER OF LONDON TASK

	PATIENTS	CONTROLS
Number	40	22
Age	36.10	32.23
(S.E.)	(1.76)	(2.21)

ANOVA F-ratio (1,62) = 1.81 P < 0.18

TABLE 2: MEAN VERBAL IQ OF PATIENTS AND CONTROLS IN TOWER OF LONDON TASK

	PATIENTS	CONTROLS
Number	40	22
NART Verbal IQ	109.9	109.2
(S.E)	(1.62)	(1.87)

ANOVA F-Ratio (1,62) = 0.06 P < 0.80

TABLE 3: NUMBER OF PATIENTS AND CONTROLS BY SEX IN TOWER OF LONDON TASK

	PATIENTS	CONTROLS	TOTAL
Male	17	15	32
Female	23	7	30
Total	40	22	62

Chi-Square = 2.79 (after Yates Correction) P < 0.10

In the Tower of London task, there was no significant impairment in the mean number of excess moves that the patients took to solve the problems (Table 4).

TABLE 4: MEAN NUMBER OF EXCESS MOVES TAKEN TO SOLVE PROBLEM BY DIFFICULTY OF PROBLEM IN PATIENTS AND CONTROLS

DIFFICULTY OF PROBLEM	PATIENTS	CONTROLS
2 MOVE	0.0	0.0
(S.E)	(0.0)	(0.0)
3 MOVE	0.2	0.1
(S.E)	(0.06)	(0.05)
4 MOVE	1.5	1.3
(S.E)	(0.15)	(0.2)
5 MOVE	1.6	1.4
(S.E.)	(0.19)	(0.2)

ANOVA	F-Ratio	df	Probability
By group	1.33	(1,62)	0.25
By difficulty	70.05	(3,62)	0.000*
Group by difficulty	0.37	(3,62)	0.76

Both patients and controls solved the same proportion of problems in the minimum number of moves possible (Table 5 - overleaf). Both groups solved the same proportion of problems in the maximum number of moves permissible (Table 6). This suggests that regardless of the measure of accuracy, the patient group was unimpaired. For all of the analyses on accuracy, there was a significant main effect in terms of task difficulty (i.e. whether the problem required 2,3,4 or 5 moves to solution) but no interaction between the group and difficulty factors.

TABLE 5: PROPORTION OF PROBLEMS SOLVED IN MINIMUM NUMBER OF MOVES IN PATIENTS AND CONTROLS

DIFFICULTY OF PROBLEM	PATIENTS	CONTROLS
2 MOVE	1.0	0.95
(S.E)	(0.0)	(0.05)
3 MOVE	0.85	0.84
(S.E)	(0.05)	(0.06)
4 MOVE	0.59	0.68
(S.E)	(0.04)	(0.05)
5 MOVE	0.58	0.61
(S.E)	(0.04)	(0.06)

ANOVA	F-Ratio	df	Probability
By group	0.27	(1,62)	0.61
By difficulty	37.65	(3,62)	0.00*
Group by difficulty	1.01	(3,62)	0.39

TABLE 6: PROPORTION OF PROBLEMS SOLVED IN MAXIMUM NUMBER OF MOVES ALLOWED IN PATIENTS AND CONTROLS

DIFFICULTY OF PROBLEM	PATIENTS	CONTROLS
2 MOVE	1.0	1.0
(S.E)	(0.00)	(0.0)
3 MOVE	0.77	1.0
(S.E)	(0.03)	(0.0)
4 MOVE	0.77	0.82
(S.E)	(0.03)	(0.04)
5 MOVE	0.9	0.93
(S.E)	(0.02)	(0.03)

ANOVA	F-Ratio	df	Probability
By group	1.57	(1,62)	0.22
By difficulty	37.70	(3,62)	0.000*
Group by difficulty	0.61	(3,62)	0.61

There was no difference between OCD patients and controls in the initial thinking time (Table 7 and Figure 7 overleaf). There is a however a non-significant trend for the patients to appear slower especially on the 3 move problems).

TABLE 7: MEAN INITIAL THINKING TIME IN SECONDS IN PATIENTS AND CONTROLS

DIFFICULTY OF PROBLEM	PATIENTS	CONTROLS
2 MOVE	2.94	2.72
(S.E)	(0.59)	(0.60)
3 MOVE	11.94	6.94
(S.E)	(1.87)	(1.17)
4 MOVE	12.32	9.53
(S.E)	(1.70)	(1.52)
5 MOVE	14.58	14.12
(S.E)	(2.39)	(3.26)

ANOVA	F-Ratio	df	Probability
By group	1.31	(1,61)	0.26
By difficulty	16.62	(3,61)	0.000*
Group by difficulty	0.90	(3,61)	0.44

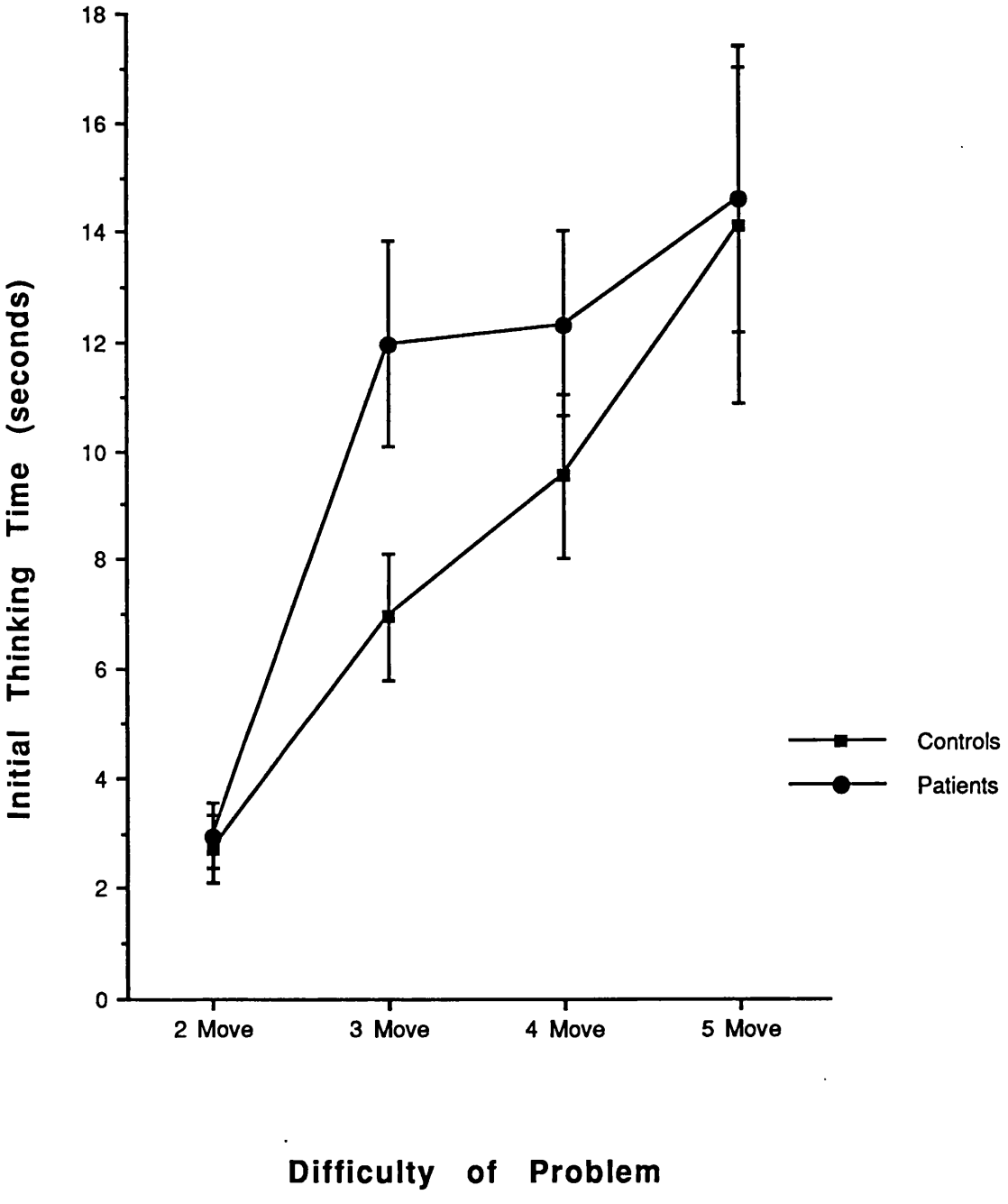

Initial Thinking Time (seconds)
18
16
14
12
10
8
6
4
2
0
2 Move
3 Move
4 Move
5 Move
Controls
Patients
Difficulty of Problem

Figure 7

Latencies were then reanalysed for perfect solutions only and there was still no significant difference between the groups for the initial thinking time (Table 8).

TABLE 8: MEAN INITIAL THINKING TIME IN SECONDS FOR PERFECT MOVE SOLUTIONS IN OCD PATIENTS AND CONTROLS

DIFFICULTY OF PROBLEM	PATIENTS	CONTROLS
2 MOVE	2.94	2.74
(S.E)	(0.59)	(0.60)
3 MOVE	9.66	6.88
(S.E)	(1.16)	(1.18)
4 MOVE	12.15	8.47
(S.E)	(1.69)	(1.37)
5 MOVE	14.78	10.26
(S.E)	(2.43)	(1.68)

ANOVA	F-Ratio	df	Probability
By group	2.77	(1,61)	0.10
By difficulty	15.44	(3,61)	0.000*
Group by difficulty	0.77	(3,61)	0.52

The patients were markedly slower in their subsequent thinking time on the Tower of London ($F(1,61) = 8.33$, $P < 0.005$) (Table 9 and Figure 8 - overleaf) when all the problems were considered. There was a significant effect of task difficulty and the interaction between the group and task difficulty factors was significant ($F(3,61) = 2.59$, $P < 0.05$). The main effects analysis revealed that the deficits were at the 4 move problem.

TABLE 9: MEAN SUBSEQUENT THINKING TIME IN SECONDS PER MOVE IN OCD PATIENTS AND CONTROLS

DIFFICULTY OF PROBLEM	**PATIENTS**	**CONTROLS**
2 MOVE	0.98	0.41
(S.E)	(0.52)	(0.14)
3 MOVE	1.13	0.49
(S.E)	(0.27)	(0.15)
4 MOVE	5.51	2.41
(S.E)	(0.84)	(0.51)
5 MOVE	2.67	1.47
(S.E)	(0.45)	(0.35)

ANOVA	**F-Ratio**	**df**	**Probability**
By group	8.33	(1,61)	0.005*
By difficulty	17.15	(3,61)	0.00*
Group by difficulty	2.59	(3,61)	0.05*

MAIN EFFECTS ANALYSIS

Difficulty of problem

2 MOVE $F(1,61) = 0.23$

3 MOVE $F(1,61) = 0.28$

4 MOVE $F(1,61) = 6.87$ $p < 0.01$

5 MOVE $F(1,61) = 1.04$

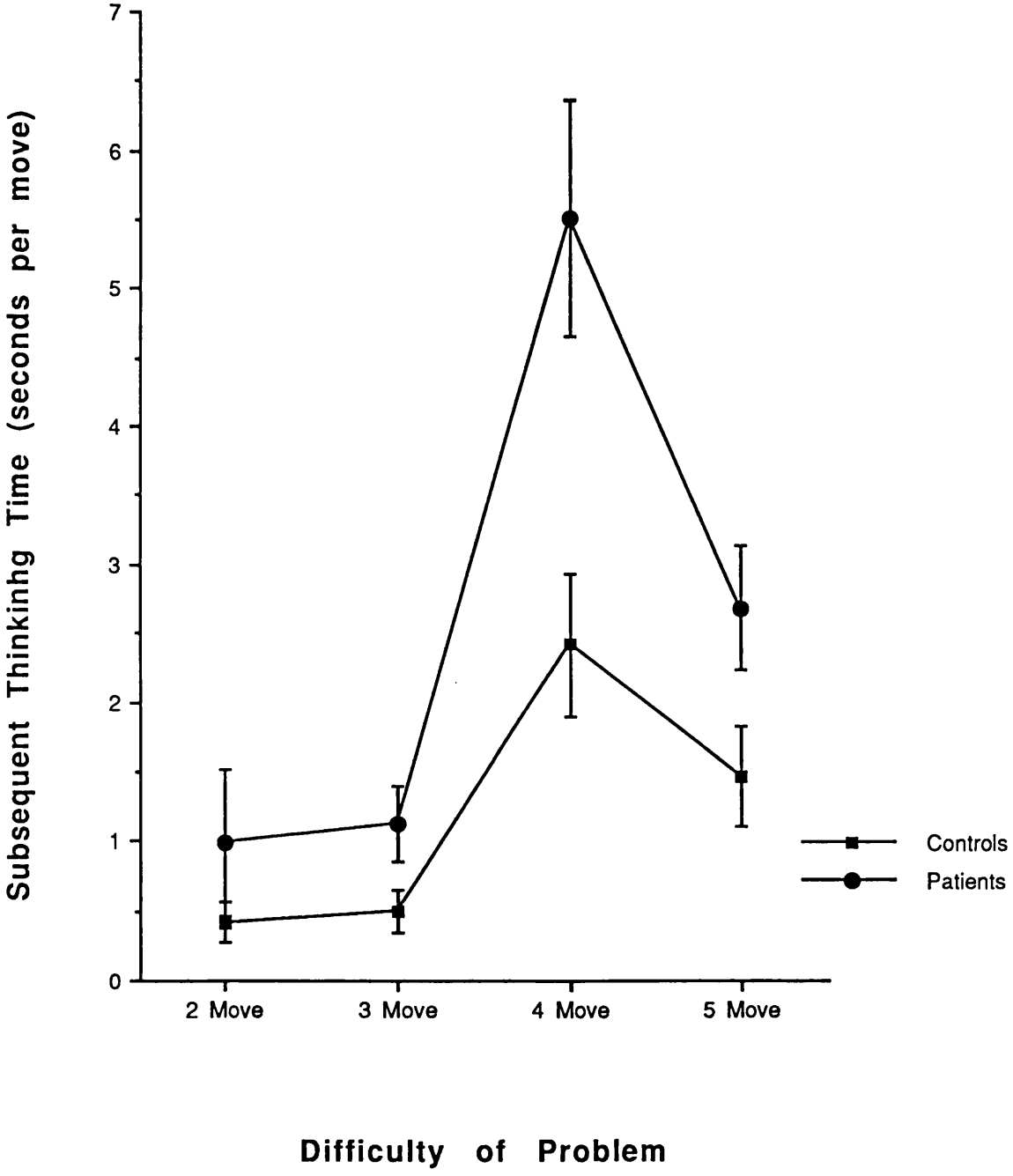

Subsequent Thinkinhg Time (seconds per move)
7
6
5
4
3
2
1
0
2 Move
3 Move
4 Move
5 Move
Controls
Patients
Difficulty of Problem

Figure 8

If perfect move solutions only were considered for subsequent thinking time this result changed and there were no significant differences between the groups (Table 10).

