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Executive Functions in Obsessive-Compulsive Disorder:

A Neuropsychological and Event-Related Potential Investigation

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EXECUTIVE FUNCTIONS IN OBSESSIVE-COMPULSIVE DISORDER: A NEUROPSYCHOLOGICAL AND EVENT-RELATED POTENTIAL INVESTIGATION

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Concordia University, 1999

A number of authors have argued that obsessive-compulsive disorder (OCD) is associated with a significant disturbance of executive functions (e.g., response inhibition, mental flexibility). The present investigation employed both neuropsychological tests and event-related potentials (ERPs) to evaluate this hypothesis.

In experiment one 23 outpatients with OCD and 23 normal control participants (matched for age, gender, education and handedness) completed a battery of neuropsychological tests assessing the domains of executive functions, verbal memory, nonverbal memory, language abilities, visuospatial and motor functioning. Data were evaluated for group differences on raw test scores, composite scores formed by averaging standardized tests scores grouped according to sensitivity to areas of neuropsychological functioning, and effect size. Results have revealed poorer language ability in the context of overall adequate functioning in the OCD group. This finding may have been due in part to subtle disturbances in other cognitive functions as statistical evidence of differential deficit was not observed. Results could not be accounted for by demographic or clinical characteristics of the participants.

In experiment two 16 outpatients with OCD and 18 normal control participants completed a visual go/nogo task while ERPs were recorded. Results failed to support previous observation of nogo P300 topographic differences implicating impaired response inhibition in OCD. In contrast, controls demonstrated shorter posterior N100 latency, suggesting that OCD may be characterized by less efficient recruitment of posterior cortical pathways involved in the encoding of visual stimuli. In addition, the OCD group demonstrated shorter N200 and P300 latencies related to task parameters, consistent with previous investigations. The functional significance of the N200 and P300 findings is unclear but may reflect disturbances in the monitoring of self-generated actions and dysregulation of stimulus evaluation processes, respectively. Finally, unmedicated OCD patients demonstrated larger P300 amplitude to go than nogo stimuli suggesting that this group may have been composed largely of individuals who would show a positive response to treatment with selective serotonin reuptake inhibitors. Again, results could not be fully accounted for by demographic or clinical characteristics of the participants. The pattern of findings suggest that OCD may be related to a subtle disturbance of response monitoring. Further investigations addressing the potential influence of symptom subtypes, level of insight and comorbid diagnoses on executive functions in OCD are likely to prove fruitful.

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Introduction and Literature Review

The introduction and literature review has been presented in three parts. The first part was concerned with the definition and phenomenology of obsessive-compulsive disorder (OCD). The second part consisted of a review of only those studies that have evaluated executive functions in OCD. These studies were reviewed individually rather than having presented review articles in the area. All studies that were not directly concerned with executive functions in OCD were excluded from the review of literature. The third part was concerned with the nature of the investigation that has been reported in this dissertation.

Definition and Phenomenology

Obsessive-compulsive disorder (OCD) has been characterized as involving the presence of obsessions and/or compulsions (American Psychiatric Press, 1995). Obsessions have been defined as intrusive and recurrent thoughts, ideas, images or impulses, that seem to enter awareness involuntarily. Obsessions are usually abhorrent to the person, yet they are difficult to dismiss or control. Compulsions are repetitive, stereotyped behaviors or mental acts that one feels compelled or driven to perform, usually in response to obsessions. Although compulsions are carried out in order to reduce the discomfort or prevent some feared consequence associated with obsessions, they are clearly excessive and difficult to resist performing. Anxiety usually results when performance of the compulsion is prevented. Current diagnostic criteria (American Psychiatric Press, 1995) have required that the obsessions and compulsions be recognized

as excessive or unrealistic at some point over the course of the illness, and that the symptoms cause significant distress or functional impairment.

Most individuals who suffer from OCD have reported multiple obsessions and compulsions. Only a small percentage of individuals have reported obsessions in the absence of compulsions, and an even smaller number have reported compulsions in the absence of obsessions (Rasmussen & Tsuang, 1986; Rasmussen & Eisen, 1992). In addition, the type and severity of an individual's obsessions and compulsions can vary over the course of illness (Eisen & Steketee, 1997; Skoog & Skoog, 1999). Although the prevalence of various forms of obsessions and compulsions has varied from study to study, some consistency has been noted across investigations (Rasmussen & Eisen, 1992; Summerfeldt, Antony, Downie, Richter, & Swinson, 1997). The most common obsessions have been related to contamination, aggressive thoughts, need for symmetry or exactness, somatic fears and sexual thoughts. The most common compulsions have consisted of checking, cleaning and counting.

Prevalence

Until the mid-1980's, OCD was believed to be a relatively rare condition. Early investigations have reported prevalence estimates as low as 0.05% within the general population (Rudin, 1953). Even within psychiatric inpatient and outpatient populations the prevalence of OCD was estimated to fall between approximately 1% and 4% (Coryell, 1981; Ingram, 1961; Kringlen, 1965; Lo, 1967; Pollitt, 1957; Welner, Reich, Robbins et al., 1976). A number of early authors suspected that the above figures were likely to be underestimates given that many individuals who suffer from OCD do not seek treatment

due to fear, guilt or shame. The reluctance of individuals with OCD to reveal their illness to others has been noted since at least the first decade of the twentieth century (Freud, 1906-1908; cited in Freud, 1959). In addition, early investigations have generally employed hospital chart review to establish diagnoses with little standardization of diagnostic criteria.

More recent epidemiological investigations of OCD have obtained higher community prevalence rates than previous work. These studies have employed more objective diagnostic criteria and structured or semi-structured interviews. A number of large adult community studies have been conducted using the Diagnostic Interview Schedule (DIS; Karno, Golding, Sorensen, & Burnam, 1988; Robins, Helzer, Croughan, et al., 1981) as part of the Cross National Collaborative Group on the epidemiology of psychiatric disorders (Weissman et al., 1994). The DIS is a structured interview that was developed for use by lay interviewers in epidemiological surveys. Countries included in the survey consisted of Canada, Germany, Korea, New Zealand, Puerto Rico, Taiwan and the United States. Results of the cross national survey were highly consistent across sites, with annual prevalence rates ranging from 1.1% to 1.8%, and lifetime rates from 1.9% to 2.5%.

Two community surveys of OCD have been conducted in Canada. The first study was conducted with a sample of 3,258 adults living in Edmonton as part of the cross national collaborative survey (Bland, Orn, & Newman, 1988; Kolada, Bland, & Newman, 1994). Results revealed annual and lifetime prevalence rates of 1.4% and 2.3%, respectively. The second survey evaluated 2, 261 adults in four regions of Canada and

found a one-month prevalence rate of 3.1% (Stein, Forde, Anderson, & Walker, 1997; cited in Antony, Downie, & Swinson, 1998).

The higher prevalence rates found in recent epidemiological studies must be interpreted with some caution. The reliability of the DIS diagnosis of OCD over one year (Nelson & Rice, 1997) and almost three years (Newman & Bland, 1998) has been reported to be low. The use of lay interviewers was related to over-diagnosis in a study in which individuals with OCD were re-interviewed by trained clinicians (Stein et al., 1997). Furthermore, although recent research has indicated that the relative frequency of OCD as a discharge diagnosis rose significantly from 1969 to 1990, this increase was significantly correlated with the relative increase in scientific publications on the treatment of the disorder (Stoll, Tohen, & Baldessarini, 1992). This latter finding has been interpreted as suggesting that clinicians may be more willing to diagnose OCD given the availability of innovative or effective treatments. Increased public awareness of OCD subsequent to heightened media coverage of the disorder in the early 1980s may have also led to higher rates of self-diagnosis and self-referral for treatment (Ricciardi, 1993).

Demographic Correlates

The relationship between prevalence rates, symptoms and a variety of demographic characteristics has been examined in OCD. Most studies have focused their investigation on gender differences. With respect to gender, epidemiological general population studies which have been conducted in a number of countries have observed either a slightly higher prevalence rate for women than men (Bebbington, 1998; Henderson & Pollard, 1988; Weissman et al., 1994) or no significant difference (Nastadt,

Samuels, Romanoski, Folstein, & McHugh, 1994). The majority of studies of adult clinical samples have not found significant gender differences in prevalence rate (Black, 1974; Rasmussen & Eisen, 1992). In addition, few gender differences in the prevalence of specific OCD symptoms have been noted (Castle, Deale, & Marks, 1995; Lensi, Cassano, Correddu, Ravagli, Kunovac, & Akiskal, 1996).

A number of studies have investigated the relationship between OCD and other potentially salient demographic characteristics. OCD has been consistently reported to be more prevalent among Caucasians than other ethnic groups (Bebbington, 1998; Karno & Golding, 1991; Nastadt et al., 1994). A clear theoretical basis for this finding has not been offered at this time. The religious background of individuals with OCD within a given culture has not been found to differ significantly from the general population (Raphael, Rani, Bale, & Drummond, 1996; Rasmussen & Eisen, 1992; Steketee, Grayson, & Foa, 1987). Data with regards to the relationship between OCD and such sociodemographic characteristics as education, marital status, employment and income has remained equivocal in both general (Bebbington, 1998; Karno et al., 1988; Karno & Golding, 1991) and clinical (Antony et al., 1998; Steketee et al., 1987) populations.

Age of onset and Course of OCD

Age of onset has been investigated in several studies of OCD. An insidious rather than an abrupt onset has been reported to be much more common in idiopathic OCD (Rasmussen & Tsuang, 1986). The mean age of onset has been observed to fall within the early twenties (Burke, Burke, Regier, & Rae, 1990; Castle et al., 1995; Lensi et al., 1996; Minichiello, Baer, Jenike, & Holland, 1990). These findings have been observed

both in general and clinical samples. The mean age of onset has tended to be somewhat earlier for men than women (Burke et al., 1990; Castle et al., 1995; Lensi et al., 1996; Minichiello et al., 1990). The latter finding has been interpreted by some authors as reflecting some as yet undetermined gender divergent etiological variable(s) (Noshirvani, Kasvikis, Marks, Tsakiris, & Monteiro, 1991).

The course of OCD subsequent to onset has been observed to be somewhat variable. Improvement rates have ranged from about 32% to 74% (Berrios & Chiu, 1989; Coryell, 1981; Goodwin, Guze, & Robins, 1969; Lo, 1967; Kringlen, 1965; Rudin, 1953). It should be noted that most of the long-term studies have been limited by reliance on retrospective information. In addition, the criteria used to define improvement has varied significantly rendering cross-study comparisons difficult.

A prospective study was recently conducted in Sweden in which 251 patients with OCD were re-evaluated forty-years after they were initially diagnosed (Skoog & Skoog, 1999). Results revealed that 83% of the sample experienced a reduction in the severity of their symptoms by the end of the study period. Despite these promising findings, of the 83% that improved 35% have continued to have clinically significant symptoms and 28% have continued to experience symptoms at a subclinical level. An additional 9% have not demonstrated any improvement, and another 8% have had a deteriorating course. These results are generally consistent with most retrospective investigations, although the study suffers from a number of methodological limitations. Most individuals with OCD have continued to experience their obsessions and compulsions even after relatively extended periods of time.

Personal and Social Costs

Given the relatively chronic nature of OCD, it is not surprising that the disorder has been associated with a variety of social and personal costs. OCD has often been associated with marked distress and functional impairment (Steketee, 1997). OCD has also been associated with impoverished health-related quality of life (Koran, Thienemann, & Davenport, 1996), social adjustment (Hollander, Kwon, Stein, Broatch, Rowland, & Himelein, 1996; Khanna, Rajendra, & Channabasavanna, 1988) and impaired family functioning (Calvocoressi, Lewis, Harris, Trufan, Goodman, McDougle, & Price, 1995; Cooper, 1996; Hollander et al., 1996). The World Health Organization has recognized OCD as the eleventh leading cause of disability among physical and psychological (Murray & Lopez, 1996).

OCD has also been observed to have important societal consequences. The disorder has been associated with high health care costs (Dupont, Rice, Shiraki, et al., 1995; Hollander et al., 1996; Simon, Ormel, VonKorff, & Barlow, 1995) that include significantly greater use of mental health services (Leon, Portera, & Weissman, 1995; McCusker, Boulenger, Boyer, Bellavance, & Miller, 1997), and greater likelihood of receiving disability payments (Leon et al., 1995) than the general population.

OCD and Executive Functions

Theories

It is a relatively recent phenomenon that etiological hypotheses of OCD have been based on other than psychodynamic or behavioral theories (Jenike, 1990). Moreover, psychosocial stress has been reported to be associated with the onset of OCD symptoms and increases in symptom severity, but has not been found to be of direct relevance to the etiology of the disorder (DeSilva, 1988; Reed, 1985).

Recently, the recurrent, persistent and stereotyped nature of obsessions and compulsions have led several authors to question the integrity of brain regions involved in the inhibition and modulation of ongoing behavior in OCD. The idea that OCD is related to impoverished inhibitory control has been particularly common in neurobiologically based theories, although Freud's psychodynamic theory (1909, cited in Freud, 1959) postulated that the failure to fully repress unacceptable primitive impulses is an important aspect of the disorder. Neurobiological theories implicating impoverished inhibitory control in the etiology of OCD have hypothesized that the disturbance has occured secondary to a deficit in serotonin (Yaryura-Tobias, Bebirian, Neziroglu, & Bhagavan, 1977); is due to impoverished left frontal lobe integrity leading to poorly modulated verbal ideation and subsequently to recurrent and stereotyped thoughts (Flor-Henry, 1983); or is the result of disruption of the developmental maturation of frontal lobe-basal ganglia circuitry resulting in a primary disturbance in the ability to suppress contextually inappropriate responding (Rosenberg & Keshavan, 1998).

Several other theories have been proposed that indirectly implicate impoverished inhibitory control in the etiology of OCD. These theories have still emphasized in one manner or another a disturbance in the modulation of behavior or sensory information in the disorder. Impoverished modulation has been argued to result from a disconnection between the frontal lobes and limbic system resulting in a failure to correctly monitor ongoing activity in relation to the environment in order to terminate behaviors when they are no longer appropriate (Malloy, 1987); innocuous or inappropriate stimuli having acquired excessive emotional meaning for individuals with OCD because of a failure of the basal ganglia-limbic circuit to properly filter all of the afferent information coming from the orbitofrontal cortico-thalamic circuit (Modell, Mountz, Curtis, & Greden, 1989); or a neurologically based bias toward responding to socially and biologically relevant stimuli such as sex and aggression, which has rendered switching to more contextually appropriate behaviors difficult (Saxena, Brody, Schwartz, & Baxter, 1998).

Although these neurobiological theories of OCD have differed with respect to the emphasis they have placed on specific neuroanatomical circuits, as well as the specific functional disturbances resulting from the particular neural abnormality, they have all been consistent with the idea that OCD is related to a disturbance of executive functions. The construct of executive functions was therefore discussed prior to reviewing the empirical literature pertaining to executive functions in OCD.

Definition of Executive Functions

The term executive functions has been used with increasing frequency in the neuropsychology literature. Despite its frequent use, the term has continued to lack precise operationalization as there remains some controversy among theorists and investigators with regards to what exactly comprise executive functions.

Lezak (1983; 1995) has argued that executive functions are comprised of four main components: (1) volition; (2) planning; (3) purposive action; and (4) effective performance. Volition refers to the capacity to formulate goals or at least form an intention to act. Planning is related to volition in that it consists of the ability to determine and organize the steps needed to achieve a goal. Purposive action refers to the implementation of a plan, including the ability to initiate, maintain, alter and discontinue complex behavior sequences in an orderly and integrated manner. Effective performance requires that a person be continuously aware of the goal of a plan and the extent to which current actions are leading to the goal. The ability to self-monitor and self-correct are therefore necessary in order to attain a goal in the most efficient manner possible.

Stuss and Benson (1986) included as executive functions the capacities of anticipating future events and consequences, establishing goals, planning, monitoring the results of behavior and the use of feedback. Welsh and Pennington (1988) have defined executive functions as "the ability to maintain an appropriate problem solving set for attainment of a future goal." These authors have argued that executive functions consist of inhibition, planning, and the ability to mentally represent tasks. Daigneault, Braun and Whitaker (1992) have argued that executive functions consist of planning and execution of sequences of planned responses; self-regulation of behavior in response to

environmental contingencies; maintenance of a cognitive and behavioral set that is not carried out automatically; spontaneous and sustained mental productivity; and segmentation and organization of events over time and space. Denkla (1996) has argued that executive functions consist of inhibition, maintenance of a preparedness to act, responding following delays, as well as the planning of sequences of actions.

Roberts and Pennington (1996) have proposed that the ability to maintain and manipulate information in short-term memory in order to be used for upcoming action (also referred to as working memory), and the ability to inhibit inappropriate action are core executive functions that are likely to be necessary for other executive functions such as planning. A similar view has been expressed by other authors (Barkley, 1996; Cohen & Servan-Schreiber, 1992; Diamond, 1990; Fuster, 1989; Kimberg & Farah, 1993).

Elsinger (1996) has attempted to provide a cohesive definition of executive functions based on behaviors that have been argued to be representative of the term by members of a working group on executive functions (Barkley, 1996; Borkowski & Burke, 1996; Denckla, 1996; Graham & Harris, 1996; Hayes, Guifford, & Ruckstuhl, 1996; Pennington, Bennetto, McAleer, & Roberts, 1996). The behaviors most consistently enumerated were: self-regulation, performance of behaviors in an appropriate sequence, flexibility, response inhibition, planning and organization of behavior. Based on these behaviors, Elsinger defined executive functions as "psychological processes that have the purpose of controlling the implementation of activation-inhibition sequences, that is guided by diverse neural representations (verbal rules, biological needs, somatic states, emotions, goals, mental models), for the purpose of meeting a balance of immediate

situational, short-term, and long-term future goals, that span physical-environmental, cognitive, behavioral, emotional, and social spheres."

Tranel et al. (1994) have also attempted to achieve a cohesive operationalization of executive functions. In contrast to Elsinger (1996), Tranel et al. produced a list of concepts based on an extensive review of the theoretical and experimental work on executive functions over the past century, including the theories listed above. Concepts enumerated by Tranel et al. included planning, decision-making, working memory, self-monitoring, self-modulation, and the capacity to utilize feedback to direct and alter responding. Despite being based on somewhat different bodies of information, the concepts enumerated by Elsinger and Tranel et al. are quite similar and have appeared to capture the essential elements of what most theorists have considered to be executive functions.

Neuroanatomical Basis of Executive Functions

Controversy over what comprises executive functions has stemmed at least in part from the practice of using of the terms executive and frontal lobe functions interchangeably. This use of the terms has promoted confusion between a neuroanatomical region of the brain and a psychological construct referring to several cognitive operations.

It has been generally accepted that the frontal lobes play a major role in the cognitive operations subsumed under the rubric of executive functions (Barkley, 1997; Fuster, 1989; Goldman-Rakic, 1987, 1995; Roberts & Pennington, 1996; Stuss & Benson, 1986; Stuss, Eskes, & Foster, 1994; Tranel, Anderson, & Benton, 1994). In both

human and animal research damage to the frontal lobes has been generally accompanied by disturbances on tasks designed to assess various aspects of executive functions (for reviews see Fuster, 1989; Miller & Cummings, 1999). Damage to different regions of the frontal lobes has also been reported by some investigators to result in impairments in different executive functions. For example, disturbances in working memory have been more likely to occur following damage to the dorsolateral prefrontal cortex, while impoverished behavioral inhibition has been more common following orbitofrontal damage (Duffy & Campbell, 1994; Fuster, 1999; Malloy & Richardson, 1994).

Nevertheless, poor performance on executive function tasks has also been observed in individuals without evidence of damage to the frontal lobes. For example, focal basal ganglia infarctions have been associated with executive disturbances (Dubois, Defontaine, Deweer, Malapani, & Pillon, 1994; Strub, 1989). Such evidence does not preclude the possibility that subtle frontal lobe abnormalities such as metabolic disturbances rather than structural damage are present. It has thus been increasingly recognized that executive functions are likely to be the product of an interaction between the frontal lobes and other cortical and subcortical regions of the brain (Elsinger, 1996).

Neuroimaging and Executive Functions in OCD

Neuroimaging studies have provided indirect support for executive function disturbance in OCD. Specifically, one of the most consistent neurobiological findings in the OCD literature has been that of abnormal cerebral metabolism in the frontal lobes on PET and SPECT scans when individuals with OCD were tested at rest (Baxter, Phelps, Mazziotta, Guze, Schwartz, & Selin, 1987; Harris, Hoehn-Saric, Lewis, Pearlson, &

Streeter, 1994; Nordahl, Benkelfat, Semple, Gross, King, & Cohen, 1989; Rubin, Villanueva-Meyer, Ananth, Trajmar, & Mena, 1992; Swedo, Schapiro, Grady, Cheslow, Leonard, Kumar, Friedland, Rapoport, & Rapoport, 1989). The precise region of the frontal lobe that is abnormal has varied across studies. A trend in the data has suggested that the right frontal lobe may be particularly disturbed (Benkelfat et al., 1990; Harris et al., 1994). Cerebral metabolism has also been noted to be abnormal in other brain regions such as the caudate nuclei and cingulate gyrus. Such findings have been observed with less consistency that for the frontal lobe data (Saxena et al., 1998).

Further support for a frontal lobe involvement in OCD has been found in studies in which cerebral metabolism has been measured using positron emission computed tomography both before and after a standard course of treatment. Several investigations have observed that the treatment of individuals with OCD with either a selective serotonin reuptake inhibitor such as Fluoxetine or cognitive-behavioral therapy results in significant decrease of abnormal frontal metabolism and synptom severity (Benkelfat, Nordahl, Semple, King, Murphy, & Cohen, 1990; Swedo, Pietrini, Leonard, Schapiro, Rettew, Goldberger, Rapoport, Rapoport, & Grady, 1992; Saxena et al., 1998).

Symptom provocation studies in which patients with OCD are presented with symptom-related stimuli (e.g., pictures of dirty clothes) during the measurement of cerebral metabolism have also indicated involvement of the frontal lobes in OCD. In particular, OCD patients have demonstrated abnormal metabolism in either both or just the right orbitofrontal cortex during provocation (Breiter, Rauch, Kwong, Baker, Weisskoff, Kennedy, Kendrick, Davis, Jiang, Cohen, Stern, Belliveau, Baer, O'Sullivan,

Savage, Jenike, & Rosen, 1996; McGuire, Bench, Frith, Marks, Frackowiak, & Dolan, 1994; Rauch, Jenike, Alpert, Baer, Breiter, Savage, & Fischman, 1994).

In summary, the neuroimaging findings have been generally consistent with the hypothesis that the neuroanatomical circuitry believed to subserve executive functions is disturbed in OCD. The neuroimaging data has not, however, provided functional demonstration of impoverished executive functions. In contrast, a number of studies have been conducted with OCD patients using neuropsychological tests which place considerable demands on executive functions. These will be reviewed below.

Neuropsychological Assessment of Executive Functions in OCD

Literature Search

Empirical investigations in which neuropsychological tests of executive functions were administered to individuals with OCD were located using the *MedLine* (National Library of Medicine) and *PsychLIT* (American Psychological Association) computerized literature databases for the years 1975 through 1999. The search terms "obsessive" and "compulsive" were used in order to obtain as complete a list of publications on OCD as possible. In addition, the reference lists of all the articles identified through the computerized literature searches that pertained to neuropsychological functioning in OCD were explored for the presence of any additional articles germane to the present topic.

Determination of whether a specific neuropsychological test is a measure of executive functions or of other cognitive domains was based on factor analytic studies (Ernst, Warner, Hochberg, & Townes, 1988; Francis, Fletcher, Rourke, & York, 1992; Larrabee & Curtis, 1995; Leonberger, Nicks, Larrabee, & Goldfader, 1992; Robertson,

Ward, Ridgeway, & Nimmo-Smith, 1996; Shute & Huertas, 1990; Swiercinsky & Hallenbeck, 1975; Swiercinsky & Howard, 1983), as well as the widely referred to functional classifications provided by Lezak (1995) and Spreen and Strauss (1998). Following this guideline a total of thirty publications were identified that investigated OCD using neuropsychological tests with strong executive function components. It should be noted, however, that there are no "pure" tests of executive functions. Tasks that are purported to measure executive functions are also likely to place some demands on other functional domains such as verbal memory and visuospatial skills.

Several investigations have appeared to have not used completely independent subject samples. These are the studies by Behar and colleagues (Behar, Rapoport, Berg, Denckla, Mann, Cox, Fedio, Zahn, & Wolfman, 1984; Cox, Fedio, & Rapoport, 1989); Scarone and colleagues (Abbruzzese, Bellodi, Ferri, & Scarone, 1995a; Abbruzzese, Ferri, & Scarone, 1995b; Cavedini, Ferri, Scarone, & Bellodi, 1998; Gamnini, Abbruzzese, & Scarone, 1993); Hollander and colleagues (Aronowitz, Hollander, DeCaria, Cohen, Saoud, Stein, Liebowitz, & Rosen, 1994; Cohen, Hollander, DeCaria, Stein, Simeon, Liebowitz, Aronowitz, 1996; Hollander, Cohen, Richards, Mullen, DeCaria, & Stern,1993; Hollander & Wong, 1996); Martin and colleagues (Martin, Pigott, Lalonde, Dalton, Dubbert, & Murphy, 1993; Martin, Wiggs, Altemus, Rubenstein, & Murphy, 1995); and Purcell and colleagues (Purcell, Maruff, Kyrios, & Pantelis, 1998a; Purcell, Maruff, Kyrios, & Pantelis, 1998b). Nevertheless, all of the studies were reviewed since they provided somewhat different information with regards to neuropsychological functioning in OCD. Descriptive information for these studies has been presented in Table 1.

Table 1

Methodological Characteristics of Neuropsychological Studies of Executive Function in OCD Patients

Study	Samples	Medication Status	Methodological control CD	A	G	E	Domains	Data analysis	Comment
Flor-Henry et al. (1979)	11 adult OCD 11 control	Not reported	Schizophrenia or primary affective disorder.	+	-	+	A, EF, I, L, M, V, VIM.	Multiple univariate	Groups also matched for WAIS full-scale IQ.
Insel et al. (1983)	18 adult OCD No control group	Unmedicated	Schizophrenia or primary affective disorder.	-	-	-	A, EF, I, L, M, VIM.	Patient scores compared to normative data	
Behar et al. (1984)	16 adolescent OCD 16 control	Not reported	Psychotic symptoms, primary depressive disorder.	+	+	-	A, EF, L, V, VEM, VIM,.	ANOVA	Groups also matched for race, handedness and WISC-R full-scale IQ.
Cox et al. (1989)	42 adolescent OCD 35 Normal control.	Not reported	Psychotic symptoms, primary depressive illness.	+	+	-	A, EF, I, V, VEM, VIM	ANOVA	Groups also matched for race, handedness and WAIS or WISC full scale IQ. IQ lower than 85 also exclusion criterion.
Harvey (1986)	19 adult OCD No controls	No medication for 24-36 hrs prior to testing.	Psychosis, alcoholism.	-	-	-	EF, I, L.	Patient data compared to published normative data.	
Malloy (1987)	17 adult OCD No controls	Not reported	Not reported	-	-	-	A, EF, I, L, V, VEM, VIM.	Patient data compared to normative data.	

Table 1 continued...

Study	Samples	Medication Status	Methodological control CD	A	G	E	Domains	Data analysis	Comment
Head et al. (1989)	15 adult OCD 15 normal control	Unmedicated	"important additional psychiatric symptoms."	+	+	+	EF, I, L, V	Multiple t-tests.	Groups also matched for handedness, and NART verbal IQ
Gambini et al. (1993)	23 adult OCD 27 normal control	13 medicated 10 no medication for at least 1 week	No other Axis I or Axis II.	-	-	-	A, EF.	MANCOVA and F-tests.	11 patients had history of tic disorder. Controls significantly more years of education.
Abbruzzese et al. (1995a)	47 adult OCD 33 normal control	33 medicated 14 unmedicated	Statistical control for comorbid mood or anxiety disorder.	+	+	+	EF, I, L.	Multiple ANOVAs.	Groups also matched for handedness.
Abbruzzese et al. (1995b)	25 adult OCD 25 Paranoid schizophrenia 25 Normal control	Medicated	-	+	+	+	EF.	MANOVA, ANOVA and Scheffe t-tests.	Groups also matched for handedness.
Gross-Isseroff et al. (1996)	15 adult OCD 15 Normal control	Unmedicated for at least 14 days prior to testing.	HDRS ≤ 16.	+	+	+	EF, I.	Wilcoxon	Groups also matched for intelligence. Only women as subjects.
Cavedini et al. (1998)	28 adult OCD 29 Major Depression	Unmedicated for at least one month.	Other Axis I.	-	+	+	EF, L, VEM, VIM.	ANOVA	Groups also matched for handedness.
Martinot et al. (1990)	14 adult OCD 17 Normal control	10 medicated 5 tested after 2-week drug washout 1 drug-naive.	Current MDE, substance abuse, ECT in last six months or gross pathology on CT	-	-	-	A, EF, L, V, VIM.	Multiple t-tests.	Groups also matched for handedness.

Table 1 continued...

Study	Samples	Medication Status	Methodological control CD	A	G	E	Domains	Data analysis	Comment
Boone et al. (1991)	27 adult OCD 16 Normal control	Unmedicated for at least 4 weeks prior to testing.	Affective, schizophrenia-spectrum or organic mental disorders.	+	-	+	A, EF, I,L, V, VEM, VIM.	t-tests with Bonferroni correction.	Nine controls siblings of OCD patients. 2 in each group with learning disability.
Zielinski et al. (1991)	21 adult OCD 21 Normal control	9 medicated 12 unmedicated for at least two weeks prior to testing.	Affective disorders, schizophrenia, substance abuse, pure obsessionals and OCD with pure obsessional slowness.	+	+	+	A, EF, I, L, VEM, VIM,	ANOVA	Groups also matched for race, socioeconomic status and handedness.
Christensen et al. (1992)	18 adult OCD 18 Normal control	Unmedicated for at least 2-4 weeks prior to testing.	DSM-III Axis I.	+	+	+	ACH, EF, I, L, M, V, VEM, VIM.	MANOVA and ANOVA	
Martin et al. (1993)	17 adult OCD 11 Trichotillomania 16 Normal control	Unmedicated for 6 weeks prior to testing.	Not reported.	+	-	+	EF, I, L, M, V, VEM.	ANOVA	Groups also matched on NART Verbal IQ.
Martin et al. (1995)	18 adult OCD 18 Normal control	Unmedicated for 6 weeks prior to testing.	Not reported.	+	+	+	EF, I.	ANOVA	Groups also matched on NART Verbal IQ.
Aronowitz et al. (1994)	31 adult OCD 22 Normal control	Medication free for at least 4 weeks.	MDD	+	+	+	A, EF, I, VIM.	t-tests	Groups also matched on occupational level.
Hollander et al. (1993)	37 adult OCD 35 Parkinson's disease 27 Normal control	Not reported	Not reported for OCD group.	+	-	-	A, EF, V.	ANOVA and t-test	Each patient group had own age-matched normal control groups. Comparison of OCD and PD used sub-samples to age-match.

Table 1 continued...

Study	Samples	Medication Status	Methodological control CD	A	G	E	Domains	Data analysis	Comment
Hollander & Wong (1996)	50 adult OCD 31 Normal control	Unmedicated for 4-6 weeks	Not reported.	+	+	+	EF	t-tests	
Cohen et al. (1996)	65 adult OCD 17 Social phobia 32 Normal control	Unmedicated for at least 2 weeks.	HRSD ≤ 16.	+	-	-	A, EF, I, V, VIM.	MANOVA, ANOVA and Scheffe.	
Schmidtke et al. (1998)	29 adult OCD 58 Normal control	Unmedicated or washout for at least 1 week prior to testing.	8 OCD with past or current MDD, 12 with personality disorders, two with history of eating disorder and two history of alcohol abuse.	+	+	-	A, EF, I, L, M, VEM.	MANOVA, t-tests and logistic regression.	Groups also matched for WAIS-R full-scale IQ. Two controls were matched to each patient.
Veale et al. (1996)	40 adult OCD 22 Normal control	8 medicated	Any comorbid psychiatric disorder.	+	-	-	EF, I.	ANOVA	Groups also matched on NART verbal IQ.
Purcell et al. (1998a)	30 adult OCD 30 Panic disorder 20 MDD 30 Normal control	23 OCD medicated	DSM-IV Axis I.	+	+	+	A, EF, I, V, VIM.	MANOVA, ANOVA, type I error adjusted for number of domains.	Groups also matched on handedness and NART verbal IQ.
Purcell et al. (1998b)	23 adult OCD 23 Normal control	17 medicated 6 unmedicated for at least 8 weeks prior to testing.	DSM-IV Axis I.	+	+	+	A, EF, I, V, VIM.	MANOVA, ANOVA, and alpha set at .01.	Groups also matched on NART verbal IQ.

Table 1 continued...

Study	Samples	Medication Status	Methodological control CD	A	G	E	Domains	Data analysis	Comment
Hymas et al. (1991)	16 adult OCD 15 Normal control	2 OCD taking neuroleptics the rest not reported.	-	+	+	-	EF, I, L, M, V.	t-test	All patients tested had significant obsessional slowness. Groups also matched on NART verbal IQ.
Galderisi et al. (1995)	22 adult OCD 21 Normal control	Medication free for at least 15 days.	Substance abuse and MDE.	+	-	+	A, EF.	MANOVA and ANOVA	Groups also matched on handedness.
Thienemann & Koran (1995)	21 adult OCD No controls	Unmedicated for at least 2 weeks.	Any other current psychiatric disorder.	-	-	-	EF, L, M, V.	Patient scores compared to normative data.	
Clayton et al. (1999)	17 adult OCD 13 Panic Disorder 14 Normal control	Medicated.	-	+	-	-	A, EF, I.	ANOVA and Scheffe.	Groups also matched for NART verbal IQ

Note. Domains: A = attention, ACH = achievement, EF = executive functions, I = intellectual, L = language, M = Motor, V = Visuospatial, VEM = vebal memory, VIM = visual memory. HDRS = Hamilton Depression rating Scale. ECT = Electroconvulsive therapy. MDE = major depressive episode. MDD = major depressive disorder. NART = National Adult Reading Test.

In addition to the investigations using patient samples, three studies of executive functions have tested university students with elevated scores on self-report measures of OCD symptomatology (Goodwin & Sher, 1992; Roth & Baribeau, 1996; Zohar, LaBuda, & Moschel-Ravid, 1995). These studies were discussed given their relevance to the present topic.

Executive Functions in OCD Patients

The first published neuropsychological investigation of OCD was conducted by Flor-Henry, Yeudall, Koles, and Howarth in 1979. These authors administered a battery of neuropsychological tests, including the Halstead-Reitan Neuropsychological Test Battery (HRB; Reitan, 1959), that provided 28 variables for analysis to OCD patients and normal controls. Results revealed significantly poorer performance by the OCD group on tests of attention (Digit Span subtest of the Wechsler Adult Intelligence Scale, WAIS: Seashore Rhythm Test), psychomotor speed (WAIS Digit Symbol), language (Wepman-Jones Aphasia), spatial learning (Tactual Performance Test, bilaterally), visuospatial skills (Symbol Gestalt), and fine motor coordination and speed (Purdue Pegboard, bilaterally). Performance on executive function tests was variable with OCD patients being worse on the Halstead Category Test but not the Trail Making Test or an oral word fluency task. Flor-Henry et al. interpreted the pattern of findings as reflecting left frontal lobe dysfunction (Reitan, 1959; Royce, Yeudall, & Bock, 1976), and hypothesized that OCD was the result of poor inhibitory control over verbal ideation.

Insel, Donnelly, Lalakea, Alterman, and Murphy (1983) determined the number of OCD patients who scored below a scaled score of eight on the WAIS and within the impaired range on the HRB using normative data from healthy volunteers (Russell, Neuringer, & Goldstein, 1970). No evidence of impaired executive functions was observed. Consistent with Flor-Henry et al. (1979), the OCD patients as a group were bilaterally impaired on the Tactual Performance Test. No other impairment was noted for the patient group. WAIS Performance IQ was observed to be lower than Verbal IQ by at least 15 points in a subset of patients. In addition, a small subset of patients were observed to have HRB average impairment ratings (AIR) within the impaired range. The AIR is a measure of the overall integrity of neuropsychological functioning. These findings were interpreted as suggesting a relatively diffuse disturbance of the right hemisphere.

Behar and colleagues (1984) administered neuropsychological tests to adolescents with OCD and normal controls. The OCD group demonstrated significantly poorer performance on the Money Road Map and Stylus Maze Learning tasks. These findings were interpreted as suggesting disturbances in set-shifting and visuospatial ability. The groups did not differ on tests of auditory verbal learning, visual memory, visuoconstruction ability, tactual perception, or processing speed (reaction and decision time tasks). Essentially the same findings were observed by these investigators in an expanded sample of adolescents with OCD and normal control subjects (Cox et al., 1989). The patient group in the latter study also performed poorly on the Wisconsin Card Sorting Task (WCST), providing further evidence for executive function disturbance. The disturbance was not selective as the OCD group also performed poorly on

visuoconstruction, visual memory, and timed visual word recognition tasks. Severity of OCD symptoms, as assessed using both self-report and interview measures, was not significantly related to task performance in either study. These findings were interpreted as reflecting frontal lobe and possibly right hemisphere disturbances.

Harvey (1986) evaluated the mental flexibility of adults with OCD using a modified version of the WCST (MWCST; Nelson, 1976), as well as verbal fluency and category alternation tests (Newcombe, 1969). Results revealed a significantly greater number of perseverative responses on the MWCST in the OCD group as compared to Nelson's (1976) normative sample, indicating a disturbance in set-shifting ability. No information was provided about the performance of the patients on the verbal fluency and category alternation tests with respect to normal controls.

Head, Bolton, and Hymas (1989) also evaluated set-shifting ability in patients with OCD and normal controls using a variety of tests including the MWCST, word fluency, category alternation, Money Road Map and Stylus Maze tests. Participants were also administered tests of visuospatial and visuoconstruction. The pattern of group differences was interpreted as being consistent with a set-shifting deficit. The patient group also performed worse on the Block Design subtest of the WAIS-R (Wechsler, 1981) suggesting a disturbance of visuospatial and visuoconstruction ability.

Malloy (1987) administered tests of intelligence, attention, memory and executive functions to patients with OCD and compared their performance to normative data. Poor performance was observed only on the WCST, and this only for a subsample of patients.

The patients who performed poorly were characterized by lower intellectual functioning, poorer prognosis and more psychotic symptoms than the OCD patients who performed well on the WCST.

A series of investigations by Scarone and colleagues also focused largely on the ability of OCD patients to shift set (Gambini, Abbruzzese, & Scarone, 1993; Abbruzzese, Bellodi, Ferri, & Scarone, 1995a; Abbruzzese, Ferri, & Scarone, 1995b). Gambini et al. (1993) evaluated the performance of OCD patients and normal controls on the WCST and the Toulouse-Pieron Test, the latter being a measure of attention and concentration. No significant group differences were observed after the effects of education were covaried out (Gambini, Macciardi, Abbruzzese, & Scarone, 1992).

In a subsequent study, Abbruzzese et al. (1995b) again evaluated WCST performance in OCD but also attempted to provide greater control over potential confounding variables. The authors matched patient and normal control groups for age, gender, education and handedness. Both medicated and unmedicated patients were evaluated. No significant differences were noted between the patient and normal control groups on any of the six WCST measures employed. Comparison of OCD patients subgrouped according to their predominant symptoms (checking, washing, mental checking, mixed), as measured using the Yale-Brown Obsessive Compulsive Scale (YBOCS; Goodman, Price, Rasmussen, Mazure, Delgado, Heninger, & Charney, 1989a; Goodman, Price, Rasmussen, Mazure, Fleischmann, Hill, Heninger, & Charney, 1989b), also failed to reveal any significant differences. In addition, patients with and without comorbid mood and/or anxiety disorders performed in a similar manner. The unmedicated group was observed to have significantly more total errors and a lower

percentage of conceptual level responses than the medicated patients. The latter finding was attributed to the potential influence of "state" effects (e.g., anxiety, inattention) on task performance.

The Scarone group have also conducted two investigations in which OCD patients were compared to psychiatric control groups using test batteries with multiple executive function measures. Abbruzzese et al. (1995a) compared patients with OCD, patients with schizophrenia and normal controls on the WCST, Weigl Sorting test (Weigl, 1941), Controlled Oral Word Fluency (Benton & Hamsher, 1976) and an Object Alternation Test (OAT; Freedman & Oscar-Bergman, 1986a, b). OCD patients were observed to make significantly more perseverative errors on the OAT than either the schizophrenia or normal control group, but did not differ from normals on the other tasks. The pattern of findings was interpreted as being consistent with a disturbance of the orbitofrontal cortex in OCD given that damage to this area of the brain has been observed to result in impaired performance on the OAT in both humans and animals (Freedman & Oscar-Bergman, 1986; Mishkin, Vest, Waxler, & Rosvold, 1969).

Cavedini et al. (1998) compared patients with OCD or major depressive disorder on the Wechsler Memory Scale (Wechsler, 1945), as well as on the battery used in the Abbruzzese et al. (1995a) study. No normal control group data was provided. Consistent with the Abbruzzese et al. (1995a) study, results revealed that the OCD group made a significantly greater number of perseverative responses than the major depression group on the object alternation task. Although the OCD group was significantly younger than the depression group, this finding could not be accounted for by age, gender or Hamilton Rating Scale for Depression score (Hamilton, 1960),

Gross-Isseroff, Sasson, Voet, Hendler, Luca-Haimovici, Kandel-Sussman, & Zohar (1996) administered the WCST and a somewhat longer version of the OAT to patients with OCD and normal controls. Results revealed that the OCD group was significantly slower in completing the WCST. This finding was nonspecific as the patients were also slower in completing a test of intellectual functioning. Generalized slowness has been previously observed in a number of studies of OCD patients (Sawle, Hymas, Lees, & Frackowiak, 1991). The OCD group also made less alternations on the OAT and needed more trials to achieve the criterion of five consecutive alternations. Group differences for the number of perseverative errors on the OAT was not reported precluding direct comparison with the studies by Scarone and colleagues. Severity of OCD symptoms, as measures by the YBOCS, was significantly correlated with OAT performance. These findings were interpreted as providing further albeit tentative support for orbitofrontal dysfunction in OCD.

Martinot and colleagues (Martinot, Allilaire, Mazoyer, Hantouche, Huret, Legaut-Demare, Deslauriers, Hardy, Pappata, Baron, & Syrota, 1990) compared non-depressed inpatients with OCD with normal controls on a battery of tests tapping several neuropsychological domains. Results revealed poorer performance by the OCD group on most (Stroop task, graphic alternating sequence and Trail Making Test) but not all (word fluency) executive function tests. A generalized pattern of neuropsychological impairment was noted as the patient group also performed worse on tests of auditory and visual attention, verbal and visual memory, as well as visuospatial and visuoconstruction ability. Martinot et al. (1990) reported that the patient group's poor Stroop performance was significantly correlated with lower glucose metabolic rate in the lateral prefrontal

cortex as evaluated using PET. The authors interpreted the latter finding as being consistent with a disturbance in the ability of individuals with OCD to inhibit inappropriate responses such as obsessions and compulsions.

Boone and colleagues (Boone, Ananth, Philpott, Kaur, & Djenderedjian, 1991) compared non-depressed OCD patients and normal controls on a battery of tests that included a number of executive function measures (Auditory Consonant Trigrams, WCST, Stroop, Design and Word Fluency). Findings indicated that the OCD group had lower Full-Scale and Performance IQ than controls, as well as poorer performance on tests of nonverbal memory (Rey Figure) and visuospatial skills (Hooper Visual Organization Test). Only the group difference in Performance IQ remained significant after controlling (Bonferroni) for the large number of statistical comparisons. The authors interpreted their results as indicating impoverished visuospatial ability implicating basal ganglia and/or right hemisphere dysfunction in the disorder.

Zielinski, Taylor and Juzwin (1991) compared patients with OCD and normal controls on tests of intelligence, attention, memory and executive functions. Results revealed that the OCD group was characterized by significant disturbances in visual attention and visuospatial processing, but did not differ from controls on measures of executive functions. Findings were unrelated to the presence of either depression or anxiety. No differences were noted between medicated and unmedicated patients. Although the patient group did not differ from controls on standard tests of executive functions, they made significantly more intrusion errors during both the immediate and delayed recall trials of a visual memory test (Recurring Figures Test; Kimura, 1963), as well as on a word-list learning task (California Verbal Learning Test; Delis, Kramer,

Ober, & Kaplan, 1986). An intrusion error occurs when a subject produces items that were not previously presented in a task. Zielinski et al. indicated that their patients often produced the same incorrect word over several trials of the word-list learning task. They interpreted this finding as possibly reflecting a disturbance in the ability to self-correct. As noted previously, the ability to monitor and correct one's actions is considered to be an executive function (Barkley, 1997).

Christensen, Kim, Dysken and Hoover (1992) administered a battery of neuropsychological tests to non-depressed OCD patients and normal controls matched for age, education and gender. The OCD group demonstrated significantly poorer performance on a task of delayed memory for visual material. Poor performance on visuospatial tasks was also noted but the authors attributed this finding to a general reduction in performance on all timed tasks. In addition, the authors reported that group differences on executive function tasks (WCST, word fluency, Category Test) only reached "borderline significance." It is unclear why the authors reported the latter finding as being of only "borderline significance" given that group differences on tasks reflecting other domains of cognitive functioning (e.g., delayed visual memory) were considered significant at the same level of alpha that executive function tests were considered of borderline significance (i.e., $p \leq 0.05$).