TABLE 10: MEAN SUBSEQUENT THINKING TIME IN SECONDS FOR PERFECT MOVE SOLUTIONS IN OCD PATIENTS AND CONTROLS

DIFFICULTY OF PROBLEM	PATIENTS	CONTROLS
2 MOVE	0.99	0.41
(S.E)	(0.52)	(0.14)
3 MOVE	0.46	0.47
(S.E)	(0.47)	(0.15)
4 MOVE	1.52	1.33
(S.E)	(0.38)	(.46)
5 MOVE	0.83	0.87
(S.E)	(0.26)	(0.34)

ANOVA	F-Ratio	df	Probability
By group	0.21	(1,61)	0.65
By difficulty	2.23	(3,61)	0.08
Group by difficulty	0.29	(3,61)	0.83

There was no difference in the initial movement time between patients and controls (Table 11) but the patients were slower in their subsequent movement time ($F(1,61) = 5.19$, $P < 0.026$) (Table 12 and Figure 9 - overleaf).

TABLE 11: MEAN INITIAL MOVEMENT TIME IN SECONDS IN PATIENTS AND CONTROLS

DIFFICULTY OF PROBLEM	PATIENTS	CONTROLS
2 MOVE	2.24	1.83
(S.E)	(0.20)	(0.23)
3 MOVE	2.24	1.71
(S.E)	(0.15)	(0.16)
4 MOVE	1.82	1.43
(S.E)	(0.12)	(0.10)
5 MOVE	1.76	1.60
(S.E)	(0.15)	(0.13)

ANOVA	F-Ratio	df	Probability
By group	2.18	(1,61)	0.14
By difficulty	4.84	(3,61)	0.003*
Group by difficulty	0.55	(3,61)	0.65

TABLE 12: MEAN SUBSEQUENT MOVEMENT TIME IN SECONDS IN OCD PATIENTS AND CONTROLS

DIFFICULTY OF PROBLEM	PATIENTS	CONTROLS
2 MOVE	2.14	1.73
(S.E)	(0.12)	(0.11)
3 MOVE	2.28	1.93
(S.E)	(0.12)	(0.14)
4 MOVE	2.38	2.00
(S.E)	(0.11)	(0.11)
5 MOVE	2.19	1.94
(S.E)	(0.07)	(0.11)

ANOVA	F-Ratio	df	Probability
By group	5.19	(1,61)	0.026*
By difficulty	5.05	(3,61)	0.002*
Group by difficulty	0.54	(3,61)	0.653

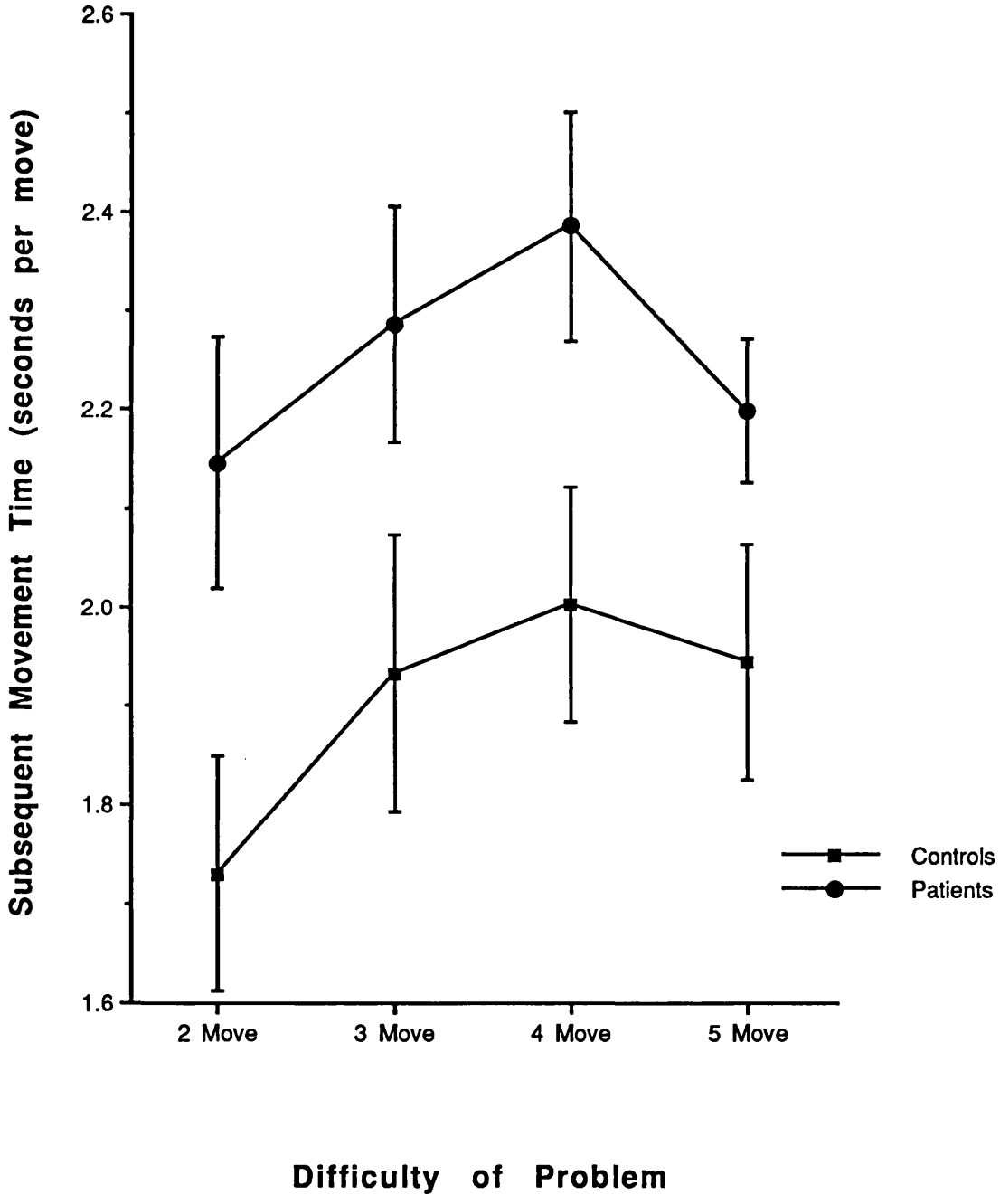

Subsequent Movement Time (seconds per move)
2.6
2.4
2.2
2.0
1.8
1.6
2 Move
3 Move
4 Move
5 Move
Controls
Patients
Difficulty of Problem

Figure 9

The presence of OCPD made no difference to the results when the two patient groups were reanalysed separately. There were 15 patients with OCD and OCPD, 25 patients with OCD alone, and 22 subjects in the control group. All three groups were matched as there was no significant difference in the mean age (Table 13), mean verbal IQ (Table 14) or in the sex distribution (Table 15) or in the severity of obsessional symptoms as measured by the CAC. There was no significant difference on the mean of the CAC between those with OCPD (mean 40, S.E 4.93) and those without OCPD (mean 32.7, S.E 2.86).

TABLE 13: MEAN AGE OF PATIENT GROUPS AND CONTROLS IN TOWER OF LONDON TASK

	OCD	OCD/OCPD	CONTROLS
Number	25	15	22
Age (S.E.)	34.5 (2.1)	38.8 (3.0)	32.2 (2.2)

ANOVA F-ratio (2,62) = 1.66 P < 0.19

TABLE 14: MEAN NART VERBAL IQ OF PATIENT GROUPS AND OF CONTROLS

	OCD	OCD/OCPD	CONTROLS
Verbal IQ (S.E)	109.1 (2.1)	111.2 (2.57)	109.2 (1.8)

ANOVA F-Ratio (2, 62) = 0.25 P < 0.78

TABLE 15: NUMBER OF MALE AND FEMALE SUBJECTS IN PATIENT GROUPS AND CONTROLS

	OCD	OCD/OCPD	CONTROLS	TOTAL
Male	8	9	15	32
Female	7	16	7	30
Total	15	25	22	62

Chi-Square = 4.87 P < 0.08

There was no difference in the number of moves that the patient groups and controls took to solve the problems (Table 16).

TABLE 16: MEAN NUMBER OF EXCESS MOVES TAKEN BY PATIENTS AND CONTROLS

DIFFICULTY OF PROBLEM	OCD	OCD/OCPD	CONTROLS
2 MOVE	0.0	0.0	0.0
(S.E)	(0.0)	(0.0)	(0.0)
3 MOVE	0.27	0.07	0.11
(S.E)	(0.1)	(0.05)	(0.05)
4 MOVE	1.54	1.43	1.3
(S.E)	(0.2)	(0.2)	(0.2)
5 MOVE	1.83	1.33	1.4
(S.E)	(0.3)	(0.3)	(0.3)

ANOVA	F-Ratio	df	Probability
By group	1.69	(2,62)	0.19
By difficulty	74.25	(3,62)	0.000*
Group by difficulty	0.60	(6,62)	0.73

Both patient groups and controls solved the same proportion of problems in the minimum number of moves possible (Table 17).

TABLE 17: PROPORTION OF PROBLEMS SOLVED IN THE MINIMUM NUMBER OF MOVES IN PATIENT GROUPS AND CONTROLS

DIFFICULTY OF PROBLEM	OCD	OCD/OCPD	CONTROLS
2 MOVE	1.0	1.0	0.95
(S.E)	(0.0)	(0.0)	(0.05)
3 MOVE	0.79	0.93	0.84
(S.E)	(0.07)	(0.05)	(0.06)
4 MOVE	0.57	0.62	0.68
(S.E)	(0.05)	(0.05)	(0.05)
5 MOVE	0.58	0.57	0.61
(S.E)	(0.05)	(0.08)	(0.06)

ANOVA	F-Ratio	df	Probability
By group	0.54	(2,62)	0.58
By difficulty	43.61	(3,62)	0.000*
Group by difficulty	0.99	(6,62)	0.43

All groups solved the same proportion of problems in the maximum number of moves permissible (Table 18). There was no difference in initial thinking time when all the solutions were considered (Table 19 and Figure 10, overleaf)

TABLE 18: PROPORTION OF PROBLEMS SOLVED IN MAXIMUM NUMBER OF MOVES IN PATIENT GROUPS AND CONTROLS

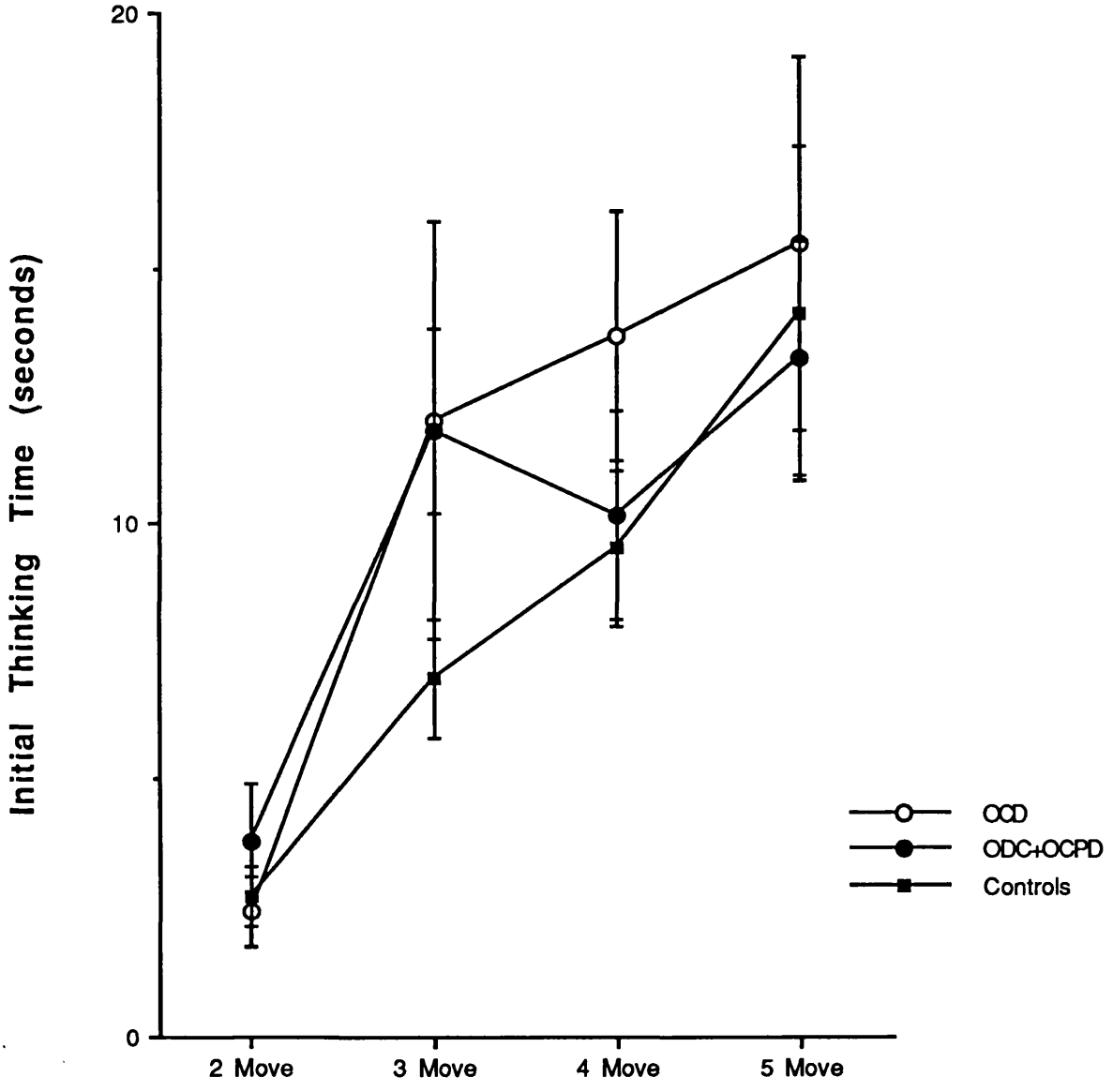
DIFFICULTY OF PROBLEM	OCD	OCD/OCPD	CONTROLS
2 MOVE	1.0	1.0	1.0
(S.E)	(0.0)	(0.0)	(0.0)
3 MOVE	1.0	1.0	1.0
(S.E)	(0.0)	(0.0)	(0.0)
4 MOVE	0.78	0.75	0.82
(S.E)	(0.04)	(0.06)	(0.04)
5 MOVE	0.86	0.95	0.93
(S.E)	(0.03)	(0.03)	(0.03)

ANOVA	F-Ratio	df	Probability
By group	0.99	(2,62)	0.37
By difficulty	43.64	(3,62)	0.000*
Group by difficulty	1.13	(6,62)	0.35

TABLE 19: MEAN INITIAL THINKING TIME IN SECONDS FOR PATIENT GROUPS AND CONTROLS

DIFFICULTY OF PROBLEM	OCD	OCD/OCPD	CONTROLS
2 MOVE	2.41	3.80	2.72
(S.E)	(0.68)	(1.09)	(.60)
3 MOVE	12.01	11.82	6.95
(S.E)	(1.78)	(4.07)	(1.17)
4 MOVE	13.67	10.17	9.53
(S.E)	(2.45)	(2.04)	(1.52)
5 MOVE	15.42	13.24	14.12
(S.E)	(3.65)	(2.29)	(3.26)

ANOVA	F-Ratio	df	Probability
By group	0.76	(2,61)	0.47
By difficulty	16.74	(3,61)	0.000*
Group by difficulty	0.71	(6,61)	0.64



Difficulty of Problem

Figure 10

There was no difference in initial thinking time when only perfect solutions were considered (Table 20).