Thienemann and Koran (1995) observed that in their group of patients with OCD 10% obtained Stroop scores and 14% controlled oral word fluency task scores below published cutoff values for abnormal performance. They interpreted these findings as being consistent with impoverished executive functioning in a subset of the sample. No normal control group was employed. No information was provided with regard to

possible differences in clinical or other characteristics between patients who performed well and those who performed poorly on the tasks.

Martin and colleagues (Martin, Pigott, Lalonde, Dalton, Dubbert, & Murphy, 1993) compared unmedicated patients with OCD and those with trichotillomania to normal controls on tests of intelligence, reaction time, visuospatial skills, verbal learning and memory as well as executive functions. No significant difference was observed in any functional domain. Martin et al. (Martin, Wiggs, Altemus, Rubenstein, & Murphy, 1995) also compared unmedicated OCD patients and matched controls on the self-ordered pointing task, a task that places significant demands on the ability to monitor ones actions. Results revealed that the OCD group took a significantly greater amount of time to complete the task than the control group but did not demonstrate poorer performance. This finding may have been due to the presence of secondary depression as a significant positive correlation was observed between completion time and depression as measured using the Hamilton Depression Rating Scale.

Aronowitz et al. (1994) compared non-depressed outpatients with OCD to normal controls on a battery of tests designed to assess auditory and visual attention, visual memory, set shifting, visuospatial and visuoconstruction abilities. The OCD group obtained poorer scores on visuospatial tasks as well as the Trail Making Test, a task that requires set shifting, sequencing and visual scanning. Further analyses indicated that male but not female OCD patients performed poorly on visuoconstruction and visual attention tasks. Hollander et al. (1993) also observed poorer visuospatial and visuoconstruction ability in an expanded sample of OCD outpatients and normal controls. The groups did not differ in their performance on measures of auditory attention or

response inhibition (Stroop). Hollander and Wong (1996) observed poorer Trail Making Test performance in OCD in a further expanded sample of patients and normal control subjects.

Cohen et al. (1996) compared unmedicated OCD and social phobic patients to normal controls on tests on auditory and visual attention, visuospatial and visuoconstruction ability, as well as the Trail Making Test. Comparison of the OCD and normal control group revealed significantly poorer performance by the former group on tests of visual attention, visuospatial and visuoconstruction ability. The social phobia group performed worse than controls on the Trail Making Test suggesting impoverished visual scanning and/or mental flexibility. No significant correlations were noted between test performance and a measure of anxiety, although it should be noted that the anxiety measure was administered between one and fourteen days prior to the test battery.

Schmidtke, Schorb, Winkelmann and Hohagen (1998) compared unmedicated OCD patients and normal controls on tests of attention, verbal memory and executive functions. Results revealed significantly poorer performance by the patients on tests of visual attention, letter and figural fluency, concept formation and set shifting. Further analysis of task performance indicated that the OCD group made a significantly larger number of perseverative errors on the letter and figural fluency tasks, as well as the concept formation task. Groups did not differ with respect to reaction time or accuracy on a choice reaction time task. Although a subset of the patient group had a current or past diagnosis of major depression, Hamilton Depression Rating Scale scores did not correlate significantly with test performance.

Veale, Sahakian, Owen and Marks (1996) administered computerized versions of the Tower of London and a set-shifting task to OCD inpatients and normal controls. Results revealed that the patient group spent significantly more time generating alternative problem solving strategies on the Tower task following errors, but did not actually make more errors than controls. In addition, the OCD group demonstrated poor set-shifting ability and heightened distractibility during the set-shifting task. These findings were interpreted as being consistent with a disturbance of fronto-striatal circuitry.

Purcell, Maruff, Kyrios and Pantelis (1998a) evaluated the accuracy and speed of performance of OCD patients on a series of computerized neuropsychological tests, including the Tower of London and set-shifting tasks administered by Veale et al. (1996). The OCD group was observed to perform more poorly than controls on measures of spatial working memory and spatial recognition, as well as the initiation and execution of motor movements. The latter findings in combination with the observation that poor spatial working memory in OCD was largely due to a failure to develop effective strategies for remembering the material, were interpreted as suggesting disturbances of attention and executive functions. No group differences were noted on tests of short-term memory, visual memory, pattern recognition, set shifting or planning ability. Medicated and unmedicated patients did not differ with respect to neuropsychological test performance. In addition, group differences could not be accounted for by depression, anxiety, IQ or level of education.

Purcell and colleagues (Purcell, Maruff, Kyrios, & Pantelis, 1998b) administered the same computerized test battery to an expanded sample of OCD patients and normal controls, as well as major depression and panic disorder psychiatric control groups. Comparison of the OCD and normal control groups revealed essentially the same findings as Purcell et al.'s previous investigation (1998a). In contrast, only set-shifting was noted to be poorer for patients with major depression relative to normal controls. The panic disorder group did not differ from normal controls on any of the measures.

Consistent with the findings of Purcell et al. (1998a, 1998b), Hymas, Lees, Bolton, Epps and Head (1991) observed significant difficulty initiating goal-directed actions in a subsample of their sample of OCD patients. This sub-sample was also noted to have considerable difficulty inhibiting perseverative responding, and performed poorly on some of the tests visuospatial and visuoconstruction abilities. Low scores on the tests were unrelated to depression, psychomotor slowness, treatment with neuroleptics or comorbid neurologic illness.

Galderisi, Mucci, Catapano, Colucci and Maj (1995) compared OCD patients and normal controls on the spatial and non-spatial versions of the conditional associative learning tasks, and the word and drawing versions of the self-ordered pointing task. Implicit auditory and verbal learning tasks were also administered. Results revealed significantly slower performance by the patient group on the executive but not the implicit learning tasks. Groups did not differ with respect to the accuracy of performance on any task. No correlation between task performance and depression was noted. Galderisi et argued that slowness in OCD cannot be fully accounted for by either

meticulous concern for correct performance or the presence of intrusive thoughts during task performance since slowness was only observed on the executive tasks.

Finally, Clayton, Richards and Edwards (1999) administered the Test of Everyday Attention (TEA) to patients with OCD, panic disorder, and normal controls. The TEA consists of a series of neuropsychological tasks designed to assess selective attention, sustained attention. divided attention and set-shifting. Patients with OCD performed significantly worse than the panic and normal control groups on the measures of set-shifting, sustained and selective attention. The latter finding was interpreted as being consistent with the hypothesis that people with OCD have a disturbance in the ability to selectively ignore external and internal stimuli.

Findings with Nonclinical Samples

Three studies have investigated executive functions in nonclinical populations with elevated scores on self-report measures of OCD symptomatology. Several studies have supported the use of such populations for analogue research on OCD (Gibbs & Oltmanns, 1996). Such studies may be informative given the control over medication history and the presence of chronic psychopathology.

Goodwin and Sher (1992) administered the WCST to university students who scored high or low on the checking subscale of the Maudsley Obsessional Compulsive Inventory (MOCI; Rachman & Hodgson, 1980). The high group made significantly more errors overall, more perseverative errors and took longer to complete the task than the low group. These findings were essentially replicated at a five month follow-up, although self-report level of anxiety accounted for the relationship between checking and WCST

performance during the initial but not the follow-up assessment. In summary, these findings were interpreted by the authors as suggesting that poor set-shifting may be a state rather than a trait variable.

Zohar et al. (1995) also observed a significant relationship between the checking subscale of the MOCI and WCST performance in a sample of university students. Specifically, checking was correlated with WCST perseverative errors and total number of trials to task completion, but not mean reaction time. The potential influence of affective variables on these findings was not evaluated.

Roth and Baribeau (1996) evaluated the performance of university students who scored high or low on the checking subscale of the MOCI on the self-ordered pointing task and tests of verbal and visual memory. Results revealed significantly more perseverative errors on the self-ordered pointing task in the checker group when abstract rather than representational drawings were employed as stimuli. In contrast, the groups did not differ significantly on tasks of verbal and visual memory. When the data were re-analyzed using trait anxiety as covariate the checkers were noted to have significantly better memory for visual stimuli after a thirty minute delay. Depression and state anxiety did not significantly influence the findings. These findings were interpreted as being consistent with a disturbance in the ability to monitor ongoing actions.

Summary and Methodological Issues in the Neuropsychological Investigations

In summary, the neuropsychological literature has provided some evidence of impoverished executive function in OCD. The disturbance may not be specific, however, as disturbances have been observed in other functional domains (e.g., visuospatial skills). In addition, the neuropsychological findings have been somewhat inconsistent for both executive and other functional domains, as well as the individual tests used to assess specific cognitive domains. Any conclusions reached with regards to the neuropsychological literature must therefore be tempered.

A number of design and statistical limitations may have impeded the determination of whether OCD is associated with a differential deficit in executive or other cognitive functions. Potential confounding variables have been inconsistently accounted for thus introducing further uncertainty into the literature. Pertinent and potential methodological and statistical limitations of previous neuropsychological studies of OCD were therefore addressed in the present dissertation.

Normal control group. The findings of a number of the studies of executive function in OCD have been difficult to interpret because no normal control group was included in the evaluation (Cavedini et al., 1998; Harvey, 1986; Insel et al., 1983; Malloy, 1987; Thienemann & Koran, 1995). Instead, these studies compared the performance of OCD patients to published normative data. Such comparisons have regularly been made for clinical purposes. Nevertheless, a number of problems have been discussed with respect to comparing the test results of individuals with those obtained from normative samples. These problems have included the use of normative data gathered from subjects

tested in different clinics or laboratories, which increases the probability of significant variations in testing conditions, and the often limited information with regard to the demographic characteristics of the normative sample (Spreen & Strauss, 1998). A further problem has been that few neuropsychological tests have been co-normed using the same population. Significant findings in a clinical sample such as OCD have thus been difficult to interpret because the pattern of significant and non-significant results may have been in part related to the characteristics of the different normative samples used for each test rather than actual differential test performance.

Demographics. Neuropsychological test performance may be related to a variety of demographic variables, particularly chronological age, gender and education (Heaton, Ryan, Grant, & Matthews, 1996). Many of the studies of OCD listed in Table 1 have attempted to match patient and control groups on one or more demographic variables in order to control for their potentially confounding influence on test performance. Only 37% percent of the investigations have matched groups on age, gender and education.

The majority of studies (73%) have matched groups for age. Significant findings on certain tests have been observed to be rendered non-significant when age was used as a covariate (Cavedini et al., 1998; Hollander et al., 1993). The effects of age as covariate, however, has not been consistent for specific tests or across investigations. Correlations between age and test scores have also generally been small and non-significant (Purcell, 1998b).

A little over half the studies (53%) have matched groups for gender composition. Despite differences between men and women with OCD in terms of age of onset and the prevalence of certain symptoms, no consistent relationship between gender and neuropsychological test performance in OCD has emerged (Abbruzzese et al., 1995a; Boone et al., 1991; Cavedini et al., 1998; Cohen et al., 1991).

About half the studied (53%) have matched groups on the basis of years of education. Control for education has been occasionally noted to reduce or eliminate test performance differences between OCD and normal control samples (Gambini et al., 1993; Gross-Isseroff et al., 1996; Hollander et al., 1993; Purcell et al., 1998b). This observation is consistent with the significant relationship between education and test performance reported in many normative studies (Spreen & Strauss, 1998). Nevertheless, the specific tests that have been rendered non-significant following statistical control for education have been inconsistent across investigations.

A number of studies (40%) have matched groups on overall intellectual functioning or verbal intelligence. Such matching has been based on the premise that intellectual functioning is significantly related to performance on neuropsychological tests, although this issue is a matter of considerable debate (Bell & Roper, 1998; Dodrill, 1997). In general, intellectual functioning has not appeared to significantly influence test performance differences between OCD and normal control subjects (Cohen et al., 1996; Purcell et al., 1998b).

A third of the studies have matched groups according to handedness, usually by employing only or a majority of individuals who are right-handed. Handedness has been noted to contribute to subtle differences in cognitive functioning in some studies of

normal, neurological and psychiatric populations (Lezak, 1995). Nevertheless, the small number of left-handers that have been employed in studies of OCD has precluded the investigation of any potential relationship between handedness and neuropsychological performance.

Treatment effects. Neuropsychological test performance in OCD may be affected by concurrent pharmacotherapy. To control for this potential confound several of the studies listed in Table 1 only included participants who were unmedicated at the time of testing, and/or compared the test performance of medicated and unmedicated OCD patients. Only Abbruzzese et al. (1995a) have observed a significant effect of medication status, unmedicated patients obtaining more total errors on the WCST than medicated patients.

Affective state. Neuropsychological studies of psychiatric disorders have often attempted to exert experimental control over the potential influence of affective variables such as depression and anxiety on test results. Concern that comorbid depression may obscure the relationship between OCD and neuropsychological test performance has appeared to be justified. Major depression has been associated with poor performance on tests tapping a variety of neuropsychological domains such as psychomotor speed, attention and memory (King & Caine, 1996; Sweet, Newman, & Bell, 1992), although the findings have not been wholly consistent (Sweet et al., 1992).

A number of neuropsychological investigations of OCD have attempted to control for depression by excluding subjects with a comorbid major depressive disorder, or using the score on a psychometric measure of depression (e.g., Hamilton Depression Rating Scale) as a covariate in statistical analyses (see Table 1). Otto (1992) noted that studies in which OCD patients with comorbid major depression were excluded have been less likely to yield significant findings on tests of executive functions. This conclusion may be somewhat premature. A number of investigations published since Otto's review have failed to detect a statistically significant relationship between depression and neuropsychological test performance in OCD (Cavedini et al., 1998; Hymas et al., 1991; Purcell et al., 1998b; Schmidtke et al., 1998). Review of the executive function studies listed in Table 1 further revealed that exclusion of patients with comorbid major affective disorder has not been consistently related to a failure to detect poorer performance on executive function tasks in OCD.

The relationship between anxiety and neuropsychological test performance has also received attention as a potential confound in studies, albeit significantly less than depression. Research employing normal subjects has not revealed any consistent relationship between measures of anxiety and neuropsychological test performance (Buckelew & Hannay, 1986; Martin & Franzen, 1989; Waldstein, Ryan, Jennings, Muldoon, & Manuck, 1997). There have been only a few studies of neuropsychological test performance in patients suffering from anxiety disorders other than OCD. These studies have suffered from a number of methodological limitations including the use of limited test batteries. The available data has suggested that social phobia but not panic disorder may be associated with impoverished executive functions (Cohen et al., 1996;

Purcell et al., 1998). The limited findings available do not provide convincing evidence that high levels of anxiety or the presence of an anxiety disorder is associated with poor performance on tests of executive functions. Few of the studies of OCD listed in Table 1. have attempted to control for level of anxiety. Overall, these studies have not found a significant relationship between neuropsychological test performance and measures of current (state) or more pervasive (i.e., trait) anxiety in patients with OCD (Purcell et al., 1998b; Zielinski et al. 1991).

Sample size, type I error and power. Interpreting the findings of many neuropsychological studies of OCD has been rendered difficult because of the use of relatively small sample sizes, large numbers of dependent variables and an emphasis on using multiple univariate statistical analyses (i.e., multiple t-tests and analysis of variance). All these factors have contributed to an elevated probability of committing Type I error, that is, falsely rejecting the null hypothesis that the groups do not differ significantly. Although some studies have employed corrections to alpha (e.g., Bonferroni correction) in order to reduce the probability of committing Type I errors (e.g., Boone et al., 1991), using such procedures may have had the unfortunate consequence of reducing the ability to detect "true" group differences or statistical power (Cohen, 1992). Statistical power may also have been limited in the many studies that have employed relatively small sample sizes.

Unfortunately, any attempt to identify a differential neuropsychological deficit or pattern of neuropsychological performance will require the use of a large number of tests tapping multiple functional domains. The sample size required in order to achieve a high

level of statistical power in such research is likely to be highly difficult to attain (Cohen, 1988), particularly when studying clinical populations such as OCD that are relatively rare and often resistant to disclosing their illness.

Several statistical procedures may be helpful in attempting to balance the probability of Type I error and the need for statistical power. Planned comparisons may help reduce Type I error by limiting statistical analyses to those group comparisons that are of greatest interest. Unfortunately, this form of analysis is not helpful when differential deficit is being evaluated. Multivariate techniques such as multiple analysis of variance (MANOVA) may reduce the probability of Type I error by decreasing the overall number of statistical comparisons conducted. To date only seven of the thirty studies on executive functions in OCD have employed multivariate statistical procedures. For example, Christensen et al. (1992) grouped tests into functional domains and then conducted a separate MANOVA on each domain. If the MANOVA was significant only then did the authors proceed to conduct univariate analyses on the individual tests within the domains. This procedure reduced the overall number of statistical comparisons, thus reducing the probability of committing Type I error.

Differential deficit. Numerous authors have argued that OCD is related to frontal lobe, or more specifically, executive function deficits (Flor-Henry, 1979; ; Khanna, 1988; Malloy, 1987). The question thus arose as to whether the presence of an executive function disturbance is actually the most prominent disturbance in the disorder (Tallis, 1997). As reviewed above, a number of studies have noted disturbances in functional domains other than executive functions. Many of the studies listed in Table 1, however,

employed only a limited number of tasks thus precluding a detailed evaluation of differential deficit. Investigations that have assessed several domains of functioning have failed to include statistical analyses that would permit the evaluation of whether OCD is related to a differential deficit in executive functions.

Chapman & Chapman (1973a, 1973b, 1978, 1989) have argued that tests with greater reliability and difficulty are more likely to differentiate groups of subjects who differ in ability level. Such tests may also best discriminate groups in part because they may be more sensitive to generalized performance deficits in the poorer performing group. These psychometric artifacts have been noted in a number of studies where a generalized pattern of neuropsychological impairment has precluded the identification of a differential deficit (Braff, Heaton, Kuck, Cullum, Moranville, Grant, & Zisook, 1991).

Chapman & Chapman (1989) have discussed a number of strategies for dealing with the above psychometric problems. One strategy has involved closely matching all tasks on a number of psychometric characteristics that can introduce artifacts into group differences, particularly test reliability and difficulty. Standardized neuropsychological tests have not been titrated for difficulty with respect to one another nor have they been closely matched on other psychometric characteristics. Some authors have been able to successfully apply this strategy using a very small number of experimental tasks (e.g., Kwapil, Hegley, Chapman, & Chapman, 1989; Rattan & Chapman, 1973). The manipulation of task parameters and the number of normal control subjects required for adequate matching (Chapman & Chapman, 1978) of a battery of neuropsychological tests tapping a variety of functional domains is, however, clearly prohibitive.

Chapman and Chapman (1989) have proposed another strategy that can be readily applied to data obtained from neuropsychological test batteries and does not require matching tasks on psychometric properties. The strategy was based on the work of Lord (1963) and employed standardized residualized scores to answer the question "to what extent is a subject's score on task B deviant, given that subject's score on task A." This technique was designed to remove extraneous variance measured by a number of tasks (e.g., verbal memory) from the primary task of interest (e.g., executive). The technique thus took into account correlations between tests. This latter characteristic of the Chapman and Chapman method has been particularly useful as significant correlations have been commonly observed between scores on neuropsychological instruments. The technique has also assumed a full range of possible scores at all levels of accuracy in task performance. This has reduced the psychometric artifact introduced by employing tasks of unequal difficulty level with groups that are likely have different ability levels on various tasks.

The technique of standardizing residualized scores has thus provided greater confidence in the evaluation of differential deficit. It has not allowed for complete confidence that the effects of generalized performance deficit have been removed (Chapman & Chapman, 1989). The procedure has been employed in several studies to investigate neuropsychological test performance in schizophrenia (Saykin, Gur, Gur, Mozley, Mozley, Resnick, Kester, & Stafiniak, 1991; Saykin, Shtasel, Gur, Kester, Mozley, Stafiniak, & Gur, 1994) and provided results consistent with findings from the neuroimaging literature on the disorder (Crow, 1990). Nevertheless, the diffuse pattern of impairment of the schizophrenic patients has indicated that caution must be exerted

(Blanchard & Neale, 1994). In contrast, this problem is likely to have been minimized in most studies of OCD because the disorder has not be found in any neuropsychological study to have been associated with a generalized pattern of impairment. Thus while not a panacea for resolving the problem of identifying a differential deficit, the standardizing residualized score method proposed by Chapman and Chapman (1989) has provided greater confidence that such a deficit does or does not exist when it has been used in combination with other multivariate techniques.

The Present Investigation

The neuroimaging and neuropsychological literature reviewed above have provided some evidence for impoverished executive functions in OCD. It has been difficult however to render any firm conclusions with regards to the integrity of executive functions in OCD because of the statistical and methodological limitations addressed above. Although these limitations have been discussed in the context of the neuropsychological literature, they have equally applied to other areas neurobiological investigation of OCD such as biochemical and psychophysiological studies.

The present investigation consisted of two experiments that evaluated executive functions in outpatients with OCD and normal control participants. Each experiment employed a different technique for evaluating executive functions, neuropsychological tests in experiment I and event-related potentials in experiment II. Two techniques were employed as a means to evaluate whether converging evidence would be obtained for executive dysfunction in OCD. The use of a converging methods approach has been fruitful in increasing the understanding of other disorders such as schizophrenia (Baaré,

Hulshoff Pol, Hijman, Mali, Viergever, & Kahn, 1999). In Experiment I a battery of neuropsychological tests was administered in order to evaluate whether OCD is primarily associated with a disturbance in executive rather than other neuropsychological domains of functioning. Experiment II was designed to provide more specific information on executive function integrity in OCD than experiment I by focusing the evaluation on a single executive function, response inhibition. The decision to focus on response inhibition in experiment II was guided by neurobiological theories of OCD (see above). These theories have all either directly or indirectly implicated impoverished inhibitory control in the etiology of the disorder. Specifically, in experiment II event-related potentials (ERPs) that have been argued to reflect the activity of neural inhibitory control mechanisms were evaluated in outpatients with OCD and normal control participants during the performance of a go/nogo target detection task.

For the sake of clarity in presentation, experiment I was first discussed in its entirety. Experiment II was then presented in its entirety, including a review of the literature pertaining to ERP correlates of response inhibition in normal populations and OCD, as well as discussion of the specific manner in which the experiment was to advance the literature on executive functions in OCD. Both experiments were designed to address many of the statistical and methodological limitations of previous neuropsychological and ERP research on OCD. An general discussion was then presented in order to integrate the findings of the two experiments.