TABLE 20: MEAN INITIAL THINKING TIME IN SECONDS FOR PERFECT SOLUTIONS ONLY IN PATIENT GROUPS AND CONTROLS

DIFFICULTY OF PROBLEM	OCD	OCD/OCPD	CONTROLS
2 MOVE	2.41	3.79	2.74
(S.E)	(0.68)	(1.09)	(0.60)
3 MOVE	10.84	7.92	6.88
(S.E)	(1.78)	(1.54)	(1.18)
4 MOVE	13.11	13.44	8.47
(S.E)	(2.41)	(0.21)	(1.37)
5 MOVE	15.57	13.44	10.26
(S.E)	(3.66)	(2.14)	(1.68)

ANOVA	F-Ratio	df	Probability
By group	1.83	(2,61)	0.17
By difficulty	17.51	(3,61)	0.000*
Group by difficulty	0.77	(6,61)	0.60

There was a significant difference by group in subsequent thinking time for all three groups (F (2,61) = 4.17, P < 0.02) (Table 21 and Figure 11 overleaf). There was no difference between the two patient groups (those with and without OCPD).

TABLE 21: MEAN SUBSEQUENT THINKING TIME IN SECONDS FOR PATIENT GROUPS AND CONTROLS

DIFFICULTY OF PROBLEM	OCD	OCD/OCPD	CONTROLS
2 MOVE	1.22	0.60	0.41
(S.E)	(0.84)	(0.25)	(0.14)
3 MOVE	1.27	0.89	0.49
(S.E)	(0.38)	(0.38)	(0.15)
4 MOVE	5.43	5.62	2.41
(S.E)	(0.96)	(1.61)	(0.51)
5 MOVE	2.70	2.63	1.46
(S.E)	(0.48)	(0.90)	(0.35)

ANOVA for all groups

	F-Ratio	df	Probability
By group	4.17	(2,61)	0.02*
By difficulty	23.03	(3,61)	0.000*
Group by difficulty	1.35	(6,61)	0.24

ANOVA for OCD and OCPD groups only

	F-Ratio	df	Probability
By Group	0.09	(1,39)	0.76
By difficulty	15.73	(3,39)	0.000*
Group by difficulty	0.11	(3,39)	0.96

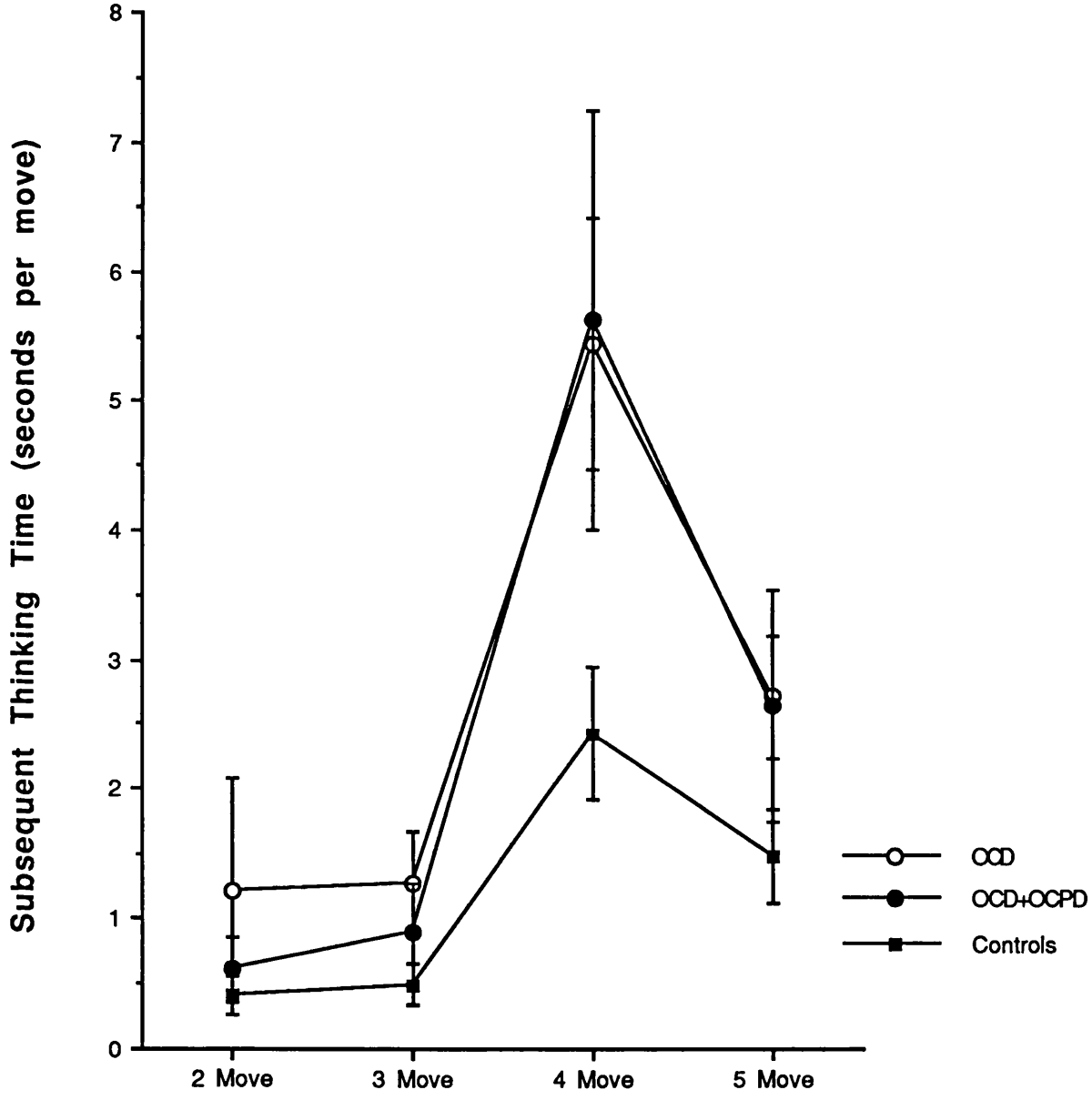

Subsequent Thinking Time (seconds per move)
8
7
6
5
4
3
2
1
0
2 Move
3 Move
4 Move
5 Move
OCD
OCD+OCPD
Controls
Difficulty of Problem

Figure 11

There was no difference between the groups when perfect solutions only were analyzed (Table 22).

TABLE 22: SUBSEQUENT THINKING TIME IN SECONDS FOR PERFECT MOVE SOLUTIONS ONLY IN PATIENT GROUPS AND CONTROLS

DIFFICULTY OF PROBLEM	OCD	OCD/OCPD	CONTROLS
2 MOVE	1.22	0.60	0.41
(S.E)	(0.84)	(0.25)	(0.14)
3 MOVE	0.47	0.45	0.47
(S.E)	(0.13)	(0.13)	(0.15)
4 MOVE	1.54	1.48	1.32
(S.E)	(0.57)	(0.40)	(0.46)
5 MOVE	1.06	0.42	0.87
(S.E)	(0.41)	(0.12)	(0.34)

ANOVA for all groups

	F-Ratio	df	Probability
By group	0.56	(2,61)	0.58
By difficulty	2.46	(3,61)	0.06
Group by difficulty	0.36	(6,61)	0.90

There was no difference in initial movement time between all the groups (Tables 23).

TABLE 23: INITIAL MOVEMENT TIME IN SECONDS FOR ALL PATIENT GROUPS AND CONTROLS

DIFFICULTY OF PROBLEM	OCD	OCD/OCPD	CONTROLS
2 MOVE	2.26	2.21	1.83
(S.E)	(0.26)	(0.34)	(0.22)
3 MOVE	1.94	1.88	1.70
(S.E)	(0.19)	(0.23)	(0.16)
4 MOVE	1.86	1.73	1.42
(S.E)	(0.16)	(0.17)	(0.10)
5 MOVE	1.67	1.90	1.59
(S.E)	(0.16)	(0.29)	(0.12)

ANOVA	**F-Ratio**	**df**	**Probability**
By group	1.07	(2,61)	0.35
By difficulty	5.31	(3,61)	0.002*
Group by difficulty	0.56	(6,61)	0.76

The subsequent movement time just failed to reach significance (F (2,61) = 2.56, P < 0.08) (Table 24 and Figure 12).

TABLE 24: SUBSEQUENT MOVEMENT TIME IN SECONDS FOR ALL PATIENT GROUPS AND CONTROLS

DIFFICULTY OF PROBLEM	OCD	OCD/OCPD	CONTROLS
2 MOVE	2.07	2.26	1.73
(S.E)	(0.16)	(0.19)	(0.11)
3 MOVE	2.29	2.26	1.93
(S.E)	(0.16)	(0.17)	(0.14)
4 MOVE	2.39	2.37	2.00
(S.E)	(0.14)	(0.18)	(0.11)
5 MOVE	2.20	2.19	1.94
(S.E)	(0.08)	(0.12)	(0.11)

For all groups

ANOVA	F-Ratio	df	Probability
By group	2.56	(2,61)	0.086
By difficulty	4.43	(3,61)	0.005*
Group by difficulty	0.69	(6,61)	0.66

For OCD and OCD/OCPD groups only

ANOVA	F-Ratio	df	Probability
By Group	0.02	(1,39)	0.88
By difficulty	2.84	(3,39)	0.04*
Group by difficulty	0.87	(3,39)	0.46

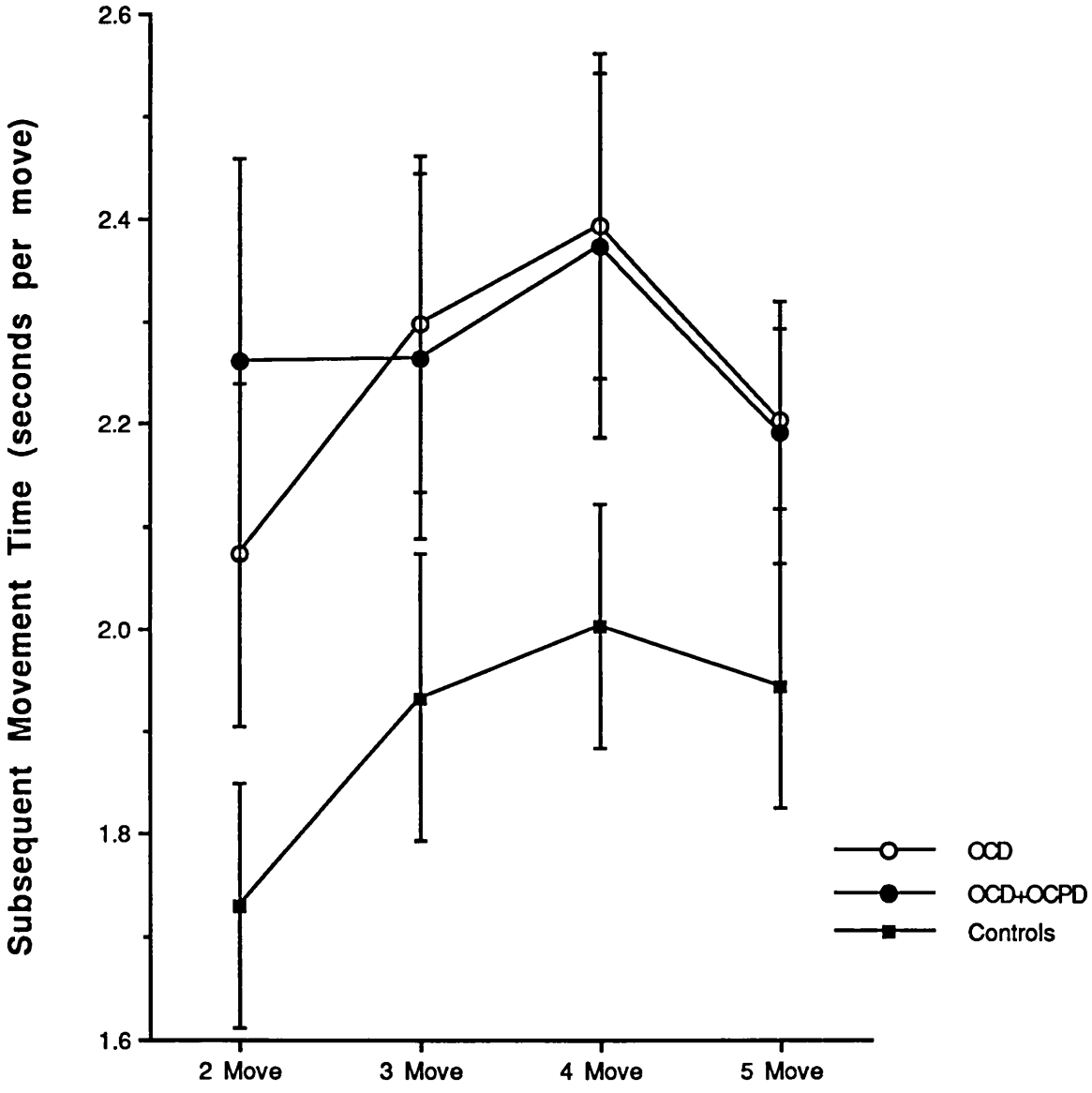

Subsequent Movement Time (seconds per move)
2.6
2.4
2.2
2.0
1.8
1.6
2 Move
3 Move
4 Move
5 Move
OCD
OCD+OCPD
Controls
Difficulty of Problem

Figure 12

There was no correlation between the severity of the symptoms of OCD (as measured by the Compulsive Activity Checklist) and any of the measures above (for all patients with OCD with or without OCPD) (Table 25) by the Pearson product moment correlation coefficient (this page) or the Spearman rank order correlation coefficient (overleaf).

TABLE 25: PEARSON CORRELATION CO-EFFICIENT BY COMPULSIVE ACTIVITY CHECKLIST

No correlations reached probability < 0.05 (n=35)

PROPORTION OF PROBLEMS SOLVED	
2 MOVE	.
3 MOVE	-.15
4 MOVE	-.10
5 MOVE	-.07
PROPORTION OF PROBLEMS SOLVED IN MINIMUM NUMBER OF MOVES	
2 MOVE	.
3 MOVE	.24
4 MOVE	.19
5 MOVE	-.09
PROPORTION OF PROBLEMS SOLVED IN MAXIMUM NUMBER OF MOVES	
2 MOVE	.02
3 MOVE	.02
4 MOVE	-.01
5 MOVE	-.01
INITIAL THINKING TIME	
2 MOVE	.01
3 MOVE	-.32
4 MOVE	-.02
5 MOVE	.03
SUBSEQUENT THINKING TIME	
2 MOVE	-.17
3 MOVE	-.20
4 MOVE	-.15
5 MOVE	.01
INITIAL MOVEMENT TIME	
2 MOVE	-.01
3 MOVE	-.04
4 MOVE	-.20
5 MOVE	-.13
SUBSEQUENT MOVEMENT TIME	
2 MOVE	.01
3 MOVE	-.04
4 MOVE	-.20
5 MOVE	-.13

SPEARMAN RANK CORRELATION CO-EFFICIENT BY COMPULSIVE ACTIVITY CHECKLIST

No correlations reached probability < 0.05 (n=35)

PROPORTION OF PROBLEMS SOLVED	
2 MOVE	.
3 MOVE	-.31
4 MOVE	-.06
5 MOVE	-.10
PROPORTION OF PROBLEMS SOLVED IN MINIMUM NUMBER OF MOVES	
2 MOVE	.
3 MOVE	.32
4 MOVE	.17
5 MOVE	-.06
PROPORTION OF PROBLEMS SOLVED IN MAXIMUM NUMBER OF MOVES	
2 MOVE	.
3 MOVE	.
4 MOVE	-.06
5 MOVE	.06
INITIAL THINKING TIME	
2 MOVE	.15
3 MOVE	.07
4 MOVE	.07
5 MOVE	.05
SUBSEQUENT THINKING TIME	
2 MOVE	.12
3 MOVE	-.19
4 MOVE	-.14
5 MOVE	-.09
INITIAL MOVEMENT TIME	
2 MOVE	-.08
3 MOVE	-.11
4 MOVE	-.09
5 MOVE	-.18
SUBSEQUENT MOVEMENT TIME	
2 MOVE	.04
3 MOVE	-.05
4 MOVE	-.20
5 MOVE	-.11

Eight patients were taking anti-depressants for the adjunctive treatment of their OCD. There were no differences on any of the statistical analyses between these 8 patients and the 32 patients who were not taking anti-depressants.

ii) Attentional set shifting task

There were 40 patients with OCD and 36 healthy subjects for comparison in the control group. The patients were the same ones who performed in the Tower of London task. The control group was made up of 14 of the same control volunteers who performed the Tower of London task and 22 new subjects. There was no difference between the groups in the mean age (Table 26), mean NART verbal IQ (Table 27) or sex distribution (Table 28).

TABLE 26: MEAN AGE OF OCD PATIENTS AND CONTROLS IN ATTENTIONAL SET SHIFTING TASK

	PATIENTS	CONTROLS
Number	40	36
Mean Age (S.E)	36.1 (1.76)	32.3 (1.27)

ONEWAY ANOVA F-Ratio (1,76) = 2.20 P < 0.14

TABLE 27: MEAN NART VERBAL IQ OF COMBINED PATIENTS AND CONTROLS FOR ATTENTIONAL SET SHIFTING TASK

	PATIENTS	CONTROLS
NUMBER	40	36
MEAN VERBAL IQ (S.E.)	109.9 (1.62)	110.0 (1.2)

ONEWAY ANOVA F-Ratio (1,76) = 0.28 P < 0.59

TABLE 28: SEX DISTRIBUTION OF COMBINED PATIENTS AND CONTROLS FOR ATTENTIONAL SET SHIFTING TASK

	PATIENTS	CONTROLS	TOTAL
Male	17	16	32
Female	23	20	43
Total	40	36	76

Chi-Square = 0.00 (1 df), P < 1.0

The patient and control group were compared in terms of the proportion of subjects reaching criterion (six consecutive correct responses) within the 50 trials allowed at each of the nine stages of the test (Table 29, Figure 13). The number of patients who fail at each stage is analyzed cumulatively. As the test becomes harder, the analysis assumes that if a subject fails an earlier stage then he or she would fail at a later stage. The data were analyzed by the likelihood ratio method of contingency tables (Kullback, 1968, Robbins, 1977). Compared to the controls, there is a steady increase in the number of patients who fail at each stage of the task. The first significant difference between the patients and controls is at the C_D stage ($2i = 3.9$, $P < 0.05$) and at all stages following the C_D stage.

TABLE 29: PERCENTAGE OF SUBJECTS REACHING CRITERION AT EACH STAGE (CUMULATIVE ANALYSIS) IN ATTENTIONAL SET SHIFTING TASK

STAGE	PATIENTS	CONTROLS	STATISTIC (2i)
SD	40 (100%)	36 (100%)	NS
SDR	39 (97.5%)	36 (100%)	NS
C_D	37 (92.5%)	36 (100%)	3.9* **P < 0.05**
CD	37 (92.5%)	36 (100%)	3.9* **P < 0.05**
CDR	36 (90%)	36 (100%)	5.47* **P< 0.02**
IDS	35 (87.5%)	36 (100%)	6.59* **P< 0.02**
IDR	34 (85%)	36 (100%)	7.99* **P< 0.01**
EDS	26 (65%)	30 (82.8%)	NS
EDR	25 (62.5%)	29 (80%)	NS

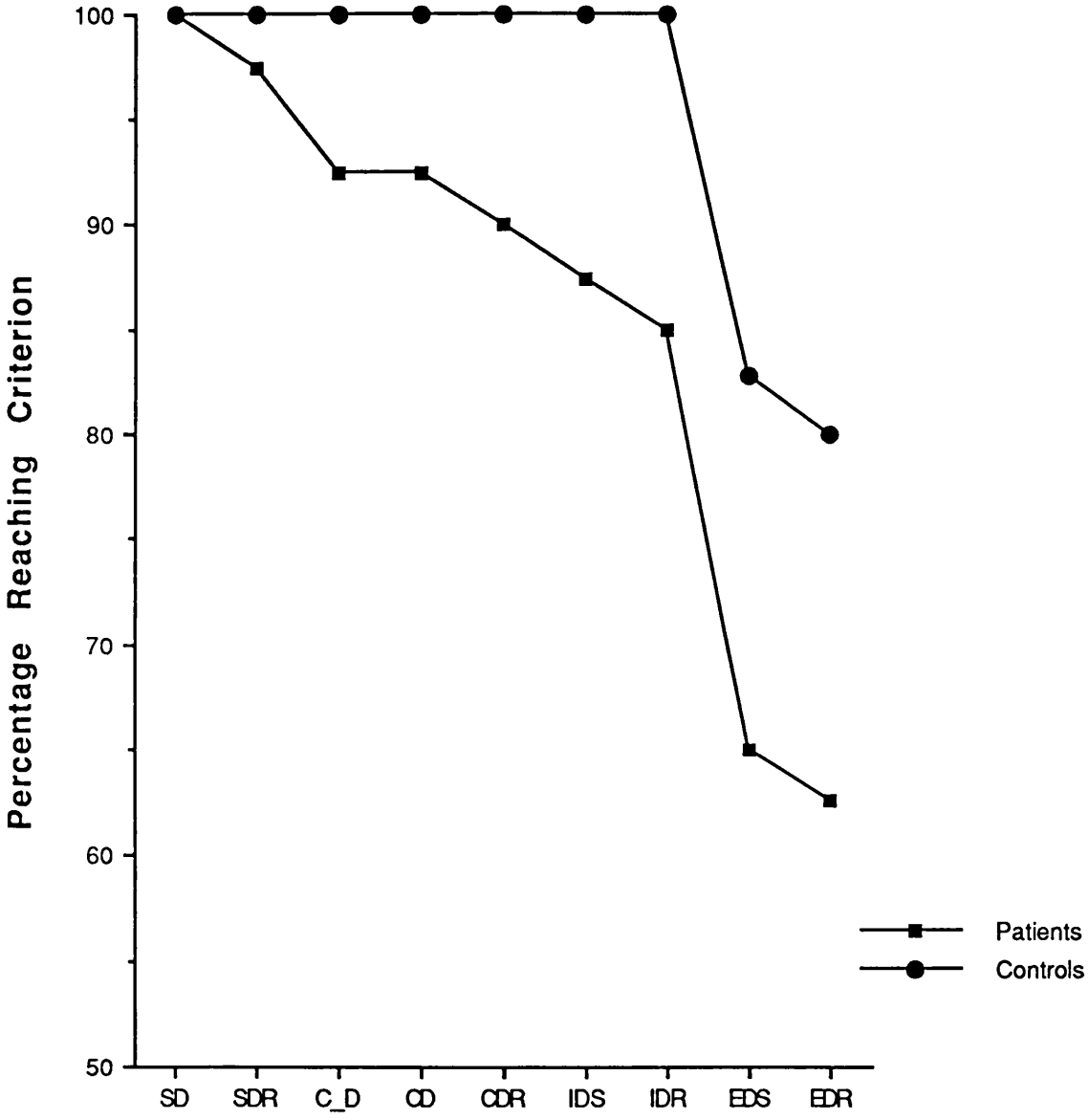

100
90
80
70
60
50
Percentage Reaching Criterion
SD
SDR
C_D
CD
CDR
IDS
IDR
EDS
EDR
STAGE
Patients
Controls

Figure 13

When only those subjects who actually attempted each stage were analyzed, there was no significant difference at any particular stage (Table 30). This suggests that there was a gradual decline in the performance of the patient group that was only significant when the data were analyzed cumulatively.

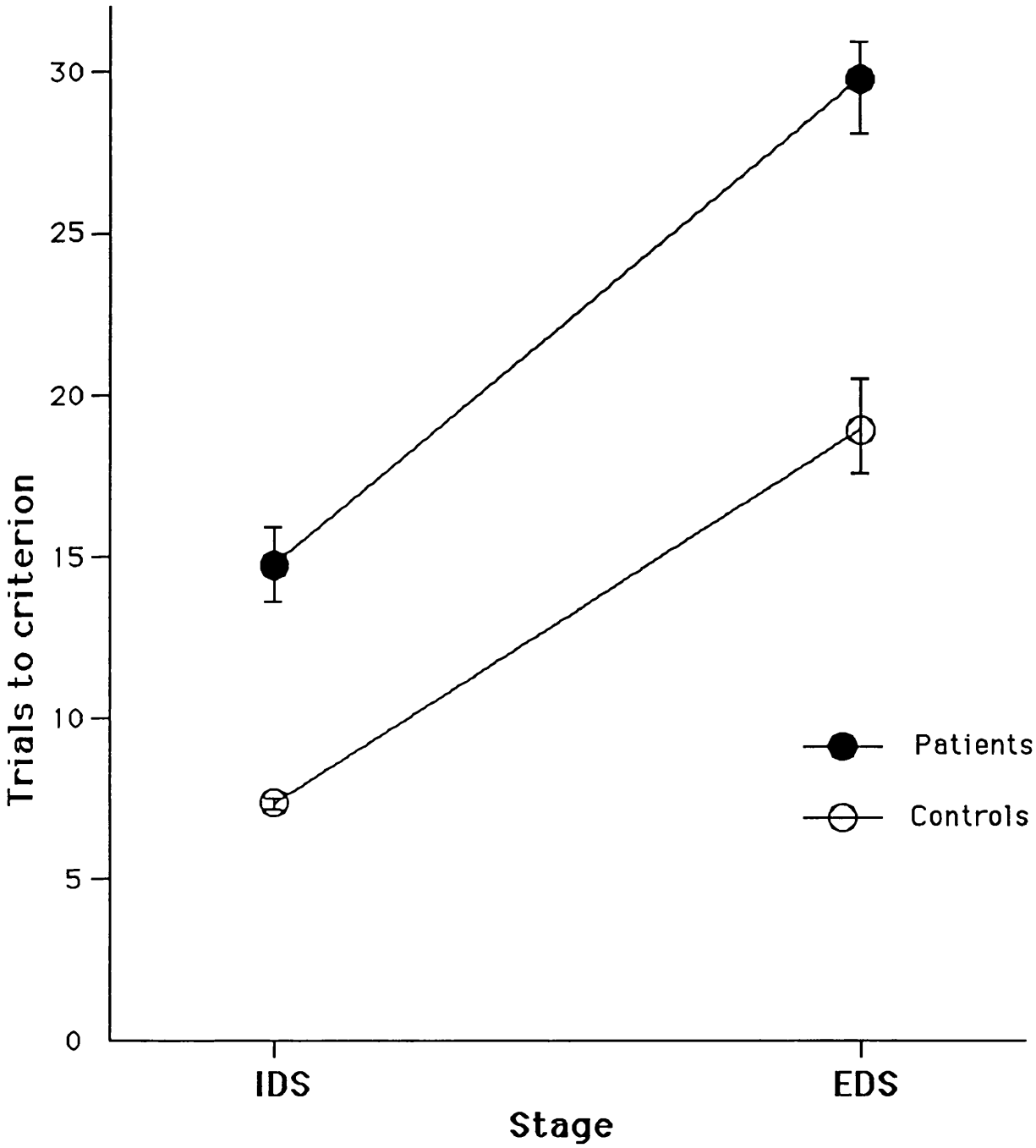
TABLE 30: NUMBER OF SUBJECTS REACHING CRITERION AT EACH STAGE (ANALYSIS BY STAGE) IN ATTENTIONAL SET SHIFTING TASK

STAGE	PATIENTS		CONTROLS		STATISTIC 2i
	Pass	Fail	Pass	Fail	
SD	40	0	36	0	NS
SDR	39	1	36	0	NS
C_D	37	2	36	0	NS
CD	37	1	36	0	NS
CDR	36	1	36	0	NS
IDS	35	1	36	0	NS
IDR	34	1	36	0	NS
EDS	26	8	30	6	NS
EDR	25	4	29	1	NS

Analysis was then focused on the two critical ID and ED shift stages to examine whether there were any differences between groups on any measures for subjects reaching those stages. The performance of the two groups on the ID and ED shifts was analyzed according to the number of trials required to reach criterion at each of these stages. The patients took more trials to reach the criterion at the IDS stage ($F(1,62) = 5.9$, $P < 0.018$) and at the EDS stage ($F(1,62) = 3.88$, $P < 0.05$) (Table 31, Figure 14 overleaf).