Several advances were included in experiment I in order to build on previous research:

First, a relatively comprehensive neuropsychological evaluation was conducted;

Second, Test scores were grouped into composite functional domains in order to reduce the overall number of statistical comparisons:

Third, a variety of procedures were employed in order to provide greater control over Type I error and simultaneously provide a more rigorous evaluation of differential deficit. These included multivariate analysis of variance and the method of standardized residual scores that was proposed by Chapman and Chapman (1989), both having been employed to provide independent checks on the pattern of findings;

Fourth, unlike many of the previous investigations methodological and statistical control over the salient and potentially confounding demographic characteristics and affective variables were employed. These variables included medication status, age, gender, education, depression and anxiety, as well as secondary diagnoses;

Fifth, to facilitate comparison with other studies the most common analytic strategies used in previous research were also carried out and the results were compared to the more rigorous analytic techniques employed in the present study;

Sixth, effect sizes were calculated for the neuropsychological test data (Cohen, 1988, Schmidt, 1996). Only one previous investigation of OCD has provided effect sizes for their neuropsychological test data (Schmidtke et al., 1998). Effect size analysis has been demonstrated to be useful in other areas of research because while the *P* values used in univariate and multivariate analyses indicate whether an effect is significant at a given alpha level (e.g., .05), no conclusion about the magnitude of group differences may be drawn from comparing *P* values between tests or test domains. This limitation has been due to the fact that the size of the F ratio used in statistical analyses may be affected by the magnitude of an effect, sample size or both (Keppel, 1991). In contrast, the effect size is a quantitative index that represents the magnitude of the relationship between two variables independent of sample size (Cohen, 1988). This characteristic of the effect size has been particularly valuable in clinical neuroscience research where sample sizes have tended to be small given the difficulties involved in the identification and recruitment of participants.

EXPERIMENT I

Method

Participants

A total of 26 outpatients with OCD and 28 normal control subjects have participated in experiment I. The fifty-four participants were between 18 and 64 years of age and Caucasian, with no history of significant neurological illness, head injury resulting in a loss of consciousness, exposure to electroconvulsive therapy or psychosurgery. All participants reported that their native toungue was French. No formal evaluation of langauge proficiency was conducted. Informed consent for participation was obtained from all participants prior to inclusion in the study (see Appendix A for sample consent forms).

Patients were evaluated by a either a psychiatrist or psychologist with extensive experience in diagnosing OCD. Patients were diagnosed using the Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV; Brown, Di Nardo, & Barlow, 1994). The ADIS-IV is a structured diagnostic interview for anxiety disorders and exclusionary conditions. Patients were excluded from the present investigation if they had any comorbid Axis I or II disorder, as defined in the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV; American Psychiatric Press, 1994), other than a secondary anxiety disorder, major depression and dysthymia. Although secondary diagnoses may be a potential confound in studies of OCD, the comorbidity of OCD with anxiety and affective disorders is very high thus rendering the recruitment of a "pure" OCD sample difficult.

Patients were also administered the Yale-Brown Obsessive-Compulsive Scale (YBOCS; Goodman et al., 1989a, 1989b). The YBOCS is structured interview specifically designed to determine the nature, extent and severity of obsessions and compulsions. The YBOCS has been demonstrated to have good psychometric properties in a number of investigations (Taylor, 1995). An overall score of sixteen or more has been generally accepted as falling within the clinical range in treatment studies of OCD. Total scores for obsessions, compulsions and overall OCD severity are reported in the present paper. All subjects completed a number of self-report questionnaires. These included a questionnaire pertaining to demographics and personal and family history of medical illness, the Beck Depression Inventory (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961; Bourque and Beaudette, 1982), and the State-Trait Anxiety Inventory-State scale (Spielberger, Gorsuch, & Lushene, 1970). A subset of the participants also completed short-form C of the Marlowe-Crowne Social Desirability Scale (MC-SDS; Reynolds, 1982) which was added to study late in the investigation.

Normal controls were recruited from a subject pool at the Centre de Recherche Fernand Seguin (a dedicated research center afficliated with Université de Montréal and Hopital Louis H. Lafontaine) and advertisements in a local newspaper (Appendix B). Potential control participants were initially screened during a phone interview (Appendix C). Normal control subjects who reported a personal history of neurological or psychiatric illness, poor physical health or head injury resulting in loss of consciousness were excluded from participation.

The final sample for each group consisted of 23 subjects. From the original sample of 26 patients, one was excluded due to concurrent severe migraine headaches and other medical problems, and two were excluded after further clinical evaluation revealed that their primary diagnosis other than OCD (Tourette syndrome and delusional disorder). Five normal controls from the original sample were excluded when matching of controls to patients as closely as possible for age, gender, education, race and handedness.

Twelve out of the remaining twenty-three patients fulfilled DSM-IV criteria for having a secondary diagnosis. Three had social phobia, one had both social phobia and dysthymia, one both social and specific (birds) phobia, one panic disorder without agoraphobia, one agoraphobia and major depressive disorder, three generalized anxiety disorder, one generalized anxiety disorder, specific phobia and hypochondriasis, and one dysthymic disorder. Nineteen of the final sample of twenty-three patients (82%) were not taking any psychotropic medications at the time of the evaluation, nor for at least four weeks prior to testing. Of the remaining four patients, two were taking Prozac, one was taking Serzone and Elavil, and one was taking Paxil. Eight of the twenty-three patients (35%) reported having had used an antidepressant or another psychotropic medication (e.g., anxiolotic), at least four weeks or more before the evaluation.

Procedure

Neuropsychological test battery.

Where necessary French translations of neuropsychological tasks (e.g., verbal memory tasks) that have been demonstrated to not differ significantly with respect to means and standard deviations from the orginal English versions were employed

(Caramanos & Leonard, unpublished data). Neuropsychological tests was administered in a fixed order due to the nature of the tasks. All tests were administered within a single session of approximately three and a half hours duration. Participants were given approximately ten minute rest break after each hour of testing, and additional breaks were taken as needed. For the purpose of the present investigation tests were grouped within the domain of functioning to which they have been found to be most sensitive. This grouping is based both on the widely cited neuropsychological texts commonly referred to in literature reviews and meta-analytic publications (Lezak, 199 ; Spreen & Strauss, 1998), as well as factor analyses (Ernst et al., 1988; Francis et al., 1992; Larrabee & Curtis, 1995; Leonberger et al., 1992; Swiercinsky & Hallenbeck, 1975; Swiercinsky & Howard, 1983). Test selection was guided by the commonality with which the tests were used in previous studies of OCD, previous research indicating that they tend to be more highly related to other tests believed to tap a particular neuropsychological function, and availability. The tests employed within each functional domain, and the specific score used if more than one score was available for a test, are as follows (a more detailed description of each test can be found in Appendix D):

Executive functions: Number of perseverative errors in card sorting on the Wisconsin Card Sorting Task (WCST; Heaton, Chelune, Talley, Kay, & Curtis, 1993); number of perseverative errors on the twelve item abstract designs version of the Self-Ordered Pointing Task (Petrides & Milner, 1982); time to complete trial B of the Trail Making Test (TMT; Reitan & Wolfson, 1985).

Verbal memory: Mean number of items recalled following a thirty-minute delay on Logical Memory subtest of the Wechsler Memory Scale-Revised (Wechsler, 1987); number of words recalled following a twenty minute delay on the Rey Auditory-Verbal Learning Test (RAVLT; Lezak, 1995)

Nonverbal memory: WMS-R Visual Reproduction thirty minute delayed recall score (Wechsler, 1987); Rey-Osterreith Complex Figure thirty minute delayed recall score (Osterreith, 1944).

Language: Number of correct items on the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983); total number of correct words produced on the Controlled Oral Word Fluency task (COWF, using letter F, A and S).

Visuospatial: Total score on the Hooper Test of Visual Organization (Hooper, 1958); total score on the Block Design subtest of the WAIS-R (WAIS-R; Wechsler, 1981).

Motor Functions: Mean weight in kilograms across two trials on the Hand Dynamometer (Reitan & Davison, 1974); mean number of pegs correctly inserted across three unimanual trials on the Purdue Pegboard (Tiffin, 1968). Left and right hand scores are reported separately for the motor tasks.

Statistical analyses of neuropsychological data.

The neuropsychological test data were subjected to a number of different analyses. In the first analysis group differences were assessed across the entire test battery using MANOVA. A significant MANOVA was followed by univariate ANOVAs in order to determine on which specific tests the groups differed. This analysis was conducted in

order to provide data directly comparable to previous investigations which have largely employed ANOVA (see Table 1). The level of significance was set at $p \leq 0.05$, although a Bonferroni correction for multiple comparisons was applied in order to provide a more stringent evaluation of the data and to reduce the risk of Type I error.

The second analytic procedure involved comparing the groups on composite indices of higher-order cognitive, perceptual, and motor functional domains. Tests were grouped into functional domains according to their sensitivity to particular areas of neuropsychological functioning (Lezak, 1995; Spreen & Strauss, 1998; Ernst et al., 1988; Francis et al., 1992; Larrabee & Curtis, 1995; Leonberger et al., 1992; Robertson et al., 1996; Shute & Huertas, 1990; Swiercinsky & Hallenbeck, 1975; Swiercinsky & Howard, 1983). Consistent with previous research (Blanchard & Neale, 1994; Saykin et al., 1991, 1994; Sullivan, Shear, Zipursky, Sagr, & Pfefferbaum, 1994) test scores were standardized (z-scores) using the means and standard deviations of the normal control group. The performance score of each normal control subject on each function was thus set to a mean of zero and a standard deviation of one. Z-scores were then transformed such that a lower score would reflect poorer performance than the normal control group for all tests. Function composite scores were formed by averaging all the z-scores from each test score included in the domain, thus giving each test equal weight within its domain. This procedure allowed the performance of the OCD group to be expressed in terms of deviation from normal. MANOVA and ANOVAs were conducted to evaluate group differences on the composite indices (Blanchard & Neale, 1994; Saykin et al., 1991, 1994). When age, education, gender, depression or anxiety were found to differ between the groups, these variables were employed as covariates in the analysis of raw

and composite scores. Patients were also partitioned into subgroups for the purpose of additional analyses based on medication status and presence or absence of secondary diagnosis. The limited sample size resulting from this partitioning indicated that the results of these analyses needed to be interpreted conservatively. Nevertheless, the sample sizes obtained after partitioning are similar to those in other studies in the literature.

The effect size index f was calculated for the ANOVA of each domain score (Blanchard & Neale, 1994). This index is a standardized measure of group dispersion recommended when one is comparing groups using ANOVA (Cohen, 1988). Effect sizes of neuropsychological test and domain scores were classified as small if falling between 0.1 and 0.24, medium if falling between 0.25 and 0.39, and large if 0.4 or more in the calculation of this value (Cohen, 1988).

Composites on which the OCD group differed significantly from the control group were subjected to analyses designed to investigate whether the finding represents a differential deficit. As an initial evaluation of differential deficit composite difference scores were formed by subtracting the mean of six of the seven composites from the remaining composite for each group. ANOVA was performed on these difference scores in order to determine whether a given domain score is higher or lower than the mean of all other domain scores relative to the control group.

Further information with regard to a potential differential deficit was obtained using the standardized residual score method recommended by Chapman and Chapman (1989). This procedure is employed because of potential limitations associated with the use of difference scores, including lower reliability than original scores. To reiterate, this

procedure asks "to what extent is a subject's score on task B deviant, given that subject's score on task A?" (Chapman & Chapman, 1989). The scores from the normal control subjects were used to compute the regression of A on B so that deviations from normal could be evaluated for the patient group. Each residualized score was standardized given that the variance of the residualized score distribution around the regression line varies with the distance from the mean. The standard error of the normal control group's B scores around the regression line was computed using Cohen and Cohen's (1983) corrected formula as suggested by Chapman and Chapman (1989). This procedure thus allowed each subject's score on task B to be expressed as a standard residualized score. The percentage of participants in each group that obtained a higher or lower score on the standard residualized score relative to the other composites was evaluated using two-tailed 2 X 2 Fisher's Exact Test's. In order to minimize the overall number of statistical comparisons, this procedure was only applied to composites on which groups differed significantly on ANOVA.

Results

Data screening

Of the 690 neuropsychological test scores (fifteen test scores for each of the 46 participants) only three (0.04%) was missing because of errors in administration, and none of the participants had more than one test score missing. Missing values were replaced with group means prior to data analysis following the recommendations of Cohen and Cohen (1983). Neuropsychological test data was also explored for outliers and fulfillment of statistical assumptions (Keppel, 1991; Tabachnick & Fidell, 1989).

Two outliers were identified, one being the Trail Making Test-B score for a patient and the other a Visual Reproduction score for a control. These data were replaced by the next most extreme score for a subject in the same group on the variable in question (Winer, 1971). Data for three variables (WCST-PE, LM, VR) violated the assumption of homogeneity of variance, while the assumption of normal distribution was violated for two variables (WCST-PE and Block Design). The violations were corrected using square root transformations.

Participant Characteristic Data

Table 2 presented the means and standard deviations for the groups on the demographic, self-report and clinical variables. Group differences were evaluated using independent-samples t-tests and Fisher's Exact Test with results having been considered significant at $p \leq 0.05$. No significant group differences were observed between the groups for age, years of education, gender composition and hand preference. These findings confirmed that the two groups were well matched on salient demographic characteristics. Participants also did not differ in terms of their scores on the MC-SDS indicating that social desirability was unlikely to have influenced the results on the other self-report measures. In contrast, the OCD group obtained significantly higher scores than the control group on the BDI [$t(44) = 4.17$, $p = .001$] and STAI-S [$t(44) = 2.29$, $p = .001$].

Table 2

Means and Standard Deviations for the Participant Characteristic Data in the Neuropsychological Study

	OCD		Control	
Variable	M	SD	M	SD
Age	39.52	10.21	36.78	9.91
Years of education	15.29	3.32	16.77	3.83
Percent women	60.9		52.2	
Percent right-handed	100		87.0	
MC-SDS[a]	6.09	1.87	5.67	1.88
BDI	14.59	8.52	5.22	6.61
STAI-S	40.17	6.17	31.87	9.11
YBOCS Total	24.09	7.16		
YBOCS Obsession	11.65	3.70		
YBOCS Compulsion	12.48	4.45		

Note. MC-SDS = Marlowe-Crowne Social Desirability Scale; BDI = Beck Depression Inventory; STAI-S = State-Trait Anxiety Inventory-State Scale; YBOCS = Yale-Brown Obsessive-Compulsive Scale.

[a]n = 11 for OCD and 12 for control group.

Analysis of raw test scores

Means, standard deviations along with F values for the raw neuropsychological test scores are presented in Table 3. A MANOVA conducted on the fifteen test scores was not significant [Pillai's F(15, 30) = 0.75, p = 0.718]. Further data analyses using ANOVA also failed to reveal any significant group differences. Only the ANOVA for the COWF test approached statistical significance [F(1, 44) = 3.84, p = 057] but without any correction for multiple comparisons. Effect sizes (f) for the fifteen test scores were generally small, the largest being for the COWF test (f = .295).

MANCOVA of raw test scores revealed significantly more perseverative errors on the WCST in the patient group when BDI [F(1, 43) = 5.73, p = .021] and STAI-S [F(1, 43) = 6.80, p = .013] were used as covariates. These findings were no longer significant, however, subsequent to the application of a Bonferroni correction (alpha of .05/15 variables = .003) for multiple comparisons (Keppel, 1991). Reanalysis after exclusion of the medicated patients did not alter the findings. Statistical comparison of patients with and without comorbid disorders, as well as controls also failed to reveal any significant differences.

Table 3

Descriptive Statistics and Results of Analysis of Variance for Raw Neuropsychological Test Scores

Variable	OCD M	OCD SD	Control M	Control SD	F[a]	p	Effect Size *f*
Executive							
Self-Ordered Pointing	6.09	2.73	5.5	2.29	0.62	.43	.119
Trail Making Test - B	71.48	40.53	65.35	24.65	0.07	.79	.039
WCST persevertive errors	15.17	11.89	9.95	7.84	2.69	.11	.247
Language							
Boston Naming Test	52.22	5.54	53.48	4.73	0.69	.41	.125
Word Fluency	37.77	7.61	42.91	10.03	3.84	.057	.295
Left-hand motor							
Grip strength	31.85	10.20	32.96	11.98	0.11	.74	.051
Purdue Pegboard	14.86	1.67	14.36	1.99	0.83	.34	.137
Right-hand motor							
Grip strength	33.98	9.93	35.60	12.66	0.23	.63	.073
Purdue Pegboard	15.54	2.19	15.78	2.38	0.13	.72	.055
Visuospatial							
Block Design	8.83	2.27	10.09	3.15	2.08	.16	.217
Hooper	24.57	4.21	26.09	2.58	2.18	.15	.050
Verbal Memory							
Logical Memory	16.33	6.58	18.96	9.28	0.84	.37	.138
Rey Verbal Learning Test	11.78	3.09	11.22	3.18	0.37	.54	.092
Nonverbal Memory							
Rey Figure	13.17	7.76	15.57	7.49	1.13	.29	.160
Visual Reproduction	29.26	8.10	30.09	8.99	0.06	.81	.036

Note. WCST = Wisconsin Card Sorting Task.

[a]df= 1, 44.

Analysis of composite scores

Means, standard deviations and F values for the seven composite scores were presented in Table 4. The MANOVA conducted on the composite scores was not significant [Pillai's $F(7, 38) = 1.76$, $p = .125$]. Exploration of the data using ANOVA revealed a significantly lower score on the Language composite for the patient than control group [$F(1, 44) = 8.90$, $p = .005$], even after Bonferroni correction for multiple comparisons (.05/7 = .007). The Language composite finding remained significant even after the covaried out the influence of BDI [$F(1, 43) = 6.42$, $p = .015$] and STAI-S [$F(1, 43) = 6.61$, $p = .014$].

Reanalysis of the composite scores following exclusion of medicated patients did not eliminate the significantly lower Language score for the patient group [$F(1, 39) = 7.04$, $p = .011$, $f = .42$]. Direct comparison of the medicated, unmedicated and control groups on the Language composite was significant [$F(2, 43) = 5.47$, $p = .008$, $f = .50$]. Post-hoc Scheffé's tests revealed that this finding was accounted for by the unmedicated group having a lower score than the normal controls. No difference was noted between the controls and medicated patients or the two patient groups. Comparison of patients with and without secondary diagnoses and controls was significant for the Language composite [$F(2, 43) = 4.67$, $p = .015$, $f = .22$]. Post-hoc Scheffé's tests revealed that this finding was due to the subset of patients without secondary diagnoses having a lower score than the normal controls.

Table 4

Standardized Neuropsychological Composite Scores[a] for the OCD Group and Results of Analysis of Variance

Variable	M	SD	F[b]	p	Effect Size *f*
Executive	- 0.31	.88	1.73	.20	.198
Language	- 0.74	.88	8.89	.005	.450
Left-hand motor	0.08	.55	.24	.63	.074
Right-hand motor	- 0.12	.62	.41	.53	.097
Visuospatial	- 0.48	1.07	2.84	.10	.254
Verbal Memory	- 0.34	.80	.02	.89	.021
Nonverbal Memory	- 0.13	.73	.30	.59	.082

[a]Composite scores for the OCD group are relative to the matched normal control group whose performance was set to a mean of 0.00 and a standard deviation of 1.00.

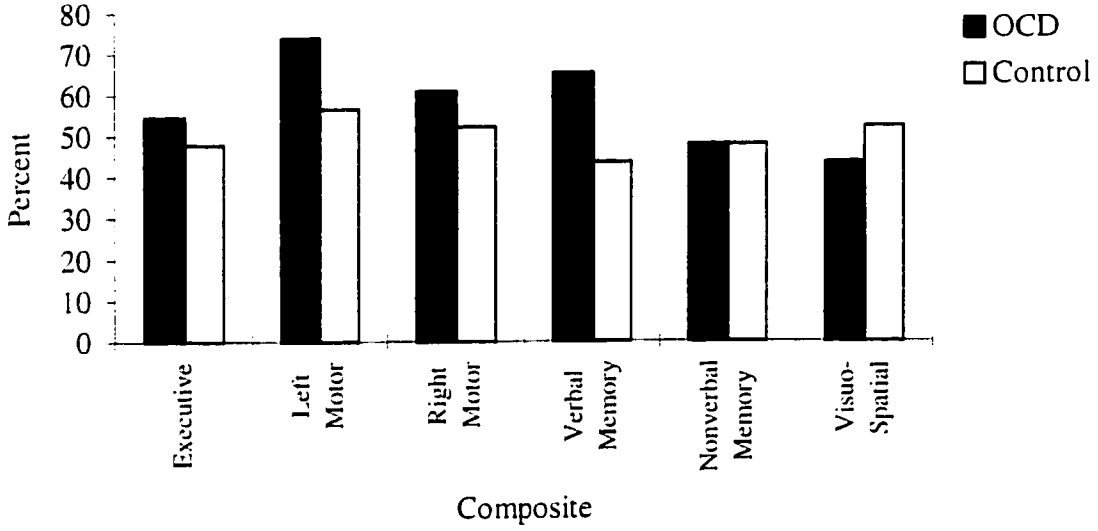
[b]df= 1, 44.

Analysis of differential deficit

Although the MANOVA on the neuropsychological composite scores was not significant, ANOVA revealed a significant group difference on the Language composite which remained even after alpha level was set conservatively using a Bonferroni correction. The finding was somewhat reduced when the effects of depression and state anxiety were covaried out. Nevertheless, exploration of whether the lower Language composite score may represent a differential deficit in OCD was pursued.

Comparison of the OCD and control groups on the Language-other composite difference score was significant [$F(1, 44) = 6.54$, $p = .014$], indicating selectively poorer language ability for the OCD group than all other functions combined. Further evaluation of differential deficit was conducted using the standardized residualized score method. Results of Fisher's Exact Test analyses revealed that the percentage of participants in the OCD and control group with lower standardized residualized Language composite scores than other composite scores did not significantly differ (all p vales above .05). Figure 1 illustrated this finding. Consistent with the ANOVA results, Fisher's Exact Tests also failed to reveal lower standardized residualized Executive composite scores than the other composite scores (all p vales above .05).

Figure 1. Percentage of OCD and control participants with language composite scores lower than other composite scores.


80
70
60
50
40
30
20
10
0
Percent
OCD
Control
Executive
Left Motor
Right Motor
Verbal Memory
Nonverbal Memory
Visuo-Spatial
Composite

Discussion of Experiment I

Neuropsychological studies of OCD have generally been fraught with a number of methodological limitations. Experiment I was designed to exert more extensive methodological control over potential confounding variables, and as well as more stringent statistical analyses, in order to determine whether OCD is characterized by a differential deficit in executive functions. Results obtained for both the raw and composite neuropsychological test scores have failed to reveal any disturbance in executive functions in the present group of patients with OCD in comparison to matched normal control participants. Furthermore, no group differences were observed on tests of verbal and nonverbal memory, motor skills or visuospatial abilities. In contrast, the patient group obtained a significantly lower score on a composite language ability measure than the controls.

The failure to observe an executive function disturbance in OCD has been reported in a number of studies (Abbruzzese, 1995b; Gambini et al., 1993). One possible explanation for this finding may lie in the limited number of patients with a secondary depressive disorder that were included in the study. Otto (1992) has noted that poor performance on executive function tasks in OCD has appeared to be more common in studies that have included patients with a secondary depressive disorder. In the present study only one patient suffered from a secondary major depressive disorder and two were diagnosed with dysthymic disorder. In addition, although the OCD group obtained significantly higher scores on the BDI than controls, it is plausible that poorer performance on executive function tasks in OCD may only be observed when the secondary depression is of clinical severity. The OCD group was, however, noted to

make significantly more perseverative errors on the WCST than the control group when the effects of depression and state anxiety were covaried-out. This finding, although contradicting the purported relationship between depression and executive functions, is likely to have been of limited significance since application of a correction for multiple comparisons rendered the WCST finding non-significant.

The presence of comorbid anxiety disorders in a subset of the present sample did not influence the present findings. This finding must be interpreted with caution as the sample sizes resulting from subdividing the patient group according to the presence or absence of secondary diagnosis were relatively small. Nevertheless, the present findings are consistent with the limited evidence for neuropsychological deficits in patients with a primary anxiety disorder other than OCD. One study has reported, however, impoverished executive functions in patients with a primary diagnosis of social phobia (Cohen et al., 1996). Five of the eleven patients in the present sample carried a secondary diagnosis of social phobia. Although the executive function deficit in social phobia is yet to be replicated, the number of OCD patients with this diagnosis in the present study is likely to have been insufficient to affect the test findings. It is unknown whether the presence of secondary social phobia may have affected the findings of other investigations as many studies did not report exclusion criteria. Studies that did not exclude patients with OCD who had secondary anxiety disorders did not addresse the potential impact of such disorders on their test findings. Further investigation of the potential impact of secondary social phobia on neuropsychological performance in OCD thus appears warranted, particularly given the relatively high degree of comorbidity between these disorders (Rasmussen & Eisen, 1992).

Differences between the present and previous studies may have also in part been related to the nature of the OCD symptoms reported by the patients (e.g., checking as opposed to washing). There has been little research on the relationship between symptom subtypes of OCD and neuropsychological performance. Few neurobiological studies have reported the prevalence of different OCD symptoms in their samples. Studies with clinical populations have relied largely on correlational analysis with relatively limited sample sizes and have tended to report the relationship between individual test scores and broad measures of OCD symptoms such as the overall YBOCS Obsession and Compulsion scores. The little work that has compared OCD patients subgrouped according to their predominant symptoms (e.g., checking, washing) has failed to reveal any significant differences (Abbruzzese et al. 1995b). Studies using subclinical populations have, however, indicated that compulsive checking but not washing may be more closely related to disturbances in the monitoring of actions and possibly other executive functions (Goodwin & Sher, 1992; Roth & Baribeau, 1996; Zohar et al., 1995). Therefore the possibility that at least some of the discrepancies between the present and previous investigations may have been related to the nature and prevalence of specific OCD symptoms in the samples cannot be completely discounted.

The inclusion of four patients (17%) who were medicated at the time of testing did not significantly alter the pattern of neuropsychological findings. Previous research has generally failed to detect significant neuropsychological differences between medicated and unmedicated patients with OCD. Consequently, discrepancies between the present and previous findings are unlikely to have been accounted for by medication effects.

The lack of executive function disturbance in the present OCD group may have at least in part been due to the use of tasks with limited sensitivity to disturbances of the orbitofrontal cortex (Eslinger & Damasio, 1985; Saver & Damasio, 1991), the frontal lobe region most consistently implicated in the disorder (Saxena et al., 1998). Unfortunately, no clinical neuropsychological test has been developed with good sensitivity and specificity to orbitofrontal dysfunction. Inclusion into test batteries of experimental tasks that have yet to gain widespread clinical use may be of benefit in identifying any differential deficit in OCD. For example, a number of the studies reviewed in Table 1 have observed poorer performance in OCD on the object alternation task, an experimental task that appears to have greater sensitivity to disturbance of the orbitofrontal cortex (Freedman & Oscar-Bergman, 1986; Mishkin, Vest, Waxler, & Rosvold, 1969).

In contrast to the lack of group differences on executive function measures and tests tapping several other functional domains, the OCD group was found to have a lower Language composite score than the normal control group. A medium effect size (.45) was obtained for this difference. The finding could not be fully accounted for by medication effects, the presence of patients with comorbid diagnoses, depression or state anxiety. In addition, the groups did not differ in terms of years of education suggesting that the Language finding is unlikely to be the result of group differences in overall verbal or intellectual abilities (Kaufman, 1990). The relatively consistent failure in previous investigations to observe significant differences between OCD and normal control groups on measures of estimated premorbid (e.g., National Adult Reading Test) and current (e.g., WAIS) intellectual functioning, and the detection of neuropsychological differences

despite matching on such measures also supports this contention (Tallis, 1997). It is also unlikely that differences in language ability between groups was due to the use of bilingual participants because French was the native toungue for all participants, no group difference was noted on the Boston Naming Test and previous research has demonstrated that brain disturbances do not differentially impair word fluency in bilingual individuals (van Lieshout, Renier, Eling, de Bot, & Slis, 1990).

Investigation of whether the Language finding represented a differential deficit revealed that the OCD group's Language composite score was significantly lower than the average of all of the other composite scores combined. This pattern of findings indicated that the OCD group was characterized by a disturbance on the Language composite in the context of overall adequate neuropsychological functioning. The group difference on the language composite was likely to be partially accounted for by the contribution of other neuropsychological functions to the performance on the tasks comprising the language composite. This was suggested because partialling out the effects of other domains of functioning from the Language composite using Chapman and Chapman's (1989) standardized residualized score method failed to reveal any differential impairment in the Language composite relative to the other domains. It remained unclear from the available data to what degree various neuropsychological functions may have influenced performance on the Language composite. One indication may lie in the observation that only the Controlled Oral Word Fluency test (COWF), part of the Language composite score, approached significance and had the largest effect size among the raw scores. Poor performance on oral word fluency tasks has been observed in previous studies of OCD (Christensen et al., 1992; Schmidtke et al., 1998). The Boston

Naming Test, the other test comprising the Language composite, did not approach significance, had a small effect size, and has not been found to differ between OCD and normal controls (Ludlow et al., 1989).

Although word fluency tasks have generally been included among tests of language abilities (Lezak, 1995; Spreen & Strauss, 1998), adequate performance appears to involve a variety of mental operations. DesRosiers and Kavanagh (1987), employing factor analysis, found that word fluency task performance loaded on a "verbal knowledge" factor together with verbal IQ and WAIS-R Vocabulary. Crockett (1996), also employing factor analysis, found that the word fluency test was most closely related to tests of naming, problem solving, sequencing, resistance to distraction, perseveration, as well as a number of memory measures. Troyer, Moscovitch and Winocur (1997) observed that better performance on the task is related to the ability to switch between producing words from different phonemic and semantic subcategories, switching being associated with executive functions. That word fluency should be associated with executive and memory functions in addition to more general verbal abilities is consistent with positron emission tomography data demonstrating bilaterally increased activity in frontal- and temporal- lobes in normal volunteers during performance of the COWF (Parks et al., 1988) and poor performance in patients with either left, right or bifrontal lobe lesions (Crowe, 1992; Ruff, Allen, Farrow, Niemann, & Wylie, 1994; Shoqueirat, Mayes, MacDonald, & Meudell, 1990). Interestingly, bilateral frontal- and temporal-lobes have also been implicated in the performance of the Boston Naming Test (Lezak, 1995; Tranel, 1992; Welsh, Watson, Hoffman, Lowe, Earl, & Rubin, 1995).

It was therefore plausible that some combination of subtle disturbances in neuropsychological functions, with perhaps particularly important contributions from executive functions and verbal memory, may have contributed to the poorer Language composite score in OCD. This suggestion is consistent with theories that argue that OCD is associated with a disturbance of frontal lobe-mediated verbal processes (Flor-Henry, 1979), electrophysiological research implicating frontal- and temporal- lobes (Malloy et al., 1989), and evidence of frontal lobe hyperactivity in some positron emission tomography studies (Baxter et al., 1987) of OCD. That abnormally high levels of glucose use during PET may be associated with poorer cognitive functioning has been noted in investigations of normal participants, and may reflect decreased processing efficiency (Haier, Siegel, Nuechterlein, Hazlett, Wu, Pack, Browning, & Buchsbaum, 1988). The present data did not however permit any firm attribution of the Language finding to a lateralized disturbance of the frontal- or temporal- lobe, given the evidence for bilateral contributions to the tasks included in the composite score.

Impoverished performance on word fluency tasks has also been observed in other psychiatric populations (Degl'Innocenti, Agren, & Backman, 1998; Mahurin, velligan, & Miller, 1998). This indicates that the present finding did not provide pathognomic information on OCD. The generalizability of the present findings to other samples of patients with OCD may be somewhat limited since the use of different tests to form composite scores may alter the pattern of findings.

The ability to detect group differences on raw and composite scores may also have been reduced due to the greater emphasis placed on avoiding Type I than Type II errors and the somewhat limited sample size. In order to obtain the conventional power of .80

(Cohen, 1992; Keppel, 1991) at an alpha of .05 and a medium effect size (f for analysis of variance) of .25, large effect sizes being relatively uncommon in behavioral research (Cohen, 1988), sixty-four participants per group would have been required. Such a large sample size in neuroscience research on clinical populations like OCD is rare and the difficulties in recruiting large samples of individuals with OCD for such research has been previously noted.

It should also be noted that the number of participants per group included in the present study was comparable to the number of patients (Mean = 21.64, SD = 7.4) and controls (Mean = 21.28, SD = 10.27) employed in previous neuropsychological investigations of OCD (Table 1). This remained true even when only sample sizes for studies conducted in the 1990's were considered (OCD: Mean = 23.29, SD = 7.51; Control: Mean = 22.31, SD = 10.43). A number of previous investigations with sample sizes similar to that employed in the present study have reported significant differences between patients with OCD and normal controls on tests of executive and/or other functions (e.g., Purcell et al., 1998b; Zielinski et al., 1991). Discrepancies between the present and previous studies are thus likely to have been at least in part due to methodological differences beyond the effects of sample size on the probability of detecting significant group differences. Nevertheless, further neuropsychological research on OCD would benefit from the use of larger sample sizes in order improve the balance between Type I error and the power to detect group differences.

In summary, experiment I did not detect evidence of impoverished executive functions in a group of outpatients with OCD. Furthermore, although the OCD group demonstrated poorer performance than normal controls on a language composite score, statistical analyses indicated that the finding could not be interpreted as reflecting a differential deficit. These findings could not be readily accounted for by either the demographic or clinical characteristics of the participants.

EXPERIMENT II

Inhibitory Control and OCD

A variety of mental operations have been subsumed under the term executive functions including mental flexibility, response inhibition and planning. Although performance on neuropsychological tasks may require the recruitment of multiple executive functions, the sensitivity of specific tasks to particular executive functions is likely to vary. The neuropsychological test battery employed in experiment I may not have placed sufficient demands on executive functions that may be especially impoverished in OCD. In particular, most of the neuropsychological investigations of OCD have not employed tasks that place significant demands on executive functions that recruit the orbitofrontal cortex during performance. Seeking executive function tasks with greater sensitivity to orbitofrontal dysfunction may prove fruitful given the evidence for a disturbance of this brain region in OCD (Malloy, 1987; Saxena et al., 1998).

One executive function that has been closely related to the functional integrity of orbitofrontal circuitry in both human and animal research is inhibitory control (Fuster, 1999; Malloy & Richardson, 1994; Mesulam, 1998). The concept of inhibitory control

has been central to many neuropsychological theories of executive functions (e.g., Barkley, 1997; Diamond, 1989; Stuss, 1992). Inhibitory control has been conceptualized as a cognitive mechanism that prevents irrelevant information, cognitive strategies, goals, and responses from intruding into the ongoing stream on mental and behavioral activity (Logan & Cowan, 1984; Ridderinkhof & van der Molen, 1997). Furthermore, the stronger the prepotency of irrelevant information the greater has been the need for and demands placed on inhibitory mechanisms (Ridderinkhof & van der Molen, 1997).

Inhibitory control has also played a prominent role in a number of theories pertaining to the neurobehavioral etiology of OCD. These theories have generally argued that a disturbance of frontal lobe circuitry is likely to result in impoverished inhibitory control. Although the specific neural structures and associated cognitive or motor mechanisms that are disinhibited by this disturbance have varied among theories, the general idea has been one of diminished ability to inhibit intrusive and repetitive thoughts (obsessions) and behaviors (compulsions). More specifically, poor inhibitory control in OCD has been hypothesized to have resulted from a deficit in serotonin (Yaryura-Tobias et al. 1977); dysfunction of the left frontal lobe, resulting in poorly modulated verbal ideation that may be produced in a recurrent and stereotyped manner (Flor-Henry, 1983); dysfunction of the orbitofrontal cortex and possibly the anterior temporal lobe (Malloy, 1987); disruption of the developmental maturation of frontal lobe-basal ganglia circuitry in OCD resulting in a primary disturbance in the ability to suppress contextually inappropriate responding (Rosenberg & Keshavan, 1998); or dysfunction of the caudate

nucleus resulting in disinhibition and subsequent overactivity of orbitofrontal-thalamic circuits which then leads to inappropriate initiation of cognitive or motor responses (Modell et al., 1989).

Neuropsychological Evidence

Some data in the neuropsychological literature has pointed towards a disturbance in inhibitory control in OCD, albeit not consistently. Deficits in set-shifting noted in numerous studies of OCD have been interpreted by some authors as reflecting an inability to inhibit responding to stimuli that are no longer task-relevant (Diamond, 1989; Roberts & Pennington, 1996). Poor performance on the Stroop task has also been observed (Martinot et al., 1990) though not in all studies (Aronowitz et al., 1994; Boone et al., 1991). In the Stroop task (Stroop, 1935) the participant is required to inhibit the more natural tendency to report a written color-name than the color of the ink in which the word is printed, despite being required to name the latter (e.g., say "red" when reading the word blue written in red). OCD patients have also been observed to perform poorly on negative priming tasks (Enright & Beech, 1990, 1993a, 1993b; Enright, Beech, & Claridge, 1995). In negative priming tasks participants have been required to selectively respond to one (target) of two simultaneously presented stimuli. Inhibition has been measured by evaluating the reaction time to the distracter when it is subsequently employed as the target stimulus (Tipper, 1985).

Event-Related Potentials and Response Inhibition

A general limitation of neuropsychological tasks of executive functions has been that the perceptual, cognitive and motor mechanisms involved in task performance have often been difficult to discern without extensive task analysis and parameter manipulations. This limitation has rendered problematic the attribution of a disturbance on a given task to a specific mechanism. Recording event-related potentials (ERPs) during the performance of tasks designed to assess executive functions may be of considerable help in isolating the executive component(s) involved in the task.

ERPs are neuroelectric activity recorded on the scalp in relation to a wide variety of stimuli and/or responses such as light flashes and button presses. ERPs are extremely useful indices of information processing because they are time-locked events, thus permitting random neuroelectric potentials that are not directly related to the stimuli and responses of interest to be filtered out from the ongoing electroencephalographic (EEG) activity. Following the nomenclature of Donchin et al. (1977), deflections in the ERP, also referred to as components when they are associated with particular mental processes, have been labelled negative (N) for upward deflections and positive (P) for downward deflections.

ERP components have been associated with a variety of psychological processes such as selective attention, preparation for motor responding and sensory gating (Donchin, Ritter and McCallum, 1978; Hillyard and Picton, 1986; Näätänen, 1992). ERPs have proven to be of considerable value in determining whether poor performance on a variety of tasks is related to abnormalities at specific levels or stages of information processing in both normal (Picton, Campbell, Baribeau, & Proulx, 1978; Rugg & Coles, 1995) and psychiatric

(Baribeau, 1986; Baribeau & Laurent, 1986; Baribeau & Lesèvre, 1983; Oades, 1998) populations. These characteristics of ERPs indicated that they may be of considerable use for investigating whether OCD is associated with a disturbance in response inhibition.

Go-Nogo Task. Performance on a variety of behavioral tasks has appeared to require the recruitment of inhibitory control. One such task is the go-nogo task. The exact stimulus and response parameters of the go-nogo task have varied across investigations. Nevertheless, the basic structure has involved requesting that participants perform a motor response following the onset of one stimulus (go) while withholding their response following the onset of a different stimulus (nogo).

The go-nogo task may be of considerable use for investigating the neurobehavioral basis of OCD because it places significant demands on inhibitory control and has been demonstrated to be sensitive to orbitofrontal damage in animals and humans (Fuster, 1995; Malloy, Bihrlr, & Duffy, 1993; Ohta, 1984; Verfaellie & Heilman, 1987). Recent evidence from a fMRI study of normal volunteers performing a visual go-nogo task revealed, however, that significant activation occurred for both the dorsolateral and orbitofrontal cortices (Casey et al., 1997). Poor performance on the task has therefore not permitted localization of cerebral disturbance to the orbitofrontal cortex.

ERPs during go-nogo tasks in normal participants. The go-nogo task is also of potential value to research on inhibitory control in OCD because the electrophysiological responses associated with the inhibition of responding following the onset of the nogo stimulus has been extensively studied with non-clinical populations. Simson, Vaughan

and Ritter (1977) required subjects to respond (go) when the second (S2) of two stimuli, presented one second apart, was different from the first stimulus (S1) and withhold responding (nogo) when they were identical. The relative probability of go and nogo stimuli was fifty percent, as in most studies using the go-nogo task. Results revealed a positive ERP component that occurred between approximately 350 and 420 msec following S2 onset that was of greater amplitude and longer latency subsequent to the nogo than go stimulus. In addition, while this component, labeled variously as P3 or P300, elicited by the go S2 had a parietal scalp distribution, the P300 elicited by the nogo S2 had a prominent frontocentral distribution. This pattern of findings was observed regardless of whether stimuli were presented in the auditory or visual modality. Although the degree of mismatch between the perceptual characteristics of S1 and the two S2 stimuli was not equated, further research indicated that the nogo P300 could not be accounted for by a perceptual mismatch (Jodo & Inoue, 1990; Pfefferbaum & Ford, 1988).

The more frontocentral distribution of the nogo P300 and more posterior distribution of the go P300 has been replicated in a number of experiments (Eimer, 1993; Fallgatter, Brandeis, & Strik, 1997; Pfefferbaum, Ford, Wenegrat, Roth, & Kopell, 1984; Schupp, Lutzenberger, Rau, & Birbaumer, 1994). Only a few studies have failed to observe this distribution, instead locating the maximal nogo P300 at central electrodes (Jodo & Inoue, 1990; Pfefferbaum, Ford, Weller, & Kopell, 1985). Furthermore, this effect has been found to be generally independent of the modality of stimulus presentation (e.g., auditory or visual), the nature of the stimuli (e.g., words or symbols, simple or degraded), or whether a manual response was required (Simson et al., 1977;

Pfefferbaum et al., 1985; Pfefferbaum and Ford, 1988). A number of authors have thus argued that the generators of the frontocentral and parietal P300s may differ (Jodo & Inoue, 1990; Pfefferbaum & Ford, 1988).

The relative consistency with which the nogo P300 has been found to have a more frontocentral scalp distribution has implicated the frontal lobe as the neural generator of the component. ERPs recorded on the scalp do not, however, necessarily reflect activity in the neural structures underlying the electrodes where the potential is observed. This limitation of scalp recorded ERPs has been attributed to a variety of factors including volume conduction and skull thickness, (Rugg & Coles, 1995). In addition, a number of studies have suggested that scalp recorded ERPs such as the P300 may reflect the activity of neural systems distributed in various brain regions.

Strik, Fallgatter, Brandeis, and Pascual-Marqui (1998) have attempted to provide more precise information with regard to the neural generators of the nogo P300 using an electrical source localization technique. Such techniques have employed a large number of electrodes and produced mathematical models of the electrical activity generated during tasks. The end result has usually been a three-dimensional model of graded electrical activity that has provided enhanced localization of the neural source of a given component (Pascual-Marqui, 1995). Results of the Strik et al. (1998) investigation revealed a locus of significantly augmented activity in the right frontal lobe during the nogo condition of a visual task. Based on such findings the anterior P300 has been proposed as a standard index of inhibitory brain functions (Fallgatter et al., 1997).

The right frontal lobe source for the nogo P300 identified by Strik et al. (1998) was consistent with the observation of impaired go-nogo task performance associated with right but not left frontal lobe lesions (Verfaellie & Heilman, 1987). In contrast, Roberts, Rau, Lutzenberger and Birbaumer (1994) observed a left frontocentral dominance for the nogo P300 using standard ERP scalp topography analysis. Unfortunately, few of the ERP studies on P300 during go-nogo task performance have used electrode arrays covering salient regions of both hemispheres thus precluding the analysis of possible hemispheric asymmetries. Methodological limitations also precluded the evaluation of possible hemispheric asymmetries at the frontal activation sites in Casey and colleagues' (1997) fMRI study. Collectively, these findings indicated that no firm conclusion could be reached with regards to hemispheric lateralization of inhibitory control.

Although the differential scalp topography of P300 amplitude and the relationship of P300 latency to go and nogo stimuli has appeared to be quite consistent across investigations, a number of authors have raised concerns that the findings may have been confounded by the influence of overlapping slow ERPs (Kok, 1986; Simson et al. 1977; Pfefferbaum et al., 1984). Negative-going slow potentials in the ERP may be present throughout the course of a task and appear to reflect response preparation and execution processes. Negative slow potentials have been noted to be enhanced when participants were required to focus their attention on a task, were presented with a stimulus warning that a response will be shortly required or were required to produce a motor response (Andreassi, 1995).

Slow potentials during go-nogo tasks may affect measurement of P300 by reducing its amplitude to the go stimulus. This may occur because preparation to respond on each trial has been associated with a negative shift in the ERP termed the contingent negative variation (CNV; Gaillard, 1986). If a go stimulus is presented the negativity related to motor processes is likely to be sustained and P300 amplitude will be subsequently decreased. In contrast, the negativity is likely to terminate following a nogo stimulus because no response is required, thus shifting the peak towards a greater positive amplitude and shortening the latency. The nogo P300 may therefore be enlarged at frontocentral electrode sites because of the reduction in go P300 engendered by the CNV.

In addition to the CNV, negative movement-related potentials are likely to be present during go but not nogo trials due to the requirement to respond. Because the movement related potentials have usually been observed to be larger over the hemisphere contralateral to the response hand at frontal and central electrode locations (Brunia & Damen, 1988; Damen & Brunia, 1994; Rohrbaugh & Gaillard, 1983) any apparent shift in topography at electrode sites contralateral to the response hand could have been due to a reduction of the go rather than an augmentation of the nogo P300. In support of this assertion Kopp, Mattler, Goaertz and Rist (1996) observed that the lateralized readiness potential, which appeared to reflect preparation to carry out a motor response, was present during go and absent during nogo trials during the 250 to 450 msec interval after target stimulus onset. It is within this interval that the P300 has been most commonly observed (Donchin & Coles, 1988).

A number of findings have suggested that the presence of a CNV or other slow potentials could not fully account for the shift in topography. Pfefferbaum et al. (1985) found that the topography effect in a task condition in which the participants were asked to count (go) or not (nogo) count stimuli. Roberts et al. (1994) failed to replicate the elimination of the nogo P300 topography by subtraction of the CNV at each electrode noted by Simson et al. (1977). Falkenstein and colleagues (Falkenstein, Koshlykova, Kiroj, Hoormann, & Hohnsbein, 1995) noted that the time course of the ERP related to motor responding is likely to be insufficient to effect the P300 (Banquet, Renault & Lesèvre, 1991). Roberts et al. (1994) observed that the presence of a negativity related to motor responding was not associated with a greater reduction of the go P300 at electrode sites contralateral than sites ipsilateral to the response hand, while the nogo P300 was consistently larger at contralateral sites. The latter authors interpreted their findings as indicating that the P300 nogo effect is related more to response inhibition than response production.