TABLE 31: TRIALS TO CRITERION AT IDS AND EDS STAGES FOR PATIENTS AND CONTROLS

	PATIENTS	CONTROLS
IDS MEAN	14.83	7.45
(S.E)	(2.23)	(0.41)
ONEWAY ANOVA F-Ratio (1,62) = 5.9 P < 0.018*		
EDS MEAN	29.87	18.89
(S.E)	(2.84)	(2.5)
ONEWAY ANOVA F-Ratio (1,62) = 3.88 P < 0.05*		



The mean number of trials required to reach criterion at the intra-dimensional and extra-dimensional stages of learning

Figure 14

The groups were also compared regarding the mean latency per trial to respond at the IDS and EDS stage (Table 32). Latencies were recorded regarding seconds to respond. There was no significant difference between the groups at the IDS stage or at the EDS stage.

TABLE 32: MEAN LATENCY TIMES IN SECONDS AT IDS AND EDS STAGES FOR PATIENTS AND CONTROLS

	PATIENTS	CONTROLS
IDS MEAN	1.99	1.43
(S.E)	(0.11)	(0.07)

ONEWAY ANOVA F-Ratio (1,58) = 1.81 P < 0.18

EDS MEAN	2.21	2.18
(S.E)	(0.19)	(0.21)

ONEWAY ANOVA F-Ratio (1,56) = 2.73 < 0.10

All the analyses above were repeated with the patient group split into patients with or without OCPD. All the groups were matched according to age (Table 33), verbal IQ (Table 34) and sex (Table 35).

TABLE 33: MEAN AGE OF PATIENT GROUPS AND CONTROLS IN ATTENTIONAL SET SHIFTING TASK

	OCD	OCD/OCPD	CONTROLS
Number	25	15	36
Age	34.5	38.8	32.2
(S.E.)	(2.1)	(3.0)	(1.3)

ANOVA F-ratio (2,76) = 1.78 P < 0.17

TABLE 34: MEAN VERBAL IQ OF PATIENTS AND CONTROLS IN RULE FOLLOWING TASK

	OCD	OCD/OCPD	CONTROLS
NART Verbal IQ	109.1	111.2	113.9
(S.E)	(2.1)	(2.57)	(1.2)

ANOVA F-Ratio = 0.35 (2,76) P < 0.70

TABLE 35: NUMBER OF MALE AND FEMALE SUBJECTS IN PATIENTS AND CONTROLS IN RULE FOLLOWING TASK

	OCD	OCD/OCPD	CONTROLS	TOTAL
Male	8	9	16	33
Female	7	16	20	43
Total	15	25	36	76

Chi-Square = 1.15 (2 df), P < 0.56

Separation of the patient groups according to OCPD made no major differences to the results of the contingency analyses (Table 36, Figure 15 and Table 37) other than C_D, CD, CDR stages on the cumulative analyses were no longer significant.

TABLE 36: PERCENTAGE OF SUBJECTS REACHING CRITERION AT EACH STAGE (CUMULATIVE ANALYSIS) IN RULE FOLLOWING TASK

STAGE	OCD	OCD/OCPD	Controls	Statistic 2i
SD	25 (100%)	15 (100%)	36 (100%)	NS
SDR	24 (96%)	15 (100%)	36 (100%)	NS
C_D	23 (92%)	15 (100%)	36 (100%)	NS
CD	23 (92%)	14 (93%)	36 (100%)	NS
CDR	22 (88%)	14 (93%)	36 (100%)	NS
IDS	21 (84%)	14 (93%)	36 (100%)	7.41*
IDR	21 (84%)	13 (86%)	36 (100%)	8.05**
EDS	16 (64%)	10 (66%)	30 (83.8%	NS
EDR	15 (60%)	10 (66%)	29 (80%)	NS

* P < 0.05 for all 3 groups, NS between patient groups

** P < 0.02 for all 3 groups, NS between patient groups

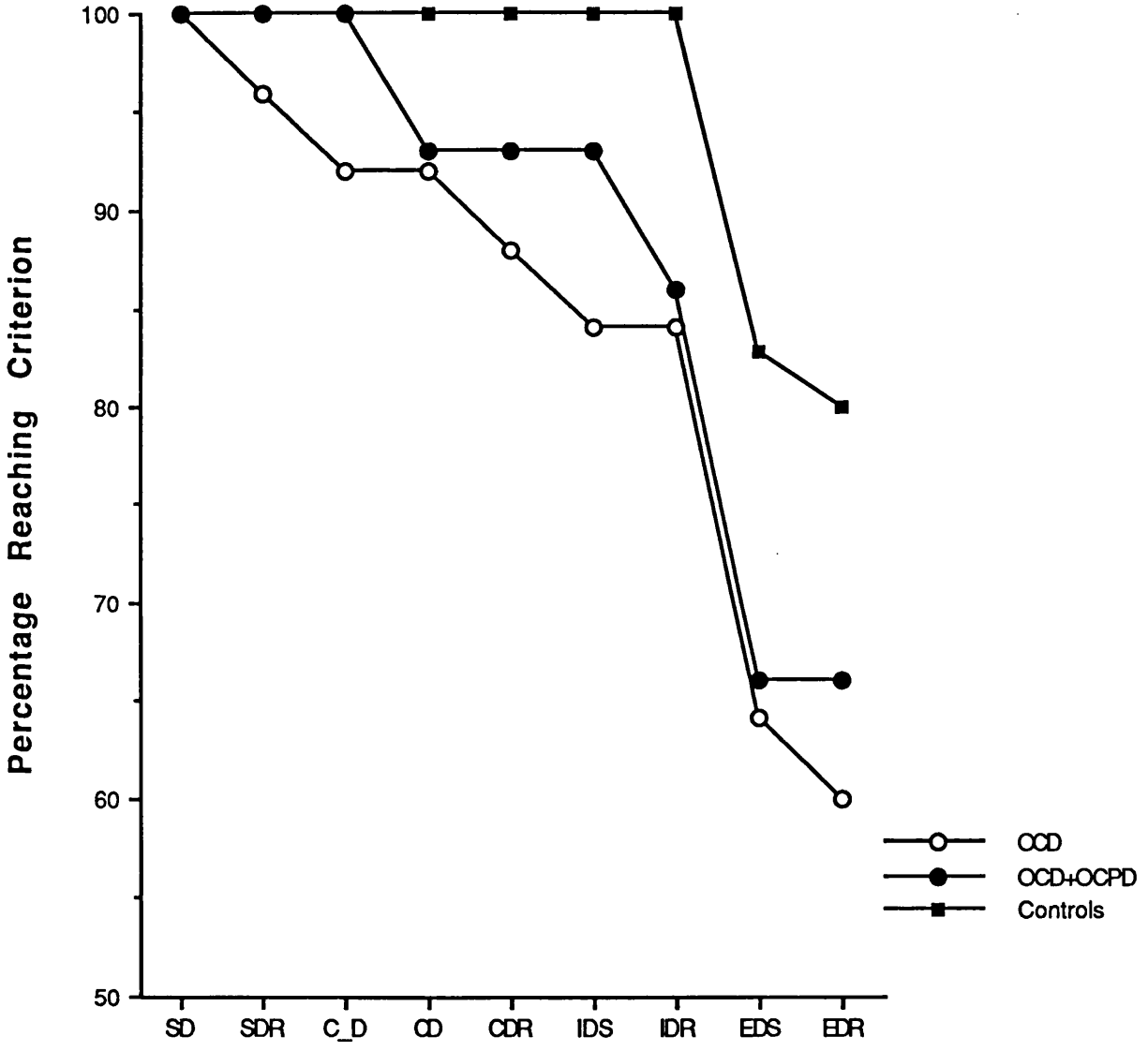

Percentage Reaching Criterion
100
90
80
70
60
50
SD
SDR
C_D
CD
CDR
IDS
IDR
EDS
EDR
STAGE
OCD
OCD+OCPD
Controls

Figure 15

TABLE 37: PERCENTAGE OF SUBJECTS REACHING CRITERION AT EACH STAGE IN RULE FOLLOWING TASK

STAGE	OCD		OCD/OCPD		Controls		Statistic 2i
	Pass	Fail	Pass	Fail	Pass	Fail	
SD	25	0	15	0	36	0	NS
SDR	24	1	15	0	36	0	NS
C_D	23	1	14	1	36	0	NS
CD	23	1	14	0	36	0	NS
CDR	22	1	14	0	36	0	NS
IDS	21	1	14	0	36	0	NS
IDR	21	0	13	1	36	0	NS
EDS	16	5	10	3	30	6	NS
EDR	15	1	10	3	29	1	NS

The number of trials to reach the criterion at the IDS stage remained significant although the number of trials at the EDS stage was no longer significant (Table 38).

TABLE 38: TRIALS TO CRITERION AT IDS AND EDS STAGES FOR BOTH PATIENT GROUPS AND CONTROLS

	OCD	OCD/OCPD	CONTROLS
IDS MEAN	15.88	13.07	7.49
(S.E)	(3.15)	(2.86)	(0.41)

ONEWAY ANOVA F-Ratio (2,62) = 3.21 P < 0.047*

EDS MEAN	30.16	29.40	18.89
(S.E)	(3.64)	(4.72)	(2.5)

ONEWAY ANOVA F-Ratio (2,62) = 1.91 P < 0.16

TABLE 39: MEAN LATENCY TIMES IN SECONDS AT IDS AND EDS STAGES FOR PATIENTS AND CONTROLS

	OCD	OCD/OCPD	CONTROLS
IDS MEAN	1.90	2.13	1.43
(S.E)	(0.12)	(0.20)	(0.07)

ONEWAY ANOVA F-Ratio (2,58)= 1.66 P < 0.20

EDS MEAN	2.21	2.22	2.18
(S.E)	(0.21)	(0.37)	(0.21)

ONEWAY ANOVA F-Ratio (2,56)= 1.34 P < 0.27

Further analysis of ED Fail group

The data for patients on the attentional set shifting task were split into two subgroups: (i) those completing the whole task ("ED pass" subgroup, n=25) and (ii) those failing at or before the final EDR stage ("ED fail" subgroup, n=15), to determine whether those patients who performed poorly on the attentional set shifting task also performed poorly on the Tower of London task or had any particular clinical features. The rationale for splitting the group at the final EDR stage is that there is a gradual deterioration of performance on the attentional set shifting task and that they are not impaired at any particular stage. The two patient groups were therefore compared against the control group in the Tower of London task. There was no difference between the groups in terms of age ($F(1, 62) = 0.98$, $P = 0.38$) or NART verbal IQ ($F(1,62) = 1.31$, $P = 0.28$). There was no difference between the patient subgroups for the severity of OCD symptoms (as measured by the Compulsive Activity Checklist (CAC) ($F(1, 34) = 0.78$, $P = 0.38$), age of onset $F(1,35) = 1.09$, $P = 0.30$), or duration of illness ($F(1,35) = 2.12$, $P = 0.15$). There was also no correlation between the CAC or any other measure on the Tower of London task within the patient subgroups (as with the group as a whole). Unfortunately the CAC cannot be broken down into any symptom type as it is essentially a measure of severity of handicap. The clinical vignettes (Appendix 4) have however

been separated into the two groups (ED pass and ED fail). Inspection of the case histories would suggest that there was no differences between the groups in terms of specific or the number of patients taking anti-depressants. symptom types. There is approximately an equal proportion of patients in each group with predominant fears of contamination or causing harm, excessive washing or checking or obsessional slowness. Unfortunately the symptom profile was not recorded systematically in a structured interview in the study design and further research will be required to answer the question of whether any particular symptom profile is associated with any specific cognitive deficits. It is also unfortunately impossible to determine whether the ED fail group had an increased number of neurological soft signs as these were unrecorded in the case notes and were not part of the study design.

There was a significant difference between the three groups (ED pass, ED fail and healthy controls) in terms of the first measure of accuracy: the mean number of excess moves required to solve the problem was significantly different ($F(2, 57) = 4.8$, $p < 0.012$). An orthonormal contrast analysis was therefore conducted, comparing each of the patient subgroups to the healthy controls. This analysis confirmed that whilst the ED pass subgroup were unimpaired on this measure ($t(57) = 0.255$, $p=0.80$), the ED fail subgroup was significantly poorer compared to controls ($t(57)= 2.88$, $p < 0.006$). There was also a significant interaction between the group and difficulty factors (F

(6,174) = 2.79, p < 0.013). Again orthonormal contrasts showed that the ED fail subgroup were impaired relative to controls (t (174) 2.51, p < 0.015) but the ED pass subgroup were not (t (174) 0.396, p= 0.69).

A similar result was found in the analysis of the second measure of accuracy: the proportion of problems solved in the minimum number of moves possible. There was a significant difference between the three groups (F (2, 57) =3.48, p < 0.037). An orthonormal contrast analysis confirmed that the whilst the ED pass subgroup were unimpaired on this measure (t (57) = 0.36, p=0.72), the ED fail subgroup was significantly poorer compared to controls (t (57)= 2.18, p < 0.033). There was also a significant interaction between the group and difficulty factors (F (6,174) = 2.52, p < 0.023). Again orthonormal contrasts showed that the ED fail subgroup were impaired relative to controls (t (174) = 2.87, p < 0.006) but the ED pass subgroup were not (t (174) = 0.36, p = 0.72).

In the most stringent measure of accuracy, both groups solved the same proportion of problems in the maximum number of moves permissible (F (1,62)= 1.62, P = 0.208) (similar to the original analysis with the combined patient subgroups). There was no difference between patients and controls in the initial thinking time (F (1,61)= 1.51, P=0.23) (also similar to the original analysis). Latencies were then reanalysed for perfect solutions only and there

was still no significant difference between the groups for the initial thinking time ($F(1,61) = 1.87$, $P = 0.168$) (similar to the original analysis). The subsequent thinking time was however significantly different when all problems were considered ($F(1,61) = 4.70$, $P < 0.013$). An orthonormal contrast analysis found that both the ED pass subgroup ($t(57) = 2.83$, $p < 0.006$), and the ED fail subgroup were significantly poorer compared to controls ($t(57) = 2.29$, $p < 0.025$) but there was no interaction with difficulty factors ($F(6,174) = 1.41$, $p = 0.21$). There was no difference in their subsequent thinking time when perfect solutions only were considered ($F(1,61) = 0.17$, $p = 0.84$). There was no difference in the initial movement time between patients and controls ($F(2, 57) = 1.53$, $p = 0.225$), but they were significantly different in the subsequent movement time when all the problems were considered ($F(2,57) = 3.39$, $P < 0.04$). Again orthonormal contrasts showed that the ED fail subgroup were impaired relative to controls ($t(174) = 2.54$, $p < 0.014$) but the ED pass subgroup were not ($t(174) = 1.60$, $p = 0.114$).