ERPs and Response Inhibition in OCD. To date there has been only one ERP investigation of response inhibition in OCD (Malloy et al., 1989). Employing a visual go-nogo task, results revealed no significant differences between the OCD and normal control group on the P100, N100, P200 or N200. Controls demonstrated an expected centroparietal maximum amplitude for the P300 to the go stimulus and a significant shift in maximal amplitude towards the frontal scalp regions for the nogo stimulus. In contrast, while the OCD group demonstrated the centroparietal P300 maximum amplitude

to the go stimulus and frontal shift in the topographical distribution of amplitude on the scalp to the nogo stimulus, the amplitude of the nogo stimulus actually decreased slightly in comparison to the go stimulus. The findings were interpreted as being consistent with impoverished frontal and possibly anterior temporal lobe mediated response inhibition in OCD.

While these findings have been of considerable interest, Malloy et al's (1989) study suffered from a number of methodological limitations. Because of technical limitations electrodes were only placed on the left side of the scalp, thus precluding the analysis of possible hemispheric differences in response inhibition. The focus on the left hemisphere was guided by theories arguing for a left-hemisphere disturbance in OCD (e.g., Flor-Henry, 1979). In contrast, some authors have suggested that the right hemisphere may be more disrupted than the left in OCD (Otto, 1992). A further limitation of the Malloy et al. (1989) study is that participants only responded with the right hand to the go stimuli. It has thus remained unclear as to whether the P300 data obtained by Malloy et al. may have been affected by slow potentials over the left hemisphere. The failure to observe group difference in P300 amplitude for both the go and nogo stimulus, as would likely occur if there were slow potential overlap, suggested that the influence of motor processes may not have played an important role. Investigation of the relationship between response hand, hemispheric laterality of electrodes and stimulus (go, nogo) would help evaluate the potential contribution of negative motor potentials to any P300 difference between patients with OCD and normal controls (Robert et al., 1994). Furthermore, a number of studies have observed higher amplitude of the contingent negative variation (CNV) in OCD relative to normal controls.

This raised the possibility that P300 findings may have been confounded by overlapping negative slow potentials (McCallum & Walter, 1968; Sartory & Master, 1984; Timsit, Konickx, Dargent, Fontaine, & Dongier, 1970).

Experiment II

The present study sought to further investigate Malloy et al.'s (1989) P300 response inhibition finding in OCD during a visual go-nogo task. A number of methodological improvements over the previous study were included:

First, ERPs were recorded over both the left and right hemisphere thus permitting an investigation of possible hemispheric asymmetry in inhibitory control in OCD.

Second, participants were required to make unimanual responses with both the left and right hands during task performance thus permitting an evaluation of the potential confounding effects of overlapping negative slow potentials.

Third, unlike Malloy et al. (1989) possible group differences in P300 latency was investigated. Information pertaining to P300 latency was of considerable interest given previous research demonstrating shorter P300 latency in OCD compared to normal controls in both auditory and visual target-stimulus detection tasks (Morault, Bourgeois, Laville, Bensch, & Paty, 1997; Towey, Bruder, Hollander, Friedman, Erhan, Liebowitz, & Sutton, 1990; Tower, Bruder, Tenke, Leite, DeCaria, Friedman, & Hollander, 1993). This finding has been argued to reflect hyperarousal, hyperattentiveness or both (Towey, Tenke, Bruder, Leite, Friedman, Liebowitz, & Hollander, 1994). Decreased P300 latency may also be specific to OCD as the latency of

this component has usually been observed to not differ from normal controls or be longer than normal in other psychiatric populations such a schizophrenia or depressive disorders (Bruder, Towey, Stewart, Friedman, Tenke, & Quitkin, 1991; Josiassen, Roemer, Shagass, & Straumanis, 1986; Roth, Duncan, Pfefferbaum, Timsit-Berthier, 1986).

Method

Participants

Participants in the present ERP experiment included 25 outpatients with OCD and 27 normal control subjects. The fifty-two participants were selected according to the same criteria as experiment I, and had undergone neuropsychological testing prior to the ERP recording session as part of the experiment I.

The final sample included in experiment II consisted of 16 patients with OCD and 18 normal controls. Nine of the patients and ten controls were excluded from experiment II for one or more of the following reasons: medical problems that may affect the central nervous system; primary diagnosis other than OCD; insufficient number of ERP trials remained for averaging; failure to return for the ERP evaluation. The number of participants excluded due to artifacts in the ERP in the present study has not been uncommon in ERP research (Unsal & Segalowitz, 1995).

Ten of the sixteen patients fulfilled DSM-IV criteria for secondary diagnoses. One had social phobia, one both social phobia and dysthymia, one social phobia and major depressive disorder, one agoraphobia and major depressive disorder, one generalized anxiety disorder and simple phobia, four generalized anxiety disorder and one dysthymic disorder.

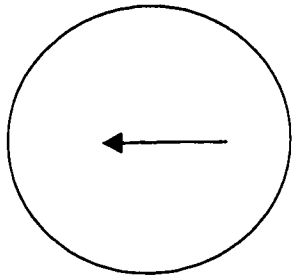
Twelve of the sixteen patients who completed the evaluation were not taking any psychotropic medications at the time of the evaluation, nor for at least four weeks prior to testing. Of the remaining four patients, two were taking Prozac, one was taking Serzone and Elavil, and one was taking Paxil. Of the total of sixteen patients, eight had used psychotropics in the past (anxiolitics) and eight had never been treated with any psychotropic medication. Because the sample of participants included in experiment I and II were not identical the demographics, self-report measures and clinical variables for the groups were analyzed for the ERP study.

Procedure

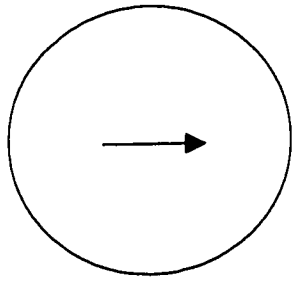
Stimuli. A slightly modified version of the task employed by Scheffers et al. (1995) was used. The task consisted of a go/nogo task in which one of four geometric visual stimuli were presented on each trial. On each trial either an oval or a circle appeared at a fixation point in the center of video monitor indicating whether the participant was required to respond (go) or withhold (nogo) responding. In the center of each circle and oval a horizontal arrow appeared. The direction of the arrow indicated to the participant which hand was to be used for responding on the trial. Each of the four stimulus types (go left, go right, nogo left, nogo right) were presented equally often and in a random order. The go/nogo assignment of the oval and circle was counterbalanced between participants in each group. Illustrations of the task stimuli were presented in Figure 2.

Figure 2. Illustration of go/nogo task stimuli.

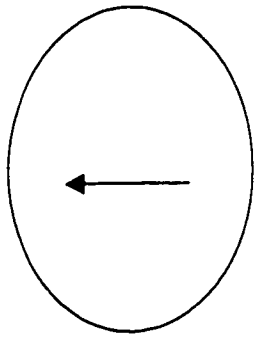
Left hand go:



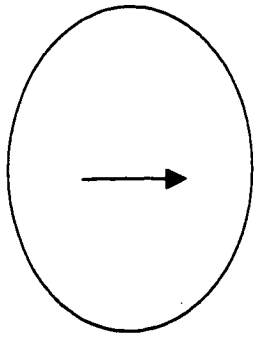
Right hand go:



Left hand nogo :



Right hand nogo:



Participants responded to stimuli using their index fingers by pressing either the left or right button of a two-button computer mouse. Only responses occurring between 100 ms and 1000 ms following go stimulus onset were considered correct. Correct responses falling outside the hit range were considered as misses. This latency range was selected because: (1) responses occurring prior to 100 msec following stimulus onset are unlikely to be voluntary responses to the stimuli; (2) given the intertrial interval of 1400 msec, 1000 msec post-stimulus onset was deemed as an appropriate upper limit of the response window given the need to allow participants sufficient time to prepare to respond to the following stimulus.

Participants were instructed on the importance of using the arrow stimuli to guide their responding. Speed of responding was stressed although participants were encouraged to try and make as few erroneous responses as possible. Participants were reminded to respond quickly if any response during the practice blocks was slower than 1000 ms after stimulus onset. Informal questioning of participants revealed, however, that many placed an equal or greater emphasis on accuracy than speed. A brief question was consequently asked of subjects in order to control for possible group differences in response style. Participants were asked to rate, at the end of each block, the degree to which they stressed accuracy or speed. Ratings were scored from one to five, with increasing emphasis on speed. Scores of one and five referred to emphasis being placed only on accuracy or speed, respectively. Scores of two and four referred to a somewhat greater emphasis being placed on accuracy or speed, respectively. A score of three indicated equal emphasis on speed and accuracy.

Participants completed three practice blocks of eighty trials each. Up to two additional practice blocks were administered to ensure that all participants attained a minimum 80% hit rate. Practice blocks were followed by five test blocks of eighty trials each. The probability of the go stimulus in practice blocks was 80%. The high frequency of go trials in the practice blocks was used to promote a strong tendency towards responding (Scheffers et al., 1995). Consistent with the previous investigation of ERP correlates of go/nogo performance in OCD, the probability of the go stimulus in the test blocks was 50%.

ERP Recording

All participants were tested in the neurophysiology laboratory at the Centre de Recherche Fernand Seguin, following the written informed consent. Participants were seated, explained the task, and Grass Gold cup electrodes placed on the scalp according to the 10-20 international system (Jaspers, 1955). EEG recording electrodes were placed along the niason-inion midline at Fz, Cz, and Pz. Other electrodes were placed over the left (F3, C3, P3) and right (F4, C4, P4) hemispheres. Electro-occulographic (EOG) activity was recorded from electrodes placed on the supra- orbital ridge of the right eye and outer canthus of the left eye. A nose tip electrode served as reference. An electrode placed between C3, C4, P3 and P4 served as electrical ground. All electrodes were affixed using a saline-based paste following mild abrasion of the scalp using OMNI cream. Electrode impedance for EEG and EOG was maintained below 5 Kohms.

Stimuli were displayed in the center of a video monitor for 100 ms with an intertrial interval (ITI) of 1400 ms during which a central fixation point (+) remained on. For both EEG and EOG the high and low bandpass cutoffs were set to .01 Hz and 100 Hz, respectively. The EEG signal was amplified by 20K and EOG by 10K. Data was recorded using the InstEP software program (Ottawa, Ontario, Canada) through a Grass polygraph. The EEG was sampled continuously throughout each block at 512 Hz and stored on hard disk.

ERP Data Processing

Prior to averaging ERP data underwent correction for eye movement artifacts (Woestenberg, Verbaten, & Slangen, 1983). EOG corrected and averaged stimulus-locked ERPs, beginning 100 ms before and ending 750 ms following stimulus onset, were obtained across the five test blocks, for correct responses to both go and nogo stimuli. Separate averaged waveforms were also obtained for left and right hand responses. Trials in which the voltage of either the EEG or EOG exceeded 100 μV were excluded from the averaged waveforms, as were any trials contaminated by other artifacts. Following averaging, the waveforms were digitally low-pass filtered down to 30 Hz (3 dB cutoff). The digital filter operated in the frequency domain using an inverse fast Fourier transform (FFT) algorithm. A minimum of twenty artifact-free trials for each averaged waveform was required for participants to be included in the analyses in order to ensure adequate signal-to-noise ratio.

For each subject, waveform and electrode, the latency and peak amplitude relative to stimulus onset of the N100, P200, N200 and P300 was scored. ERP components were sequentially identified and scored by computer using the InstEP System. Manual verification of random computer-generated scores was also done to ensure accuracy. The latency ranges in which the component was scored was determined following inspection of the individual subject's and group-averaged waveforms. The N100 was scored as the minimum voltage between 75 and 150 ms, P200 as the maximum voltage between 150 and 250 ms, N200 as the minimum voltage between 150 and 350 ms, and P300 as the maximum voltage between 250 and 650 ms post-stimulus onset.

Behavioral Data

Four types of response data were calculated across the five test blocks. The hit rate was calculated as the number of correct responses to go stimuli occurring within 100-1000 ms after stimulus onset out of a total of 100 target stimuli. Misses were calculated as the total number of failures to respond to a go stimulus and correct responses occurring between 1001 ms and 1400 ms after the onset of a go stimulus. False alarms were calculated as the total number of responses to nogo stimuli occurring within 100-1000 ms after stimulus onset. Mean reaction time to go stimuli was also obtained. Separate values were calculated for left and right hand responses. The two groups were also compared on hit rate and mean reaction time for the last practice block in order to ensure that they reached an equivalent level of proficiency in responding by the end of the practice trials.

Statistical Analyses

Mean reaction time for the practice and test blocks was analyzed using mixed-model repeated measures ANOVA with group as the between-groups factor and response hand as the within-groups factor. The number of hits during the practice and test blocks, as well as the number of false alarms and misses made during the test block, were analyzed using the Mann-Whitney U and Kruskall-Wallis tests because of excessive departures from the normal distribution that could not be adequately remedied using statistical transformations. Results were considered significant at $p \leq .05$.

Separate analyses where conducted for the latency and amplitude data for each ERP component, and separately for midline and lateral electrodes. Midline data was analyzed using a mixed-model repeated measures ANOVA in which group (OCD, Control) served as the between-groups factor, and the within-group factors consisted of response hand indicated by arrow (left, right), coronal plane (Frontal, Central, Parietal), and stimulus (go, nogo). Lateral electrodes were analyzed using a mixed-model repeated measures ANOVA in which group (OCD, Control) served as the between-groups factor, and the within-groups factors consisted of response hand indicated by arrow (left, right), hemisphere (left, right), anterior/posterior axis (Frontal, Central, Parietal), and stimulus (go, nogo). Results were considered significant at $p \leq .05$.

Significant effects involving the anterior/posterior axis factor were considered significant at $p \leq .05$, only after application of the Geisser-Greenhouse (1958) correction. This correction is recommended for any effects involving a factor with two or more degrees of freedom in the numerator, given the common violation of the sphericity assumption in ERP research (Vasey & Thayer, 1987). All reported p values are based on

corrected degrees of freedom, although uncorrected degrees of freedom along with the Geisser-Greenhouse epsilon are presented. Post-hoc evaluations were conducted using t-tests with significance level set at $p \leq .01$.

Finally, patients were also partitioned into subgroups for the purpose of additional analyses based on medication status and presence or absence of secondary diagnosis. The limited sample size resulting from this partitioning indicated that the results of these analyses needed to be interpreted conservatively. Nevertheless, the sample sizes obtained after partitioning are similar to those in other studies in the literature.

Results

Data screening

None of the 1260 data points for the P300 across the two groups and test conditions were missing. ERP data was explored for outliers and fulfillment of statistical assumptions (Keppel, 1991; Tabachnick & Fidell, 1989). Six outliers were identified. These data were replaced by the next most extreme score for a subject in the same group on the variable in question (Winer, 1971).

It was originally planned that potential group differences on earlier peaks of the ERP such as the N100, P200 and N200 would be evaluated. For many participants, however, one or more of these peaks were not detectable in the waveform. Adjusting the digital filters in order to help in the detection of these peaks (Jodo & Kayama, 1992) was unsuccessful. The P200 in particular was usually not detectable for most participants through either the computerized scoring program or visual inspection, resulting in insufficient data for statistical analyses. The P200 was therefore excluded from further

analysis. The failure to observe a clear P200 peak in go-nogo tasks may also be noted when inspecting the waveforms from a number of previous investigations (Jodo & Inoue, 1990; Simson et al., 1977). Given the number of missing data points replacing these points with group means or through statistical estimations would be inappropriate (Tabachnick & Fidell, 1989). Consequently, the groups were compared on N100 and N200 using only those participants that had all data values for all conditions. For the N100 this resulted in groups of twelve patients and nine controls for the analysis of lateral electrodes, and eleven patients and nine controls for midline electrodes. For the N200 this resulted in groups of ten patients and ten controls for the analysis of lateral electrodes, and ten patients and thirteen controls for midline electrodes. Comparison of participants that were included and excluded from the analyses due to missing data points failed to reveal any differences in age, gender, education, YBOCS, BDI or STAI-S scores. Furthermore, comparisons of the patients and controls included in the analyses for the N100 and N200 revealed significant differences on the BID and SAT-S, no differences in terms of age and education, and YBOCS data, all consistent with those obtained for participants included in the analysis of the P300. Nevertheless, results of analysis on the N100 and N200 were interpreted conservatively due to the reduction in sample size.

An alteration made to the InstEP program resulted in different amplification of the ERPs for participants tested before and after the alteration. Eleven (69%) OCD and twelve (67%) control participants demonstrated lower amplification on visual inspection of the data than the 5 OCD and 6 controls tested prior to the alteration. The groups did not significantly differ with respect to the number of participants tested before and after the alteration [Fischer's Exact Test two-tailed $p = 1.00$]. The potential influence of time

when participants were tested was evaluated using repeated measures analysis of variance on each ERP variable with Group and Time as between-group factors. Results of the ANOVAs are presented in Appendix E. No significant main effect of Time or Group X Time interaction was observed for the latency of N100 and N200 at either midline or lateral electrodes. These effects were also not significant for N100 and N200 amplitude at midline electrodes, or N200 latency and amplitude at lateral electrodes (all $p > .05$). In contrast a significant main effect of Time was observed for P300 latency and amplitude at both midline and lateral electrodes. This finding was due to participants tested prior to the alteration having larger amplitude and shorter latency then those tested afterwards. Importantly, none of the Group X Time interactions for the P300 were significant. Thus any group differences on P300 that emerged are unlikely to have been accounted for by the time when participants were tested. The only significant Group X Time interaction was found for N100 amplitude at lateral electrodes. This finding indicated that N100 amplitude was generally larger for participants tested prior to the alteration. This N100 amplitude finding was interpreted with caution, however, as only two controls and three patients tested prior to the alteration of amplification had complete N100 amplitude data. Finally, the use of different amplification precluded the construction of grand-averaged ERP waveforms across participants within each group. Representative waveforms for two participants in each group were therefore presented.

Participant Characteristic Data

Table 5 presented the means and standard deviations for the groups on the demographic, self-report and clinical variables. Group differences were evaluated using independent-samples t-tests and Fisher's Exact Test with results being considered significant at $p \leq 0.05$. No significant group differences were observed between the groups for age, years of education, gender composition or hand preference. In contrast, the OCD group obtained significantly higher scores than the control group on the BDI [$t(32) = 3.74$, $p = .001$] and STAI-S [$t(32) = 2.88$, $p = .007$].

Behavioral data

A subset of eleven patients and twelve controls completed the accuracy/speed rating. Results revealed that both groups stressed accuracy considerably more than speed. The groups did not differ significantly with respect to this rating [$t(21) = 1.89$, $p = .073$].

Means, standard deviations and results of analyses for the behavioral response data were presented in Table 6. Results revealed a significant main effect of group on reaction time in the practice block [$F(1, 32) = 5.00$, $p = .033$] indicating shorter reaction time for the control group. This finding was rendered non-significant when the influence of STAI-S was covaried-out [$F(1, 31) = 3.54$, $p = .069$] and medicated participants were excluded from the analyses [$F(1, 28) = 1.86$, $p = .183$]. Comparison of patients with and without a secondary diagnosis was not significant. The OCD and control group did not differ with respect to the number of hits during the last practice block for either the left [Mann-Whitney U = 120.0, $p = .090$] or right [Mann-Whitney U = 133.0, $p = .536$] hand.

Table 5

Means and Standard Deviations for the Participant Characteristic Data in the ERP Study

	OCD		Control	
Variable	M	SD	M	SD
Age	41.35	10.79	37.39	11.55
Years of education	14.82	3.21	16.72	3.92
Percent women	47		33	
Percent right-handed	100		89	
BDI	13.68	3.72	3.72	7.35
STAI-S	37.41	8.84	28.78	7.8
YBOCS Total	24.59	1.56		
YBOCS Obsession	11.65	.92		
YBOCS Compulsion	12.94	.95		

Note. BDI = Beck Depression Inventory; STAI-S = State-Trait Anxiety Inventory-State Scale; YBOCS = Yale-Brown Obsessive-Compulsive Scale.

Table 6

Means and Standard Deviations for Behavioral Data in the ERP Study

Variable	OCD		Control	
	M	SD	M	SD
Last practice block				
Reaction time (ms)				
left hand	510	64.79	463	51.72
right hand	494	62.32	458	47.63
Number of hits				
left hand	32.00	0.00	31.78	0.55
right hand	31.81	0.40	31.90	0.32
Test blocks				
Reaction time (ms)				
left hand	528	61.41	491	66.42
right hand	514	63.81	476	67.27
Percent hits				
left hand	98.75	1.57	98.22	1.90
right hand	98.50	1.20	99.38	1.20
Number of misses				
left hand	0.44	1.26	0.39	0.85
right hand	0.25	0.78	0.44	0.86
Number of false alarms				
left hand	1.00	1.51	0.94	1.89
right hand	1.69	2.94	1.12	1.47

In the test phase a significant main effect of response hand on reaction time was obtained [$F(1, 32) = 13.27$, $p = .001$], indicating faster response with the right than left hand. No significant group or group by response hand interaction was noted for reaction time. Comparisons on reaction time based on medication status or the presence of a secondary diagnosis were also not significant.

The control group made more hits with the right (Mann-Whitney $U = 82.0$, $p = .023$) but not left (Mann-Whitney $U = 120.0$, $p = .390$) hand than the patient group during the test phase. The right hand difference remained significant after exclusion of medicated patients [Mann-Whitney $U = 59.0$, $p = .029$]. Comparison of patients with and without a secondary diagnosis was not significant. No effects of were observed for either the number of misses or false alarms made during the test phase. Covariance analysis using the BDI and STAI-S did not alter the pattern of findings.

ERP data

Tables 7 to 9 presented the means and standard deviations for the latencies of the N100, N200 and P300. Tables 10 to 12 presented these values for the amplitudes. The results of the analyses are presented in Appendix F. Representative ERP waveforms for two OCD patients and two normal controls were presented in Figure 3. Significant effects which did not include the Group factor are presented first, followed by any findings involving the Group factor. Reanalysis of the ERP data using the number of hits made with the right hand during the test block as covariate did not significantly alter the pattern of findings. Thus only the original findings were presented below.