The analysis suggests OCD patients who pass the attentional set shifting task (ED pass) perform exactly like the OCD group as a whole on the Tower of London with no deficits on any measure except the subsequent thinking time and subsequent movement time when all the solutions were considered. However, the ED fail subgroup perform poorly on the Tower of London task in terms of the accuracy of their

solutions (unlike the group as a whole). The ED fail subgroup were not impaired in the initial thinking time but were impaired in their subsequent thinking time when all the solutions were considered (similar to the group as a whole).

DISCUSSION

This study used a large carefully diagnosed group of patients with OCD and a control group matched with the patients by age, IQ, and gender. The possible effects of OCPD were controlled for. In addition patients with either a depressive disorder or who had fears of contamination from the equipment or who had obsessional ruminations that might interfere with the task were excluded from the study. Using two clearly defined neuropsychological tests which have previously demonstrated specific patterns of deficits in disorders of fronto-striatal dysfunction, it was possible to show that patients with OCD were slower in one component of executive function when compared with normal control subjects. When the patients made a mistake in the Tower of London task, their subsequent thinking time was significantly slower. This was interpreted as a deficit in the ability to plan an alternative sub-goal to reach the final solution. In the attentional set shifting task, the patient group were significantly impaired in compound discrimination learning and reversal and at the intra- and extra-dimensional stages of the task. The interpretation of these results was similar for those of the Tower of London task in that patients with OCD appear to be less efficient at generating alternative strategies and are less flexible in attentional set shifting. A subset of patients who failed at or before the extra-dimensional shift stage also performed poorly on the Tower of London task in terms of

the accuracy of their solutions and subsequent thinking time when they made a mistake.

(i) Tower of London task

Regarding the hypotheses, patients with OCD as a whole were no different to healthy controls in the number of errors made in the Tower of London task. Both patients and controls solved the problems in the same number of moves. They solved the same proportion of problems in the minimum number of moves possible (that is the number of perfect solutions) and they solved the same proportion of problems in the maximum number of moves permissible.

Patients with OCD were no different in their initial thinking time prior to the first move but were slower than healthy controls in the subsequent thinking time. However, when perfect solutions only were considered there was no difference in the initial or subsequent thinking time. Therefore, the deficit in thinking time is more likely to be related to a difficulty in planning alternative sub-goals to reach the final solution. The thinking times were corrected by considering the actual movement time since the latter was also prolonged in the patients with OCD.

The planning component of the Tower of London task was related to the difficulty of the task as hypothesised by Shallice (1982). Thus when the problems require 2 or 3 moves, the requirements for planning are minor and do not

require planning several complex sub-goals. When the task is increased to 4 or 5 move solutions, the planning component is significantly increased. The main effects analysis of the subsequent thinking time revealed that the deficits were significant at the 4 move problem only. This is a common finding in the Tower of London task as subjects have difficulty with the 4 move problems may then improve at the 5 move problems having already practised on the 4 move problems (Sahakian, personal communication).

Patients with OCD are thus able to solve accurately the problems (and therefore generate, refine, and revise solutions) which argues against any deficits in spatial working memory. There is however a sub-group of OCD patients (ED fail) who are like patients with frontal lobe lesions who are less accurate than healthy controls on the Tower of London.

The overall pattern of results can be compared to relevant patients of different diagnoses in previous studies (Table 40 overleaf). The general pattern is different to that found in patients with frontal lobe lesions who require more moves to solve the problem and who solve fewer problems with perfect solutions (Owen et al, 1990). The results are also dissimilar to that found in autism when compared to a matched control group with a low IQ (Hughes et al, 1994). Autistic subjects require more moves to solve the problem, they solve fewer perfect solutions and take

Table 40: Summary of results of Tower of London task in different patient groups compared to matched controls

(✗ denotes significant difference compared to a control group, ? denotes not tested;
nc = normal controls, ldc = learning disabled controls)

	Accuracy (Mean number of moves)	**Initial thinking time**	**Subsequent thinking time**	**Number of perfect solutions**	**Initial thinking time** (perfect solutions only)	**Subsequent thinking time** (perfect solutions only)
Obsessive compulsive disorder	✓	✓	✗	✓	✓	✓
Multiple Systems Atrophy *(Robbins et al, unpublished)*	✓	✓	✗	✓	?	?
Autism *(Hughes et al, unpublished)*	✗	✓	✗	✗	✗ nc ✓ ldc	✓
Early Parkinson's disease *(Morris et al, 1988)*	✓	✗	✓	✓	?	?
Frontal lobe lesions *(Owen et al, 1990)*	✗	✓	✗	✗	✓	✗
Temporal lobe lesions *(Owen, 1992)*	✓	✓	✓	✓	✓	✓
Amygdalo-hippocampectomy *(Owen, 1992)*	✓	✓	✓	✓	✓	✓

more time to complete the perfect solutions. OCD patients show no impairment in accuracy compared to healthy controls and achieve the same number of perfect solutions. In contrast, more severely affected patients with Parkinson's disease seem to exhibit a decrease in accuracy and become more like patients with frontal lobe lesions (Owen, 1992).

The thinking times had been calculated by subtracting the actual movement time in a yoked control condition. OCD patients did not differ from control subjects for the time spent thinking prior to making the first move (unlike patients with Parkinson's disease who spend longer planning the first but not subsequent moves (Morris et al, 1988)). However, patients with OCD do spend significantly more time thinking about the problem for each successive move. A similar finding of increased subsequent thinking time has been found in patients with frontal lobe lesions (Owen et al, 1990), autism (Hughes et al, 1994) and multiple systems atrophy (Robbins et al, 1994).

When only perfect solutions are considered, patients with OCD do not show the increase in subsequent thinking time relative to controls; autistic subjects maintain their deficit, whereas patients with frontal lobe lesions reveal even larger differences compared to controls. (The findings in multiple systems atrophy are not known.) Thus, only when patients with OCD make a mistake do they spend a longer time to reach the solution (even though they reach it in

the same number of moves as the healthy controls).

The finding of an increased subsequent thinking time on all solutions in OCD patients may occur because they have "wrongfooted" on the first move. By contrast, patients with autism and frontal lobe excisions are less accurate and take a longer subsequent thinking time when perfect solutions only are considered. Patients with frontal lobe excisions may therefore have a more severe deficit in planning in terms of being able to evaluate a problem and then generate, refine and revise a solution before making the first move. Consequently this inadequate planning in patients with frontal lobe excisions leads to a disorganized solution involving more moves and more time. The added deficit in frontal lobe excisions may also be related to non-planning components of the task. Successful planning requires a significant load on spatial working memory. This is essential not only for the storage of a correct sequence but also in the active search process of possible solutions. Subsequently the problem solutions must be held in immediate memory and transposed into the appropriate sequence of motor movements before it can actually be executed. Patients with frontal lobe lesions might be impaired at retaining a sequence of spatial moves in immediate memory for a sufficient length of time to allow its successful execution. This explanation is unlikely as patients with frontal lobe lesions have a normal spatial span. In contrast, the spatial working

memory paradigm revealed significant impairments and was correlated significantly with impaired accuracy on the Tower of London task. The impairment was in both possible types of search error and this was related to an inefficient search strategy for solving the problem (Owen et al, 1990).

The deficit in planning in OCD on the Tower of London task is therefore more subtle than that found in autism or frontal lobe lesions. Patients with OCD are as accurate as healthy controls, but when they make a mistake, they are slower in generating alternative strategies, probably because they are less flexible in their "mental set". They are slower at setting aside the main goal and planning the necessary sub-goals.

The increased subsequent thinking may also represent an inefficient strategy that has been adopted by the patient. When OCD patients make a mistake, they are just as fast as healthy controls in generating an alternative strategy to solve the problem, but they might be spending longer time checking that it will indeed lead to a correct solution. There are three main arguments against this explanation. First, excessive checking in OCD is usually selectively focused on tasks with excessive responsibility or danger Second, previous research has found that OCD patients are not uniformly impaired on all tests, which would be expected if their performance simply reflected their

obsessional symptoms. Third, the excessive checking of performance on a neuropsychological test might be a feature of Obsessive Compulsive Personality Disorder (OCPD). However in this study, the perfectionism and meticulousness in patients with OCPD might be expected to increase latency times if they repeatedly checked to determine whether they have obtained a correct solution to the problem. In this study, however there was no difference between OCD patients with or without OCPD and this hypothesis is less likely.

The results of the attentional set shifting test, also favours the explanation that the increased subsequent thinking in the Tower of London task represents a difficulty in generating alternative strategies. This is because the patients are less flexible in switching "mental set" and slower at setting aside the main goal and planning the necessary sub-goals.

(ii) Attentional set shifting task

Regarding the hypotheses, patients with OCD are significantly impaired in another component of executive function, namely the ability to shift set and to maintain attention. Compared to the control group, there is a steady fall off in the number of patients who pass at each stage of the attentional set shifting task as well as at the crucial extra-dimensional shift stage. The earlier stages of compound discrimination and reversal requires selective attention to the relevant dimension when a second

distracting dimension is introduced and in the maintenance of an attentional set at the intra-dimensional shift stage. The results of the attentional set shifting test are consistent with the hypothesis of Norman and Shallice (1980) and a diminished supervisory frontal lobe influence (Robbins and Sahakian, 1983). It states that in the functional absence of a Supervisory Attentional System (SAS), action schemas are triggered directly by environmental features (leading to increased distractibility and loss of behavioural control) or by current activity leading to response perseveration and difficulty in shifting mental set. This "stuck-in" set perseveration is a continued use of a framework which has become inappropriate due to a failure of executive function in the frontal lobe. Sanderson & Albert (1984) have proposed two further categories of perseveration. The first of these is termed "recurrent" perseveration which is manifested at the simple reversal stage of the attentional set shifting task and consists of perseveration to a specific stimulus in the face of negative reinforcement. This form of perseveration is manifested at the first simple reversal stage of the attentional set shifting task and was not found in this study. It has however been described in patients with schizophrenia on the attentional set shifting task (Elliot et al, in press). Another form of perseverative behaviour is "continuous" perseveration which consists of the inappropriate repetition of behaviour without interruption. The current study does not directly

address this but compulsions such as excessive washing or checking are a good example of "continuous" perseveration. In this case there is a failure in the monitoring and feedback about a completed motor act as the subject is unable to confirm whether the checking or washing is sufficient.

OCD patients resemble those with unmedicated mild Parkinson's disease (Downes et al, 1989; Owen, 1992) and patients with moderate Dementia of Alzheimer's type (Sahakian et al, 1990) at the critical extra-dimensional shifting stage. In terms of showing deficits of simple discrimination learning, they resemble patients with moderate Dementia of Alzheimer's type (Sahakian et al, 1990; (Table 41, overleaf). There is of course no evidence of any dementing process in the patients with OCD in this study to account for the deficits. It cannot also be argued that the deficit was due to a perceptual problem as OCD patients successfully completed the simple discrimination and reversal stages.

The difficulties in maintaining attention may have implications for the possible deficits in visual memory reported in some OCD patients (Zielinski et al, 1991; Boone et al, 1991). An inability to maintain attention may contribute to the reported visual memory deficits as the relevant aspects of the information may not have been encoded. Patients who repeatedly check to prevent a feared

Table 41: Summary of results of Set shifting task in different patient groups

(✗ denotes significant difference compared to a control group)

	ID SHIFT	ED SHIFT
Obsessive compulsive disorder	✗	✗
Multiple Systems Atrophy *(Robbins et al, unpublished)*	✓	✗
Parkinson's disease *(Downes et al, 1989)*	✓	✗
Parkinson's disease (non-medicated, mild) *(Owen et al, in press)*	✗	✗
Frontal lobe lesions *(Owen et al, 1991)*	✓	✗
Temporal lobe lesions *(Owen, 1992)*	✓	✓
Amygdalo-hippocampectomy *(Owen, 1992)*	✓	✓
Elderly *(Owen et al, 1991)*	✓	✗
Mild Dementia Alzheimer's *(Sahakian et al, 1990)*	✓	✓
Moderate Dementia Alzheimer's *(Sahakian et al, 1990)*	✗	✗

danger occurring (for example a gas tap being left on) may be repeatedly distracted by other environmental stimuli and not encode in memory whether they prevented the danger. If a subject is easily distracted by irrelevant stimuli it may contribute to the clinical phenomenon of obsessional doubting and indecisiveness. OCD patients may be collecting too much irrelevant data in the working memory and it's subsidiary systems to efficiently encode or process the data. A patient not only needs to encode the data that an action has been completed but also to accurately recall the last completed check by discriminating the last check from all previous checks (Otto, 1992). In this respect, visuo-spatial deficits may be a factor in poorly encoding the data.

Compulsive checking or washing is usually performed with a high demand for certainty and excessive responsibility (eg "I have to know for certain that I haven't made a mistake because if I have, then I will be wholly responsible for catastrophe"). This may bias the response towards less flexibility in switching "mental set" (as switching is perceived as too risky) and subsequent repetition of the act.

The results of the ED pass or fail subgroups suggest that one group of OCD patients is relatively unimpaired neuropsychologically ("ED pass") apart from an increased subsequent thinking time when they make a mistake on the

Tower of London task. There appears to be another smaller group of OCD patients ("ED fail") who have deficits in maintaining attention in terms of increased distractability and perseveration on the attentional set shifting task and who are inaccurate in solving the problems on the Tower of London task. The results of the "ED fail" patients are very similar to patients with frontal lobe excisions. Further research will be needed to determine whether "ED fail" OCD patients have greater abnormalities in neuroimaging studies, whether they have different symptom profile, whether they have an increased number of neurological soft signs or whether they have a worse prognosis during treatment. This study suggests that the profile of clinical symptoms is no different between the two groups although it was not a hypothesis that was tested at the outset and therefore the data was not systematically collected. There was however no significant differences in age, age of onset, duration, or estimated verbal IQ.

The study reinforces the notion that OCD is a heterogenous disorder and that diagnosis and a classification based upon clinical symptoms alone is inadequate. The heterogeneity of the disorder is the most likely explanation for differences in reported deficits from previous studies (neuropsychological, neurological and neuroradiological).

The general conclusion, therefore, which is supported from the results of both tests is that some OCD patients may

have special difficulty in planning and attending to relevant dimensions of compound stimuli when they make a mistake. Mistakes may lead to less flexibility in their mental set. They appear to have difficulties in attending to feedback and altering their strategy. This suggests impaired functioning of the central executive of the working memory and it's ability to coordinate the activities of the subsidiary slave systems (the "phonological" loop and the "visuospatial sketch-pad") in complex tasks that require continuous monitoring.