Table 7

Means and Standard Deviations of N100 Latency for OCD and Normal Control Groups

	OCD				Control			
	Go		Nogo		Go		Nogo	
Variable	M	SD	M	SD	M	SD	M	SD
Left hand								
Fz	108	20.55	114	23.23	109	25.67	104	23.23
Cz	110	22.25	110	15.92	108	25.25	117	14.18
Pz	111	17.79	105	13.37	115	24.77	114	18.71
F3	112	23.18	116	21.33	114	24.77	121	20.81
C3	112	16.12	108	15.05	122	21.54	109	15.10
P3	106	13.27	103	11.88	104	15.89	101	14.31
F4	115	22.24	109	20.70	106	21.66	125	16.81
C4	111	16.14	106	10.14	109	21.97	117	18.17
P4	104	16.94	101	16.79	94	13.63	98	15.46
Right hand								
Fz	112	24.28	124	20.51	110	17.83	116	20.88
Cz	110	18.57	113	15.89	115	24.04	109	16.56
Pz	109	15.58	111	12.47	105	13.91	109	17.35
F3	111	22.56	112	21.36	118	24.11	129	18.00
C3	112	19.62	110	17.50	110	18.10	112	20.58
P3	99	14.11	106	14.30	98	12.91	98	15.20
F4	116	18.36	122	19.84	108	19.34	116	23.63
C4	109	14.50	114	13.68	111	27.23	104	14.83
P4	103	13.44	103	16.75	103	21.61	100	13.55

Table 8

Means and Standard Deviations of N200 Latency for OCD and Normal Control Groups

	OCD				Control			
	Go		Nogo		Go		Nogo	
Variable	M	SD	M	SD	M	SD	M	SD
Left hand								
Fz	206	12.65	200	19.60	203	22.17	187	18.13
Cz	205	18.90	197	18.41	205	20.83	192	16.20
Pz	195	19.32	200	34.88	196	15.10	199	14.48
F3	211	22.95	183	20.65	192	18.72	188	13.42
C3	207	24.23	214	40.53	196	19.73	193	12.66
P3	206	37.12	203	32.64	195	14.51	204	9.99
F4	214	22.90	206	22.71	201	22.28	210	27.96
C4	220	29.54	201	18.31	204	12.17	198	14.20
P4	208	35.03	191	13.17	200	13.06	205	12.22
Right hand								
Fz	205	17.23	203	27.16	207	20.33	192	27.70
Cz	207	29.53	205	21.44	204	15.74	196	27.53
Pz	204	30.14	204	25.34	202	11.31	192	25.66
F3	211	35.96	206	29.96	214	22.19	201	35.56
C3	212	38.11	197	19.99	208	17.79	198	27.39
P3	210	38.15	206	25.64	204	12.59	203	14.66
F4	218	29.43	217	35.64	203	20.55	199	28.26
C4	201	15.84	209	31.22	198	10.74	194	16.17
P4	195	14.37	212	28.51	202	10.19	205	9.07

Table 9

Means and Standard Deviations of P300 Latency for OCD and Normal Control Groups

	OCD				Control			
	Go		Nogo		Go		Nogo	
Variable	M	SD	M	SD	M	SD	M	SD
Left hand								
Fz	371	83.35	383	101.23	380	103.05	365	52.13
Cz	361	81.19	381	101.60	388	94.65	357	55.92
Pz	375	71.15	408	105.02	362	73.81	374	81.07
F3	393	94.04	416	120.36	382	108	378	74.03
C3	369	67.21	403	117.08	371	84.85	364	66.15
P3	385	88.86	378	95.76	386	93.11	358	64.26
F4	387	94.31	424	118.91	392	103.84	383	85.58
C4	365	74.20	406	108.48	384	87.04	376	72.57
P4	392	95.79	433	106.52	394	85.00	381	91.47
Right hand								
Fz	387	99.85	378	87.69	380	104.86	367	63.54
Cz	373	100.23	358	76.07	391	98.16	359	69.48
Pz	369	72.12	379	97.35	361	75.89	372	90.06
F3	385	95.02	407	101.96	391	106.96	391	67.02
C3	375	75.34	373	89.15	377	89.12	375	73.47
P3	383	77.74	395	105.16	377	89.77	388	96.47
F4	358	53.39	401	104.78	366	95.48	384	70.56
C4	361	67.29	401	104.58	360	74.68	368	72.28
P4	374	82.73	363	94.56	371	73.29	404	102.73

Table 10

Means and Standard Deviations of N100 Amplitude for OCD and Normal Control Groups

	OCD				Control			
	Go		Nogo		Go		Nogo	
Variable	M	SD	M	SD	M	SD	M	SD
Left hand								
Fz	0.17	2.26	-0.82	1.87	-0.74	0.76	-0.52	0.44
Cz	-0.36	3.42	-1.21	2.70	-0.54	1.19	-0.15	0.93
Pz	-3.55	5.12	-3.66	4.42	-2.22	3.39	-2.02	3.35
F3	-1.50	2.64	-1.74	1.89	-0.41	0.45	-0.67	0.52
C3	-3.12	3.11	-2.98	2.71	-2.06	2.32	-1.51	2.26
P3	-6.75	4.42	-6.75	4.10	-3.94	3.52	-3.52	2.56
F4	-0.61	1.43	-0.80	1.38	-0.57	0.94	-0.94	1.41
C4	-1.82	2.63	-2.30	2.39	-1.59	1.87	-1.64	1.56
P4	-6.70	5.15	-6.82	4.84	-4.38	3.97	-3.61	2.67
Right hand								
Fz	0.02	1.81	-0.10	2.06	-0.69	1.11	-0.57	0.79
Cz	-0.88	2.78	-0.77	2.96	-0.62	1.01	-0.35	0.75
Pz	-3.26	4.40	-3.09	4.71	-2.22	4.01	-1.69	3.63
F3	-1.19	1.74	-1.51	1.58	-0.69	0.75	-0.98	1.09
C3	-3.07	2.81	-3.17	2.81	-1.97	2.63	-1.86	2.62
P3	-6.71	4.78	-6.53	4.45	-3.90	3.51	-3.69	3.23
F4	-0.65	1.37	-0.69	1.55	-0.91	1.31	-0.88	1.40
C4	-2.12	2.38	-2.10	2.36	-1.86	2.36	-1.53	1.96
P4	-6.16	5.03	-5.76	5.17	-4.01	4.01	-3.62	3.31

Table 11

Means and Standard Deviations of N200 Amplitude for OCD and Normal Control Groups

	OCD				Control			
	Go		Nogo		Go		Nogo	
Variable	M	SD	M	SD	M	SD	M	SD
Left hand								
Fz	0.65	3.68	0.37	3.25	-0.18	1.25	-0.47	0.91
Cz	0.58	3.77	1.31	3.80	-0.74	1.41	-0.31	1.21
Pz	-0.51	4.55	0.53	3.26	-0.17	2.02	0.26	3.24
F3	0.85	2.55	0.25	2.18	-2.98	0.87	-0.55	1.02
C3	0.90	3.39	1.84	2.55	-0.13	2.07	0.09	2.30
P3	-2.40	5.95	-1.37	3.81	-1.61	2.11	-0.79	3.80
F4	0.76	3.56	1.09	4.00	-0.19	0.73	-0.25	0.86
C4	0.35	3.76	1.65	3.26	-0.09	1.92	0.13	1.56
P4	-2.39	5.01	-1.27	3.53	-1.13	2.34	-0.52	3.26
Right hand								
Fz	0.28	3.38	-0.55	5.05	-0.30	2.16	-0.92	0.81
Cz	0.79	3.40	1.11	5.73	-0.86	2.08	-0.60	1.15
Pz	-0.20	4.11	-0.48	3.25	0.08	3.35	-0.27	1.61
F3	0.43	2.42	-0.67	4.42	-0.65	2.59	-1.36	1.41
C3	-0.51	3.38	0.15	4.13	-0.83	3.64	-0.42	0.90
P3	-3.11	5.40	-2.57	2.90	-1.41	4.85	-1.38	2.32
F4	0.79	3.46	-0.62	4.55	0.17	0.99	-0.98	1.07
C4	1.88	3.14	0.72	3.86	0.66	2.95	-0.16	1.19
P4	-1.49	4.49	-1.31	2.70	-0.12	3.73	-0.51	2.05

Table 12

Means and Standard Deviations of P300 Amplitude for OCD and Normal Control Groups

	OCD				Control			
	Go		Nogo		Go		Nogo	
Variable	M	SD	M	SD	M	SD	M	SD
Left hand								
Fz	10.41	5.36	11.01	5.47	6.78	5.02	7.34	4.62
Cz	11.84	8.51	10.63	6.82	8.17	7.90	8.31	6.88
Pz	13.11	8.63	9.66	7.03	10.23	10.53	8.42	7.41
F3	9.04	4.76	8.56	5.50	6.22	4.51	6.14	3.32
C3	11.30	7.51	9.96	6.65	8.39	7.42	8.01	5.94
P3	10.49	7.53	6.66	6.41	6.90	7.26	5.83	5.32
F4	9.85	6.50	9.71	6.13	6.26	4.91	6.61	4.01
C4	10.31	6.40	10.10	5.97	7.71	7.18	7.82	5.91
P4	9.25	7.20	6.68	5.97	6.65	6.55	5.96	6.04
Right hand								
Fz	10.42	5.32	9.84	6.23	6.85	5.14	6.91	4.80
Cz	11.63	7.52	12.51	9.41	7.57	7.82	8.40	7.01
Pz	12.96	8.43	9.08	7.04	10.06	10.15	7.82	7.61
F3	7.84	3.93	7.38	4.79	5.46	4.04	5.72	3.68
C3	9.97	6.11	9.99	7.40	7.33	6.97	7.65	6.23
P3	9.33	7.59	6.80	6.68	7.09	7.33	5.15	5.51
F4	10.11	6.54	8.09	5.16	6.66	5.05	6.33	4.46
C4	11.23	7.23	10.01	6.84	8.24	7.79	7.63	6.41
P4	8.64	6.79	6.92	5.20	7.66	8.52	5.76	6.25

Figure 3. Representative ERP waveforms for left and right hand go (solid line) and nogo (dotted line) for OCD and control participants.

Figure 3a. ERP waveforms for go (solid line) and nogo (dotted line) stimuli responding with left hand for a participant with OCD.

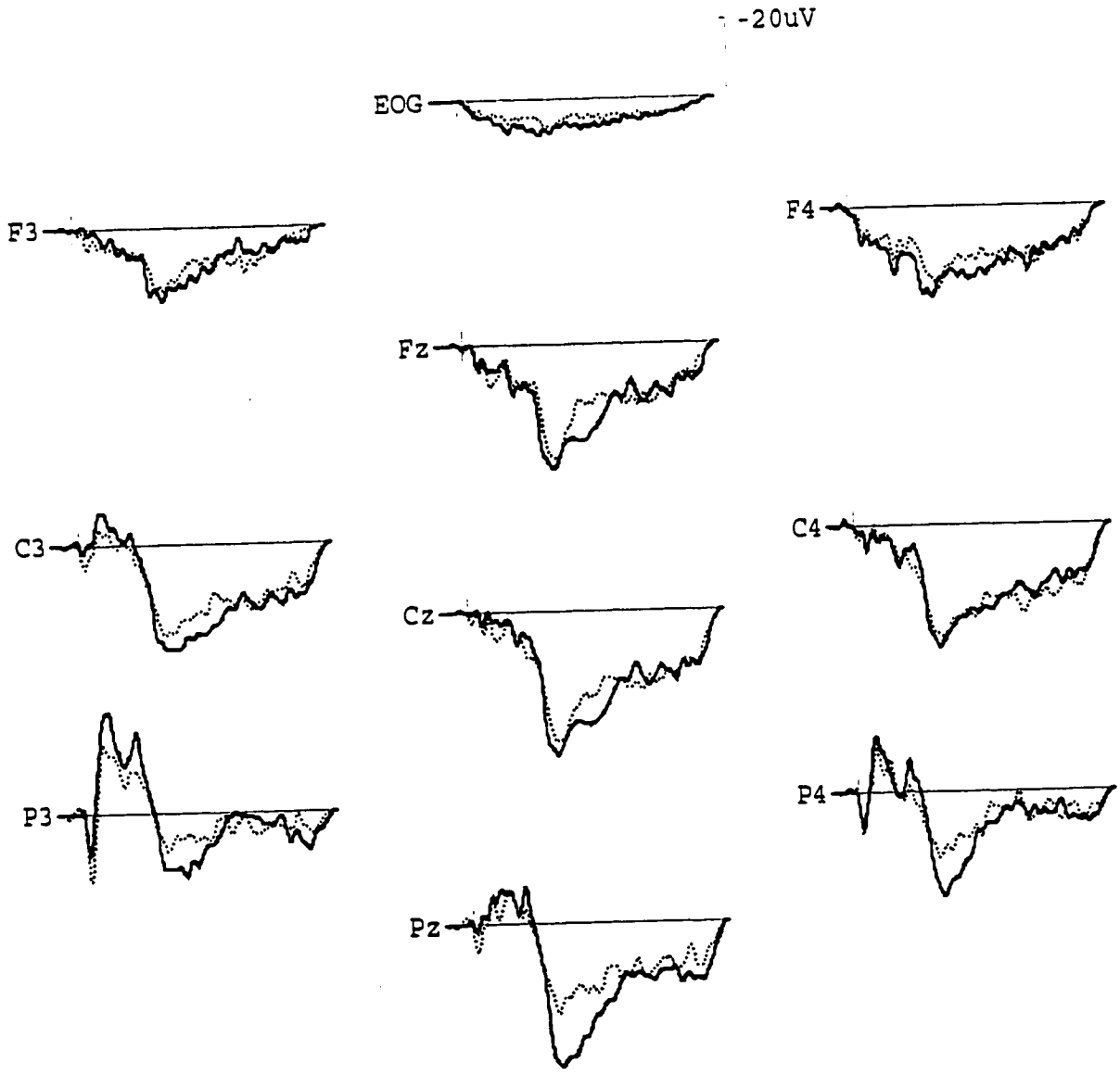

-20uV
EOG
F3
F4
Fz
C3
C4
Cz
P3
P4
Pz

Figure 3b. ERP waveforms for go (solid line) and nogo (dotted line) stimuli responding with right hand for a participant with OCD.

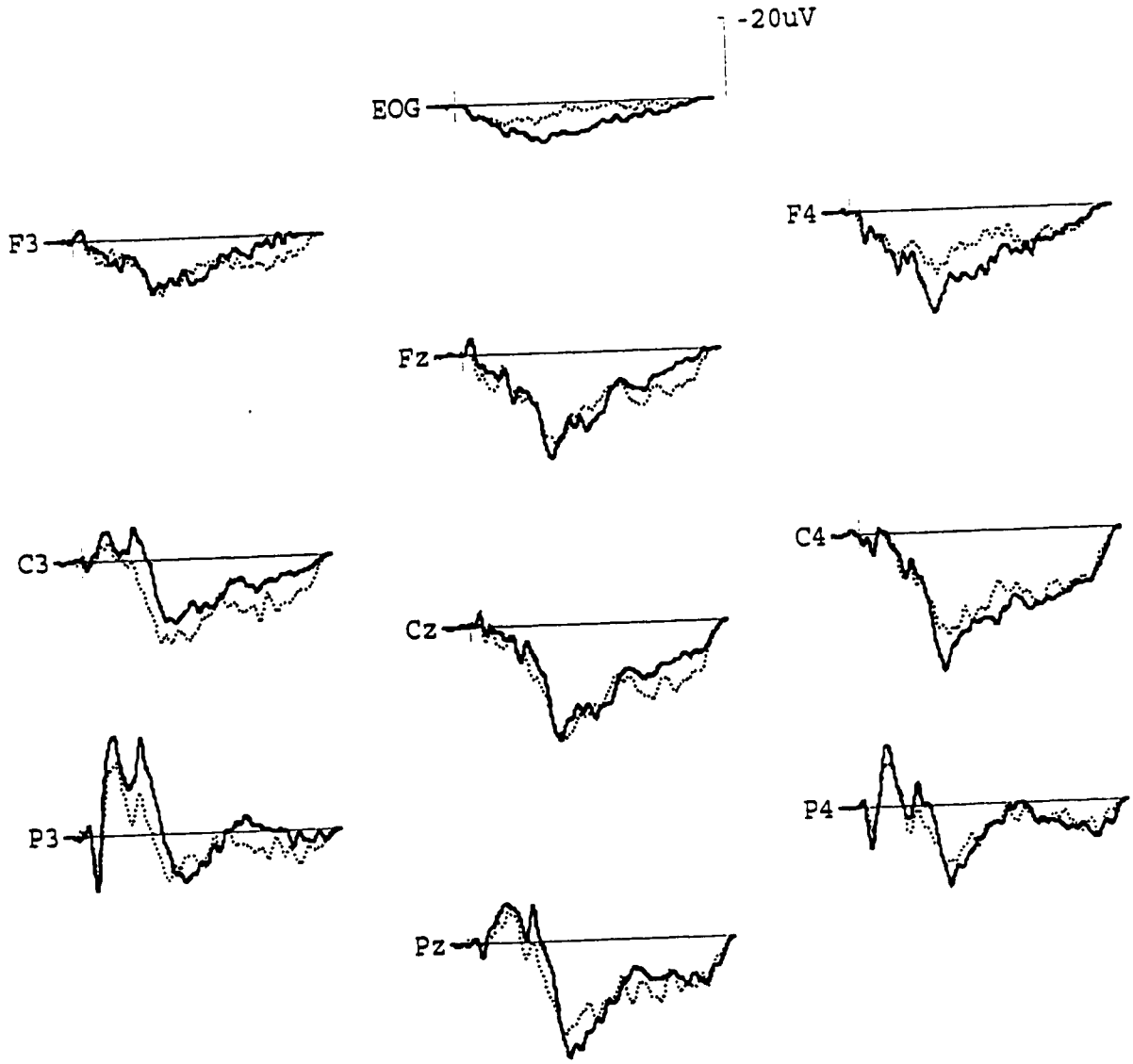

-20uV
EOG
F3
F4
Fz
C3
C4
Cz
P3
P4
Pz

Figure 3c. ERP waveforms for go (solid line) and nogo (dotted line) stimuli responding with left hand for a second participant with OCD.

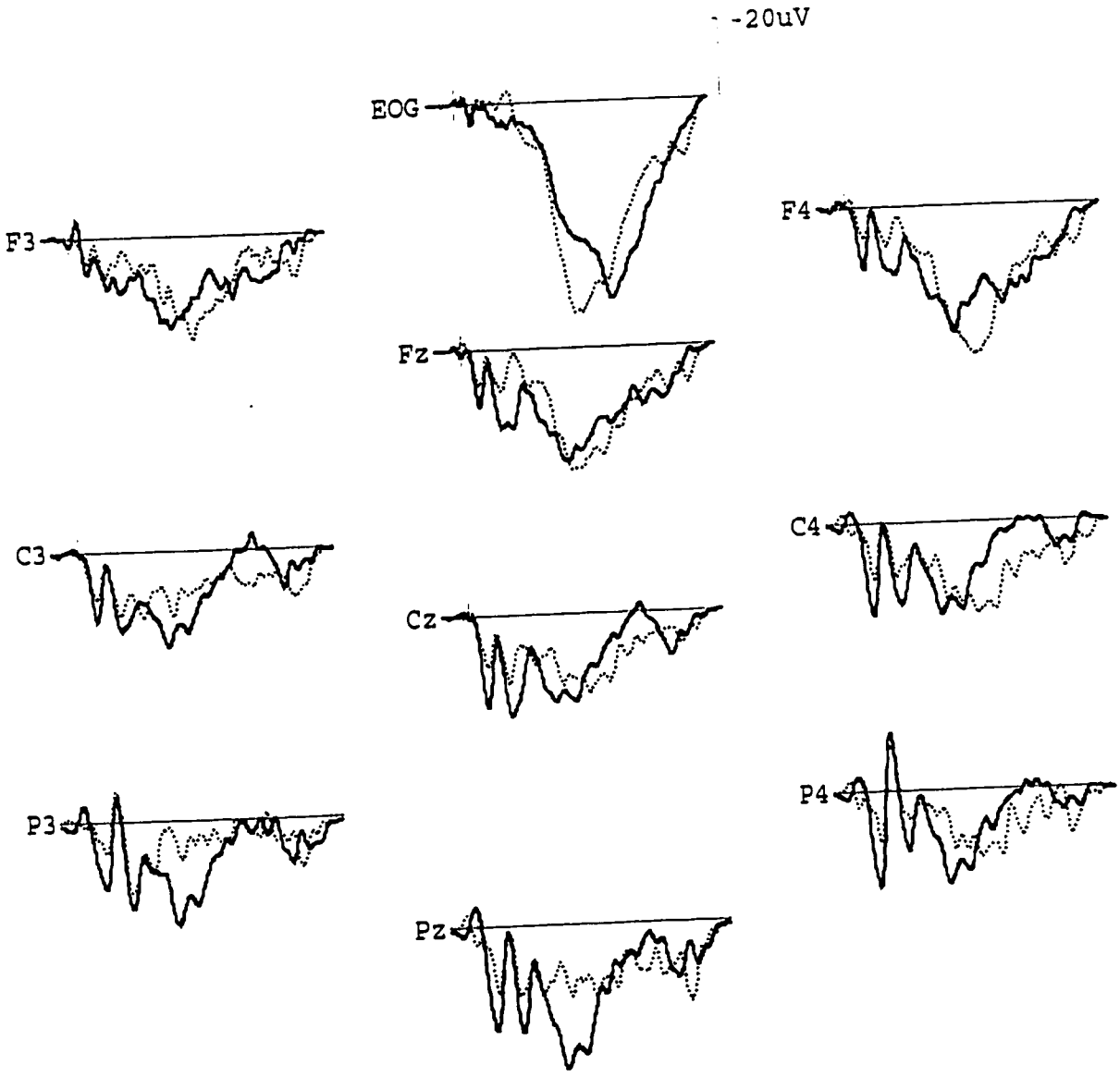

-20uV
EOG
F3
F4
Fz
C3
C4
Cz
P3
P4
Pz

Figure 3d. ERP waveforms for go (solid line) and nogo (dotted line) stimuli responding with right hand for a second participant with OCD.