It is interesting to compare some of the findings of the attentional set-shifting task with experimental studies on primates who have had lesions of cholinergic cells of the basal forebrain (Roberts et al, 1990). This lesion results in about a 40% reduction of choline acetyl transferase in the frontal cortex. It results in deficits in earlier stages except simple discriminatory learning in attentional set-shifting tests similar to the one reported in this thesis. There are no deficits in either ID or ED shifting performance. The results suggest that cortical cholinergic loss is unlikely to account for attentional set shifting deficits in basal ganglia disorders, but may account for other cognitive deficits such as visual discrimination and learning difficulties. Further studies will need to replicate these findings and to produce lesions in other neural pathways before the two can be linked. There have been no previous reports of a deficit in acetylcholine

activity of the pre-frontal cortex in OCD and the neuroimaging studies suggest hyper-metabolism in the frontal cortex. It would be of interest to determine the effect of an anticholinesterase (eg physostigmine) or acetylcholine agonist (eg nicotine) in OCD patients who fail the earlier stages of the attentional set-shifting test and the effect on obsessional symptoms. Nicotine has been shown anecdotally to be effective in treating some cases of Tourette's syndrome and has not been studied in OCD (McConville et al, 1991).

Similar studies have also been conducted in marmosets with neurochemical lesions that deplete dopamine (and to a lesser extent noradrenaline) in several areas of the prefrontal cortex, including the dorsolateral and orbito-frontal cortex. In the attentional set shifting test, there were no effects on discrimination learning nor on intra-dimensional shift tests. The performance of the lesioned animals was significantly superior to that of controls at the ED shift stage. It seems that prefrontal dopamine depletion facilitates shifting between attentional dimensions (Roberts et al, 1991). The explanation for these findings may be related to an upregulation of sub-cortical striatal dopamine activity which improves the ED set shifting performance (Robbins et al, 1994). Such an interpretation would be consistent with the effect of L-Dopa in Parkinson's disease which presumably acts in the basal ganglia. The effect of dopamine agonists such as

dextro-amphetamine in OCD was transiently to improve symptoms (Insel, 1983). It would be of interest to determine the effects of dopamine agonists in OCD on ED set shifting performance and the effect on obsessional symptoms in the long-term.

One study (Park et al, 1994) has examined the effect of l-tryptophan depletion in normal volunteers on tests from CANTAB. Tryptophan is a precursor to serotonin and is obvious interest in the pathogenesis of OCD. In the study on normal volunteers, a low tryptophan condition impaired learning in the attentional set shifting and paired associates. The low tryptophan condition has its disruptive effect mainly on the reversal stages of the task, when the subject has to learn new stimulus-reinforcement associations. Furthermore it lengthened thinking times during the Tower of London planning task, but only in subjects already familiar with the task, suggesting a retrieval deficit. There was no effect on accuracy. The results supported a role for the serotonergic system in memory and learning not directly implicated in frontal lobe function. This result is surprising in view of the high concentration of serotonergic receptors in the basal ganglia (Steinbusch, 1981; Stuart et al, 1986) and in the mesencephalic raphe nuclei that innervate the prefrontal cortex. It is difficult to extrapolate these findings to OCD patients as multiple types and sub-types of serotonin receptors and pathways make the notion of hyper or

hyposerotonergic state far too simplistic. It might be predicted that chronic tryptophan depletion should exacerbate obsessional symptoms and increase the deficits found on the attentional set shifting task in OCD patients. Tryptophan depletion might also interfere with habituation (a form of learning) in patients receiving behaviour therapy and be one reason why some patients fail to habituate. A controlled trial of l-tryptophan in OCD patients receiving behaviour therapy would therefore be of interest especially in those patients who fail the earlier stages of attentional set-shifting test.

(ii) Methodological critique

The following methodological criticisms may be made of the study:

(i) The impairment on the CANTAB tests may have occurred because some of the patients were depressed. Beats et al (in press) have found evidence of cognitive impairment in elderly depressed patients on a wide range of tests on the CANTAB (eg. visual learning and memory, attentional set shifting and planning) that are usually reversible when the patient recovers. In a visual search test where it is possible to separate out accuracy and latency of response, depressed patients show preserved accuracy at the expense of latency. On the Tower of London task, elderly depressed patients took significantly

more moves to solve the problems as compared with their matched control group and this effect was more marked with the more difficult problems. This is in contrast to patients with OCD who were no different to controls. Depressed patients show no difference in initial thinking time, but did show a slower subsequent thinking time (which is similar to patients with OCD). On the attentional set shifting task, elderly depressed patients were impaired at both the intra- and the extra-dimensional set shifting and not at the earlier stages of simple and compound discrimination learning. Again this is in contrast to the pattern of results found in patients with OCD in which there is evidence of attentional deficits. Such a study has not been conducted in non-elderly depressed patients. Watts et al (1988) has however used a non-computerised version of the Tower of London task in which depressed patients were slower at both the initial and subsequent thinking time.

One hypothesis is that depressed patients are also deficient in their central executive (Robbins et al, 1992). Preliminary research from other studies shows that depressed patients do not show specific impairments in the immediate memory of the two subsidiary slave systems (the

"visuo-spatial sketch pad" and "the phonological loop") but in the central executive of the working memory. I have already discussed how it's role is to coordinate the various components in complex tasks that require continuous monitoring. Thus depressed patients and OCD patients may share some cognitive deficits in terms of impairments of their central executive and future studies are required to unravel any specific differences in the various components to the tests.

Depressive symptoms and OCD often co-exist and no standardised measure of severity of depression was used in this study. However all the patients were screened in a clinical interview by the author and patients with a DSMIII-R diagnosis of major depressive disorder or dysthymia were excluded from the study. The pattern of results on the CANTAB for OCD and depression, at least in the elderly, also appears different.

Another hypothesis is that the patients with OCD were slower because they lacked motivation. Against this hypothesis, is that motivation is more likely to affect accuracy on the Tower of London task. Patients with OCD were just as accurate as the controls, suggesting that they

were just as motivated to seek the right solution.

(ii) The impairment may have occurred because the patients were preoccupied by obsessional thoughts and ruminations. Patients whose clinical symptoms were dominated by obsessional ruminations were excluded from the study but some patients may have denied them to please the experimenter. There may still be occasional intrusive thoughts that will increase latency times or impair concentration on a task leading to errors. It is impossible to control for this completely in any study on OCD. All the patients were however directly questioned at the end of each test whether they experienced any obsessional thoughts or images during the test that might have interfered with the task. None reported doing so. Future studies should compare OCD patients with intrusive obsessional thoughts against those without to test this hypothesis further.

In a study on depressed patients, Watts et al (1988) examined the relationship between loss of concentration because of "mind wandering" onto competing thoughts or of "mind blanking". They studied 36 depressed patients in a memory test for prose and on a non-computerised version of

the Tower of London task. The frequency of mind wandering was associated with a poor memory for prose. This requires less effortful processing than the Tower of London task. Mind wandering did not correlate with the latency times on the Tower of London task but with the frequency of "mind blanking". The latter was hypothesised to be an aspect of the Supervisory Attentional System (SAS). When the attention is properly focused the dominant activity will be left uninhibited and the competing response inhibited. However the possibility arises that the inhibitory action of the SAS becomes generalised and that this would be experienced as "mind-blanking".

The results of this study suggest that competing obsessional or depressive thoughts cannot fully account for the performance deficits on the Tower of London task or the attentional set shifting task. It is however possible that intrusive obsessional thoughts contribute to the inefficiency of the working memory and the ability to coordinate the various components (thus leading to slower thinking times on the Tower of London task).

(iii) The impairments observed in this study may have occurred because of a deficit in spatial span or

spatial working memory. In patients with frontal lobe excisions, impaired accuracy on the Tower of London task correlated significantly with accuracy on CANTAB tests of spatial working memory, suggesting that some component of spatial working memory in the frontal lobe is an important part of planning ability (Owen, 1992). Success on the task will clearly depend upon the ability to keep in mind several sequences of moves and their likely outcome before choosing the perceived solution. If there are any deficits in spatial working memory in OCD patients, then it is more likely to effect the accuracy of the 4 and 5 move solutions on the Tower of London task which in this study was unimpaired. It is possible that the "ED fail" patients had deficits in spatial working memory as they were less accurate than healthy controls and this would need to be tested in future studies.

The ability to plan also depends on spatial span. This is impaired in patients with severe Parkinson's disease, right sided temporal lobe lesions or Alzheimer's disease but not in patients with frontal lobe excisions. Deficits in spatial span represent a more global deterioration of cognition and probably involves parietal lobe mechanisms (Owen, 1992). The

measure of spatial span on the CANTAB is based on the Corsi Block Tapping test (Milner, 1971). Most healthy controls score about 5 on the spatial span and a few score 4 (Saghal et al, 1992). A score of 3 would indicate marked cognitive impairment (eg dementia) in which there would be definite impairment on the Tower of London task. One would not expect any deficits in spatial span in OCD patients as they do not have global deficits in cognition. If they did have a deficit in spatial span then again it is more likely to affect the accuracy of the solutions on the Tower of London task which in this study was unimpaired.

The mnemonic load on the attentional set shifting task is also minimal and does not appear to depend on a normal visual memory. Patient's with mild Alzheimer's disease are unimpaired on the attentional set shifting task but show gross deficits on tests of visual memory (Sahakian, 1990).

(iv) The impairments are a general measure of psychopathology and further tests on the CANTAB would reveal further deficits. Against this suggestion, previous studies have suggested that patients with OCD are not uniformly impaired on

all tests but have a relatively high degree of specificity on visual memory, visuo-spatial skills and set-shifting tasks. The second piece of evidence against this is that deficits found in this study were highly specific and not general to all measures. The third piece of evidence against this hypothesis is that there was no correlation between measures on the Tower of London task with the severity of OCD symptoms. This evidence also suggests that the findings are not secondary to OCD, that is the symptoms are not interfering with the test performance and the findings are a true indicator of the underlying neural substrate.

(v) The population of patients with OCD is unrepresentative as they were recruited from a tertiary referral centre that is likely to be biased towards a more severe sample. The sample may be biased but there was no correlation between measures on the Tower of London task and severity of OCD symptoms.

(vi) It is possible that the control subjects were unrepresentative and that they included subjects with OCPD. Although Obsessive Compulsive Personality traits are common in the general population only a minority will suffer from a

OCPD. By comparison, 15 out of 40 OCD patients had OCPD. The results in OCD patients found no significant differences for those with and without OCPD. It therefore seems unlikely that OCPD had any influence on performance in the control subjects, but this requires further testing.

Findings in relationship to other studies in OCD

There have been no previous studies using the CANTAB tests in patients with OCD. The findings of the attentional set shifting task are in keeping with the controlled study by Head et al (1989) who found that patients with OCD had a deficit in their set shifting ability on the Wisconsin Card Sorting Test (WCST). Three other studies that have used WCST found no differences (Boone et al, 1991; Zielinski et al, 1991; Christensen et al, 1992). As I have already discussed in the introduction, the WCST is not a pure measure of set-shifting ability (Downes et al, 1989). This study has used a purer measure of set shifting and demonstrated that OCD patients have significant deficits in extra-dimensional Set shifting.

Attentional deficits were suggested using the Stroop Colour Word Interference test in the study by Rosen et al (1989) but were not replicated by Hollander et al (1993) or Zielinski et al (1991). This study has demonstrated significant deficits in the ability of some OCD patients to

maintain attention when distracted.

Recommendations for further research:

Further research could extend and clarify the current findings:

i) by including tests of spatial working memory to exclude this as a factor in planning deficits.

ii) the Tower of London task could be modified to increase the planning load to determine whether with an increase in difficulty, patients with OCD are less accurate and slower in their initial thinking times.

iii) the attentional set shifting task could be modified to determine if the failure is due to an inflexibility in mental set (perseveration) or to learned irrelevance. The latter may occur during the attentional set shifting task, when one of the stimulus dimensions is randomly correlated with reinforcement for the first seven stages and only becomes relevant at the EDS stage. Thus, failure at the EDS may result from an enhanced tendency to *ignore* a previously irrelevant stimulus dimension (i.e. learned irrelevance) rather than from a failure to shift *from* a previously relevant one (i.e. perseveration). Both components are thought to play a role in the deficits found in patients with Parkinson's disease (Owen, 1992). Patients with Parkinson's

disease receiving L-Dopa show little perseveration, but are impaired on the learned irrelevance condition. Unmedicated patients with Parkinson's disease show both kinds of deficit while patients with frontal lobe lesions show perseveration only.

iv) It would be of interest to investigate the effects of patient variables further. OCD is a heterogenous condition and in future it will be important to distinguish between various sub-groups. For example, further research would be required to determine the cognitive deficits in patients with obsessional slowness, in OCD with obsessions without compulsions, in OCD with co-morbid tic disorder or in OCD with high scores on soft neurological signs. The study does also address the specificity of the the findings to OCD and the study requires replication with other anxiety disorders (for example agoraphobia) and in obsessive compulsive related disorders (for example body dysmorphic disorder and hypochondriasis).

v) Further research is required to show the stability of the current findings in a longitudinal study in which patients are treated by behaviour therapy or an SSRI anti-depressant and the tests repeated. This will help to determine whether the findings in this study are

state or trait abnormalities. It might be predicted that the deficits are state abnormalities as the abnormalities found on neuroimaging have been reversible in those patients who respond to treatment. Lastly the CANTAB tasks should be done by OCD patients during functional imaging studies with the aim of defining the neural pathways and areas for the performance on each task.

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Appendix 1

DSM IIIR criteria for Obsessive Compulsive Personality Disorder(American Psychiatric Association, 1987)

A pervasive pattern of perfectionism and inflexibility, beginning by early adulthood and present in a variety of contexts, as indicated by at least five of the following:

i) Perfectionism that interferes with task completion. e.g. inability to complete a project because of overtly strict standards.

ii) Preoccupation with details, rules, lists, order, organization, or schedules to the extent that the major point of the activity is lost.

iii) Unreasonable insistence that others submit exactly to his or her way of doing things, or unreasonable reluctance to allow others to do things because of the conviction that they will not do them correctly.

iv) Excessive devotion to work and productivity to the exclusion of leisure activities and friendships (not accounted for by obvious economic necessity) .

v) Indecisiveness: decision making is either avoided, postponed or protracted, e.g. the person cannot get an assignment done on time because of ruminating about

priorities (do not include if indecisiveness is due to excessive need for advice or reassurance from others).

vi) Over-conscientiousness, scrupulousness, and inflexibility about matters of morality, ethics or values (not accounted for by cultural or religious identification).

vii) Restricted expression of affect.

viii) Lack of generosity in giving time, money or gifts when no personal gain is likely to result.

ix) Inability to discard worn-out worthless objects even when they have no sentimental value.

Appendix 2

DSM IIIR criteria for Obsessive Compulsive Disorder (American Psychiatric Association, 1987)

A. Either obsessions or compulsions:

Obsessions: (1), (2), (3) and (4)

(1) recurrent and persistent ideas, thoughts, impulses or images that are experienced, at least initially, as intrusive and senseless, e.g. a parent's having repeated impulses to kill a loved child, a religious person's having recurrent blasphemous thoughts.

(2) the person attempts to ignore or suppress such thoughts or impulses or to neutralise them with some other thought or action

(3) the person recognises that the obsessions are the product of his or her own mind, not imposed from without (as in thought insertion)

(4) if another Axis 1 disorder is present, the content of the obsession is unrelated to it, e.g. the ideas, thoughts, impulses, or images are not about food in the presence of an Eating Disorder, about drugs in the presence of a Psychoactive Substance Use Disorder, or guilty thoughts in the presence of a Major Depression.

Compulsions: Both (1), (2), and (3)

(1) repetitive, purposeful, and intentional behaviours that are performed in response to an obsession, or according to certain rules or in a stereotyped fashion

(2) the behaviour is designed to neutralise or to prevent discomfort or some dreaded event or situation; however, either the activity is not connected in a realistic way with what it is designed to neutralise or prevent, or it is clearly excessive

(3) the person recognises that his or her behaviour is excessive or unreasonable (this may not be true for young children; it may no longer be true for people whose obsessions have evolved into overvalued ideas)

B. The obsessions or compulsions cause marked distress, are time-consuming (take more than an hour a day), or significantly interfere with the person's normal routine, occupational functioning or usual social activities or relationships with others.

Appendix 3

Consent form.

I hereby consent to participate in a study that measures my IQ and tests my mental skills on a computer. I understand that I may stop the test at any time.

Signed.....

(Patient)

Date.....

Signed.....

(Doctor)

Date.....

Appendix 4

Case vignettes

Case histories were collected retrospectively from notes at the Bethlem and Maudsley Hospital. For this reason it was not possible to trace all the records as some reported as lost. No abnormal physical or neurological findings were documented in the notes for any patient. The case histories were split into two subgroups: (i) those completing the whole task ("ED pass" subgroup, n=25) on the attentional set shifting task and (ii) those failing at or before the final EDR stage ("ED fail" subgroup, n=15).

"ED pass" subgroup

No. 1

Age 51. Age of onset 29 years. Duration 22 years. Fear of harming himself or others in his family leading to checking rituals (eg gas taps, electric switches). Avoidance of writing or reading as he becomes "stuck" with some words (e.g."horror"). Compulsive rituals of "evening up" actions to prevent a disaster happening. Past history of depression. Family History of OCD.

No. 3

Age 31. Age of onset 17 years. Duration 14 years. Fear of contamination by predominantly germs, dog mess, or HIV.

Avoidance of anything related to above (for example condoms, homosexuals) leading to excessive handwashing up to 20 times a day (lasting 2 to 3 hours a day). Takes up to 100 baths daily and avoidance of public toilets and sexual intercourse. Also fear of being responsible for disaster leading to excessive checking of taps, locks and cooker.

No. 4

Age 21. Age of onset 15. Duration 6 years. Fear of causing harm to himself and others leading to repeated checking (e.g. taps, important documents). Frequent seeking of reassurance 10-12 times a day (up to 3-4 hours a day). Avoids leaving home alone and listening to the news in case it might contain items of violence or sexual crimes. Also fear of contamination from germs leading to excessive handwashing (20 times daily). Avoids touching waste-paper bins and toilets.

No. 5

Age 31. Age of onset 25 years. Duration 6 years. Fear of "doing things wrong" and of things being brought into or taken out of the house. Did not allow husband or anyone to move or take objects away from the house. Preoccupation with order and having perfection leading to taking up to 2 hours to get dressed. Past history of depression in 1982.

No. 7

Age 46. Age at onset 29 years. Duration 17 years. Obsessional slowness as a result of checking and rechecking even smallest actions. Procrastinates endlessly about a problem until he loses sight of the goal. Goes to sleep in his clothes, stops bathing and washing as it would take too long. Was unable to prepare meals at home as even making tea would take half an hour.

No. 8

Age 22. Onset age 11 years. Duration 11 years. Feared contamination from faeces, leading to avoidance of public toilets and compulsive washing, (8 hours a day), and showering, (5 hours a day). Also checking position of household objects up to 2 hours a day for fear of not being in "right" position.

No. 9

Age 31. Age of onset 7 years. Duration 24 years. Fear of contamination leading to extensive avoidance of items perceived to be contaminated with faeces, urine, semen, saliva, avoidance of being touched by others, and compulsive handwashing up to 100 times a day.

No. 10

Age 22. Age of onset 7 years. Duration 15 years. Fears of contamination and excessive responsibility for protecting his family from dying leading to excessive handwashing

(20 to 30 times daily), repeated counting and checking of electric switches and gas taps. Avoidance of touching door handles, touching people or being touched, and toilet seats. Past history of depression and anorexia nervosa. Family history of OCD.

No. 11

Age 51. Age of onset 32 years. Duration 19 years. Fear of contamination by faeces leading to avoidance of and excessive handwashing (30 times a day) and cleaning of all door and cupboard handles (half an hour daily). Avoids visitors, door handles, sexual intercourse, and touching husband's clothes. Uses a third of a toilet roll on each visit to the toilet.

No. 15

Age 36. Age of onset 21 years. Duration 15 years. Obsessional need for orderliness and actions to be done "right", leading to indecisiveness, procrastination, perfectionism, and slowness (e.g. having a bath would lead to remaining motionless for hours).

No. 18

Age 46. Age of onset 9 years. Duration 37 years. Fear of contamination from faeces, mucous, blood, dirt, radiation and fumes. Avoidance of situations such as public toilets, hospitals and people which might be associated with such contaminants. Ritualistic handwashing 90 times

a day and washing of clothes and flat up to 50 times day. Would change clothes several times a day. Past history of depression.

No 21

Age 39. Age of onset 12 years. Duration 27 years. Fear of contamination by radio-activity leading to: excessive handwashing up to 75 times a day, bathing up to three and a half hours daily, and avoidance of social contacts and many personal belongings.

No. 22

Age 31. Age of onset 27 years. Duration 4 years. Fear of contamination from urine and dirt, (e.g. dead skin, bread crumbs), leading to avoiding friends coming to his flat and eating some foods in his flat because of the mess that would occur. Handwashing rituals 40 to 60 times daily and need for orderliness, leading him to clean and tidy his flat for 2 to 3 hours daily. Also trichotillomania, with plucking pubic hairs $1^1/_2$ hours daily.

No. 24

Age 45. Age of onset 35 years. Duration 10 years. Fear of contamination form chemicals (e.g. paint, toilet cleaner, car batteries, turps, plant feed) leading to: avoidance of shops, areas within the home, cars, and public toilets, compulsive handwashing 150 times a day, checking

rituals (1 hour at lock, 2 and half hours at heater) changing clothes 3 to 4 times a day, and counting rituals.

No. 25

Age 63. Age of onset 15 years. Duration 48 years. Obsessional slowness related to avoidance of disorder and imperfection and need for meticulousness, (50 minutes to shave, 50 minutes to clean teeth, one hour to dress, one hour for breakfast, two hours to bath), eats out to avoid cooking and preparing food, because it would take too long.

No. 28

Age 31. Age of onset 11 years. Duration 20 years. Obsession about blasphemous thoughts of Jesus Christ and God leading to compulsive handwashing, ordering and repeating of actions. Washing/dressing took 3-4 hours and eating a meal 1 hour. Checking of light switches/gas-taps.

No. 29

Age 27. Age of onset 23 years. Duration 4 years. Fear of contamination from AIDS or germs and harming family which led to: handwashing rituals (up to x 20 a day), showering rituals twice a day for 15 minutes and after intercourse, frequent demands for reassurance, excessive changing her clothes on entering home, cleaning bathroom surfaces

daily and kitchen contents bleached weekly. Also excessive checking and counting up to 4 hours a day. Avoidance of touching contaminated items around the house, entering public toilets and crowded places.

No. 31

Age 41. Age of onset 31 years. Duration 10 years. Fear of contamination of herself and others by dirt or germs leading to avoidance of touching anything directly (e.g. uses tissues to pick up objects or knees to open doors).

No. 32

Age 40. Records not traceable.

No. 34

Age 60. Age of onset 10 years. Duration 50 years. Fear of contamination of others by herself leading to avoidance of touching any item perceived as dirty, avoidance of preparation of food, handwashing up to 15 times a day, toilet rituals up to 1 hour a day, and cleaning rituals of her clothes (up to 4 hours a day).

No. 36

Age 19. Age of onset 13 years. Duration 6 years. Fear of causing cancer in self and others, leading her to avoid certain foods, touching communal objects and personal belongings. Compulsive handwashing up to 70 times a day and bathing would last one hour a day. Would open doors

and drawers with her feet. Certain areas around her house perceived as contaminating were avoided.

No. 37

Age 31. Age of onset 20 years. Duration 11 years. Fear of contamination by germs leading to compulsive hand washing in a specific order (lasting up to 2 hours a day) and throwing away clothes daily. Additional diagnosis of social phobia. Past history of depression and suicide attempts in the past.

No. 38

Age 37. Records not traceable.

No. 39

Age 34. Age of onset 24 years. Duration 10 years. Fear of contamination from dirt and germs leading to: excessive handwashing up to 70 times a day, cleaning body with Dettol and Jeyes Fluid, extensive avoidance behaviour (eg door handles, food stuffs, toilet seats).

No. 40

Age 31. Age of onset 11 years. Duration 20 years. Fear of contamination and becoming blind, losing his limbs or having a serious accidents. Compulsion to takes food in and out of his mouth repeatedly. Washing his hair 5 x a day and cleaning his hands excessively. Using up to half a toilet roll to clean his bottom in the toilet.

"ED fail" sub-group

No. 2

Age 20. Age of onset 11 years. Duration 9 years. Fear of contamination from AIDS and previously asbestos, leading to avoidance of touching clothes that had been used 3 years ago; avoidance of touching door handles and going into others' bedrooms. Would not re-use previous opened make-up and toiletries and would purchase new items each week. Avoids using toilet paper in case they have been contaminated by another person. Symptoms are worse at time of periods. Also obsessional need for perfection in written work. She would have to rewrite and check letters repeatedly.

No. 6

Age 27. Age of onset 22 years. Duration 5 years. Fear of contamination from AIDS leading to avoidance of: finding a partner, masturbating, using deodorants, razors, brushing teeth, streets with overhanging houses and bridges, toilet seats, postage stamps and red meat. Compulsive handwashing up to one hour daily and washing of utensils and crockery excessively. Repeatedly checking that windows are shut and seeking reassurance from others.

No. 12

Age 40. Age of onset 21 years. Duration 19 years. Fear of illness by contamination from dirt and germs leading to

avoidance of going in certain areas in the house and compulsive handwashing. Emptying rubbish would take up to 8 hours of compulsive checking for money that may have been lost. Hoarding of unnecessary items. Past history of post-natal depression.

No. 13

Age 39. Age of onset 18 years. Duration 21 years. Fear of contamination from dirt and dust, leading to excessive checking and tidying around the house, which would take $4^1/_2$ hours a day. She would avoid skin contact with door handles, stereo and television buttons in case she would mark them. Cleaning rituals were performed in rigid routine to minimise disorder. Past history of depression.

No. 14

Age 46. Age of onset 35 years. Duration 11 years. Fear of contamination from dirt and germs leading to extensive avoidance behaviour, handwashing 5 or 13 x (up to 60 times day), excessive cleanliness and orderliness around the house. This would take up to 7 hours daily. Also excessive checking of plugs to ensure they are switched off and the kitchen area for dirt.

No. 16

Age 32. Age of onset 24 years. Duration 8 years. Obsessional slowness in carrying out household activities as a result of need to order, exactness and tidiness.

Would repeatedly check to ensure actions were done correctly, (e.g. taking $3^1/_2$ hours daily to clean the bathroom, $1^1/_2$ vacuuming around the house and 45 minutes to make the bed. His feared consequences would be of losing control if actions were not performed.

No. 17

Age 31. Age of onset 21 years. Duration 10 years. Obsessional thoughts about committing a sexual "perversion" on his father leading to avoidance of certain people. Also fear of contamination leading to compulsive handwashing up to 30 times a day and avoidance behaviour.

No. 19

Age 45. Age of onset 16 years. Duration 29 years. Fear of going blind leading to avoidance of touching various household items. She believed that small bits of various substances (e.g. dandruff, or biscuit crumbs could get into her eyes and blind her). Frequent counting and checking rituals and excessive washing (lasting up to two hours daily). Family history of OCD.

No. 20

Age 25. Age of onset 14 years. Duration 11 years. Obsession for order and position leading to his morning routine taking 3 hours, (dressing, combing his hair, going to the toilet and shaving). Repeated checking that

there are no bits of paper, dandruff or marks on himself or his clothes. Cleaning his dishes would take half an hour. Repeated checking of kitchen cupboards up to 3 or 4 times a day.

No. 23

Age 32. Records not traceable.

No. 26

Age 41. Age of onset 36 years. Duration 5 years. Fear of harming himself and others, leading to excessive checking. Repeats actions 4 times, tapping his thumb on door locks, saying words out loud or performing a ritual 4 times. Avoids working on his car or on jobs around the home as it would take too long. Seeks frequent reassurance from his wife. Unable to work as too handicapped.

No. 27

Age 23. Age of onset 11 years. Duration 12 years. Fear of going through perceived spaces defined by open bars, gates, trollies and bicycles. Frequently becomes "stuck" as he does not believe it will lead to a space that he can trust for real. As a consequence he may take 2 hours to get to bed, dress or change clothes, go through doors, sit or rise from a chair.

No. 30

Age 45. Age of onset 28 years. Duration 17 years. Fear of contamination (e.g. grease, dirt, smells, butter, fat, oil, plaster, dirt), compulsive handwashing 50 times a day and excessive cleaning of anything perceived as dirty. Changes clothes to go out of the house and avoids wearing contaminated clothes.

No. 33

Age 37. Age of onset 25 years. Duration years 12 years. Fear of contamination from germs, leading to avoidance of touching door handles, dirty chairs, specific areas at home, litter, cigarette ends, cups and bath edges. Compulsive handwashing lasting up to 3 hours at a time. Obsessive checking and meticulousness to ensure actions are "just right", leading to excessive slowness getting dressed (taking 3 hours), and getting to bed (lasting 3 hours).

No. 35

Age 26. Age of onset 24 years. Duration 2 years. Fear of contamination from dog and human excrement leading to excessive cleaning rituals, (would spend 7 hours a day washing, bathing, cleaning her home, clothes and shoes). Avoids many areas of her home and unable to prepare food. Restricts journeys to new places and would avoid public toilets and physical contact with others.