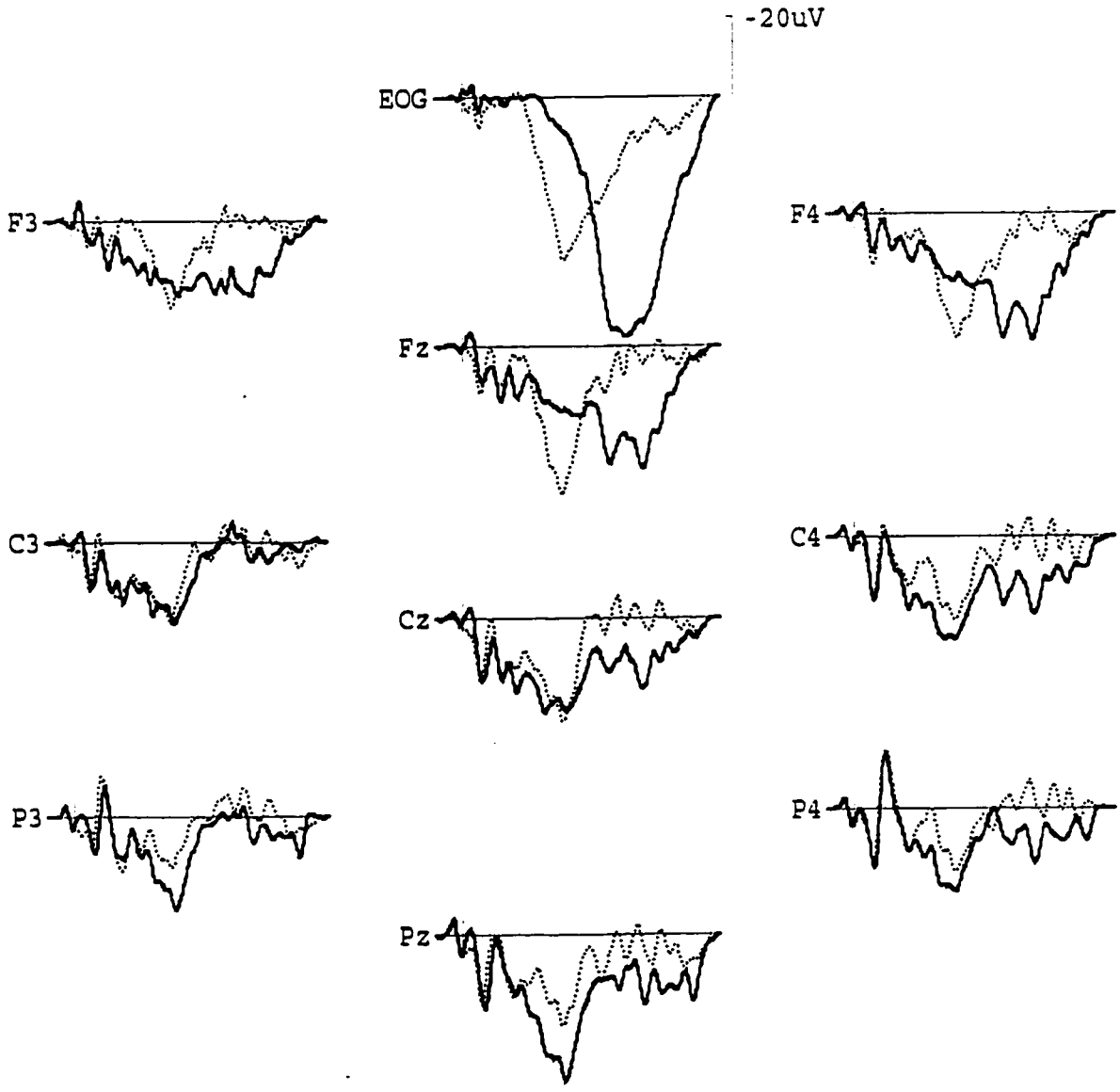

-20uV
EOG
F3
F4
Fz
C3
C4
Cz
P3
P4
Pz

Figure 3e. ERP waveforms for go (solid line) and nogo (dotted line) stimuli responding with left hand for a normal control participant.

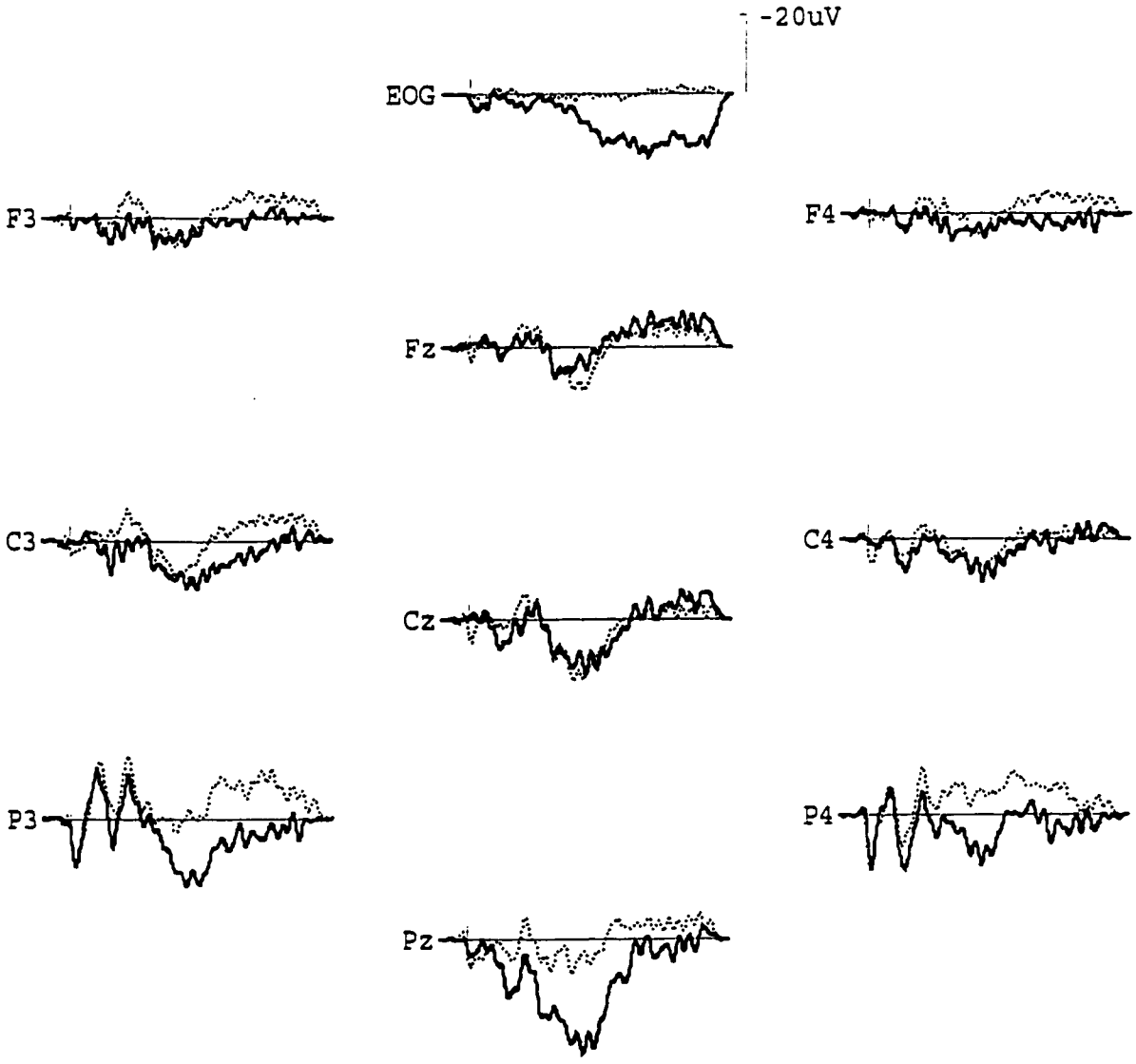

-20uV
EOG
F3
F4
Fz
C3
C4
Cz
P3
P4
Pz

Figure 3f. ERP waveforms for go (solid line) and nogo (dotted line) stimuli responding with right hand for a normal control participant.

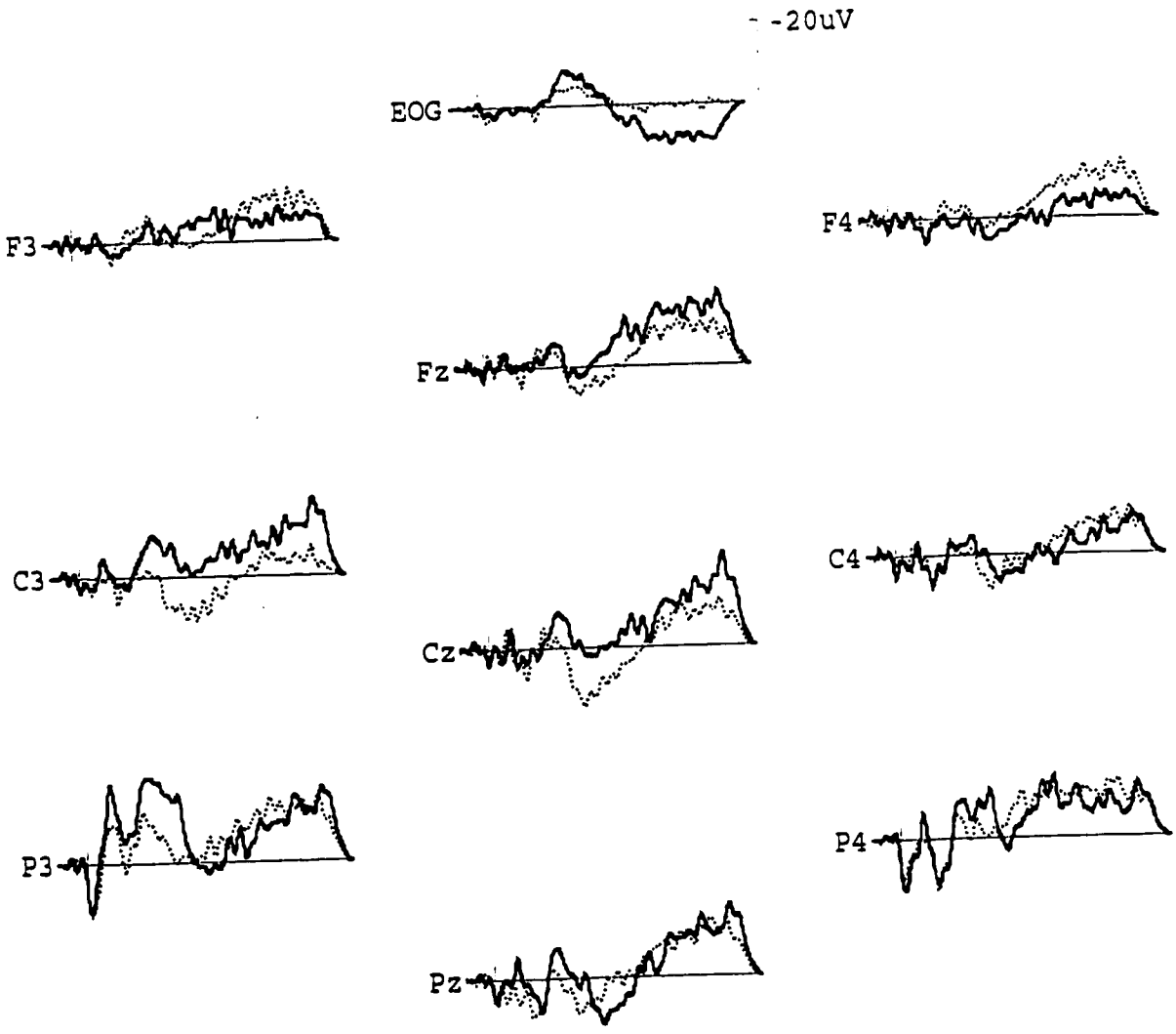

- -20uV
EOG
F3
F4
Fz
C3
C4
Cz
P3
P4
Pz

Figure 3g. ERP waveforms for go (solid line) and nogo (dotted line) stimuli responding with left hand for a second normal control participant.

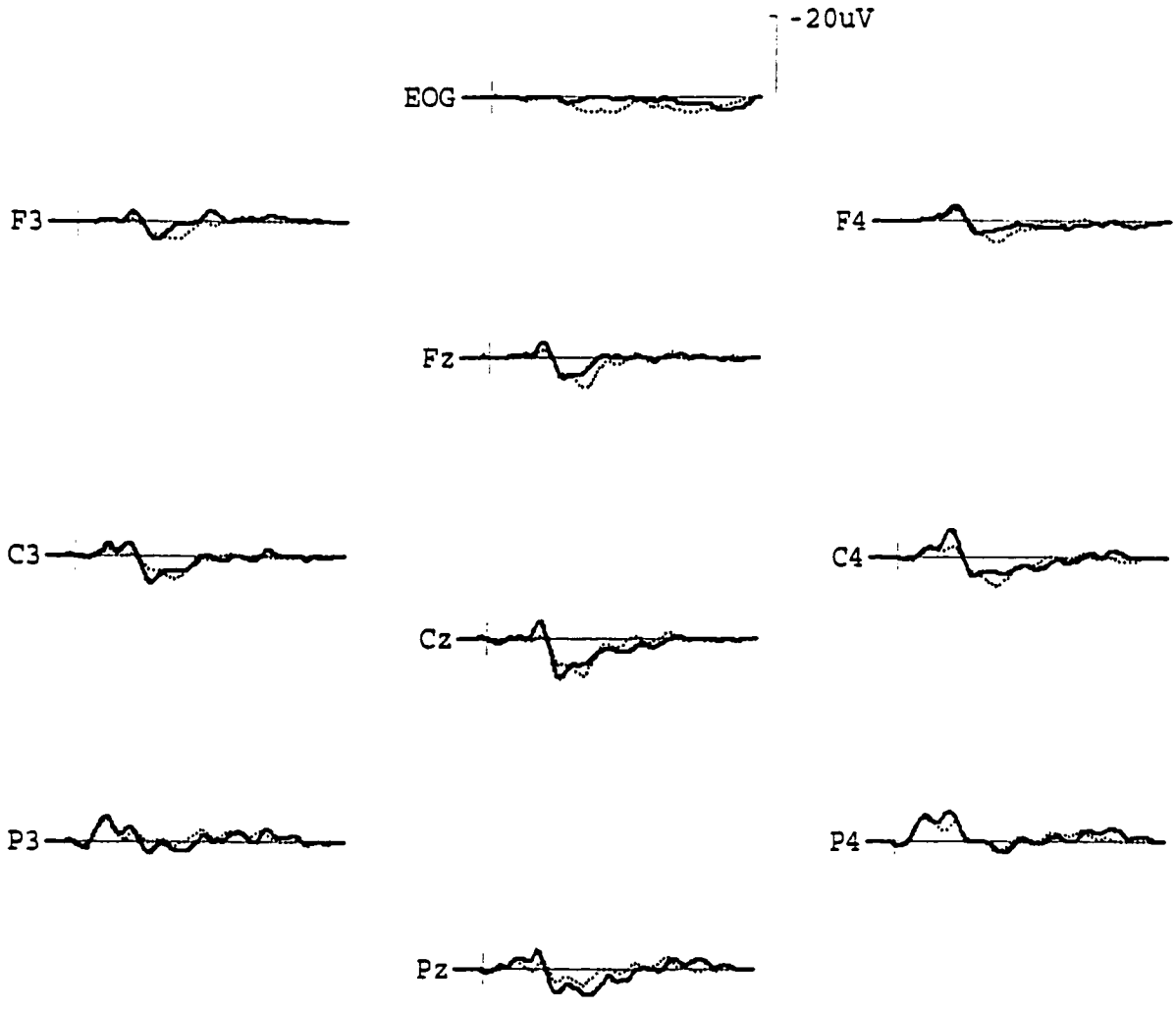
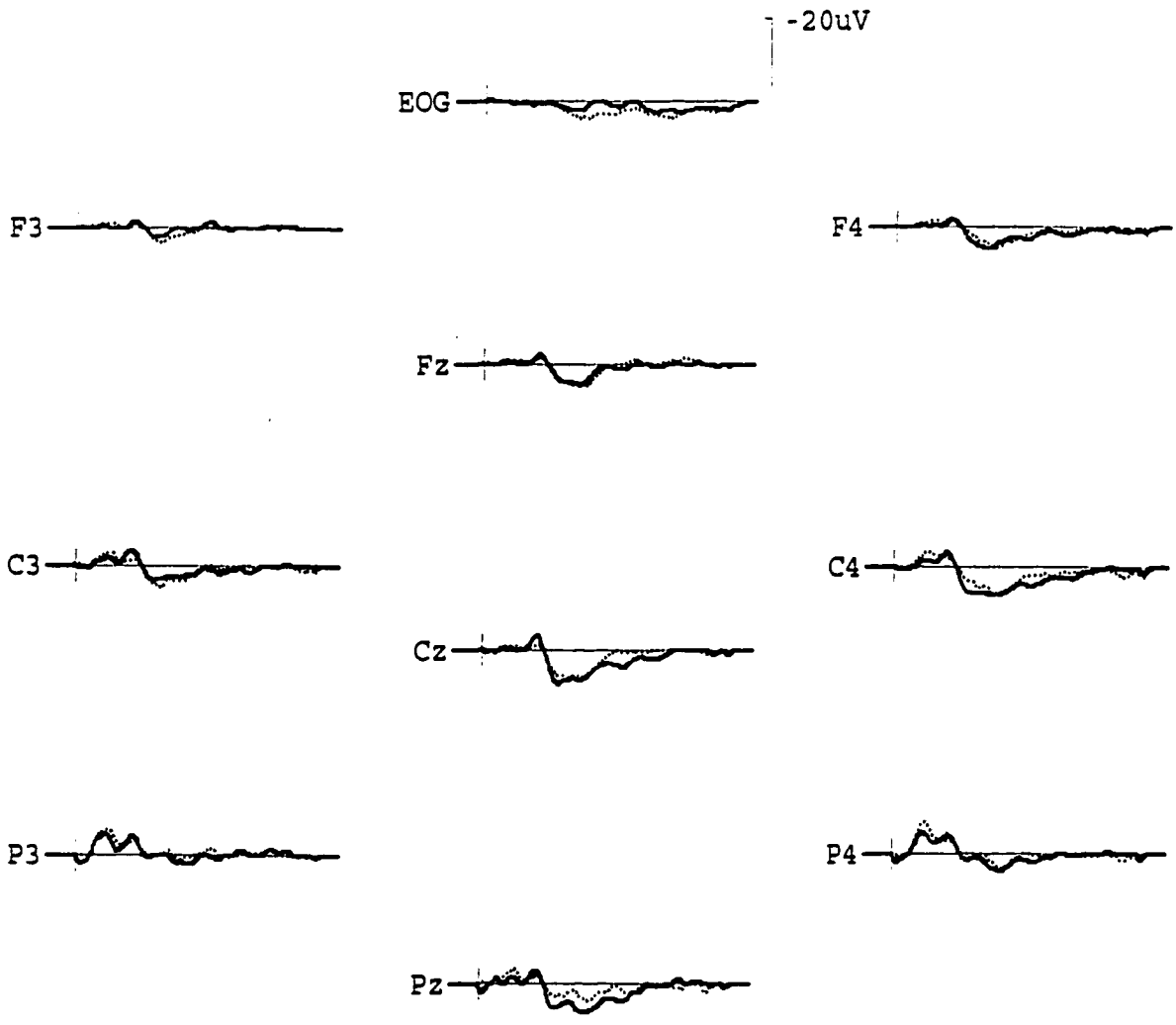

-20uV
EOG
F3
F4
Fz
C3
C4
Cz
P3
P4
Pz

Figure 3h. ERP waveforms for go (solid line) and nogo (dotted line) stimuli responding with right hand for a second normal control participant.


-20uV
EOG
F3
F4
Fz
C3
C4
Cz
P3
P4
Pz

N100 latency at lateral electrodes.

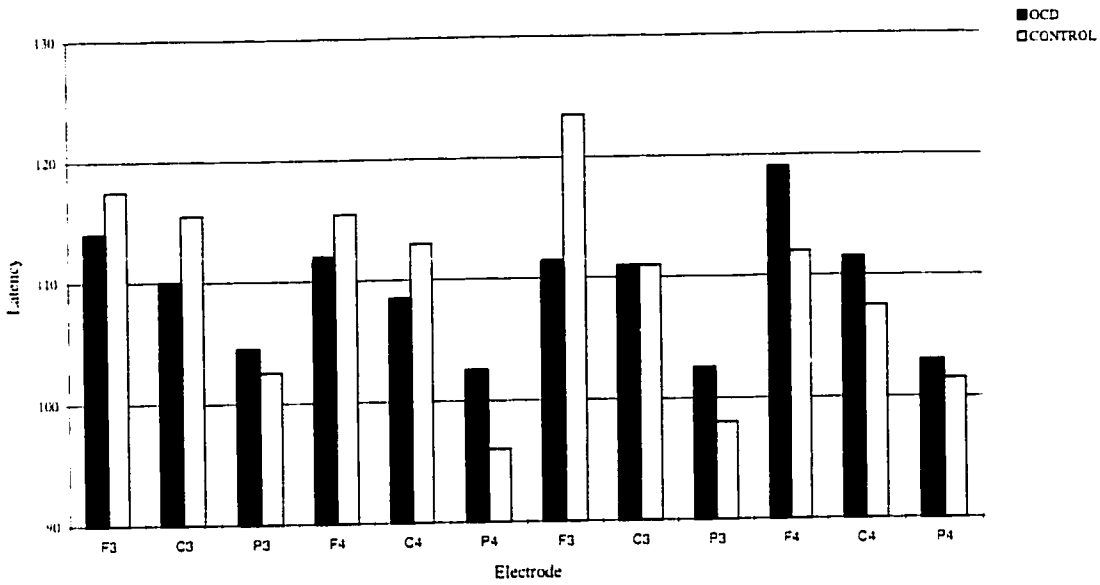
Effects not involving Group factor: A significant Anterior/Posterior Axis X Stimulus interaction was observed for N100 latency [$F(2, 38) = 4.48$, $p = .022$]. This finding was due to a decrease in nogo amplitude from the frontal (118 ms) to central (110 ms) to parietal (102) electrode plane, and go amplitude decrease only from the central (112 ms) to parietal (102 ms) electrode plane.

Effects involving Group factor: A significant Group X Hand X Hemisphere X Anterior/Posterior Axis interaction was noted for N100 latency [$F(2, 38) = 5.67$, $p = .007$]. The finding was due to latency being shorter at P3 than F3 and C3 when responding with the right hand for the control but not the OCD group (Figure 4). ANCOVA using BDI and STAI-S did not alter the results. In addition, the results remained significant when the data were reanalyzed following exclusion of the four medicated patients [$F(2, 30) = 6.12$, $p = .007$]. Comparison of patients with ($n = 8$) and without ($n = 4$) secondary diagnoses was not significant.

N100 amplitude at lateral electrodes.

Effects not involving Group factor: A three-way interaction was noted between Hand, Hemisphere and Anterior/Posterior Axis [$F(2, 38) = 3.55$, $p = .042$, $\epsilon = 0.933$]. This interaction indicated that N1 amplitude increased significantly from the frontal to central to parietal electrode plane regardless of response hand or stimulus, and amplitude at P4 was larger when responding with the left (-5.57 μV) than right (-5.04 μV) hand.

Figure 4. Mean N100 latency (ms) at lateral electrodes for the OCD and control groups as a function of response hand, laterality and anterior/posterior axis.



Left Hand

Right Hand

Effects involving Group factor: No significant main or interaction effect involving the Group factor was obtained for N100 amplitude at lateral electrodes. Reanalysis following exclusion of medicated patients also failed to reveal any significant effects involving the Group factor. These findings should be interpreted with caution as the time when participants were tested may have influenced the pattern of findings.

N100 latency at midline electrodes.

Effects not involving Group factor: No significant main or interaction effect was observed for N100 latency at midline electrodes.

Effects involving Group factor: No significant main or interaction effects involving the group factor were observed. Reanalysis following exclusion of medicated patients also failed to reveal any significant effects involving the Group factor.

N100 amplitude at midline electrodes.

Effects not involving Group factor: At midline electrode sites a significant main effect of Anterior/Posterior Axis was observed. This effect indicated larger N1 amplitude at Pz (-3.35 μV) than Cz (-1.02 μV) and Fz (-0.72 μV), but no difference between Cz or Fz.

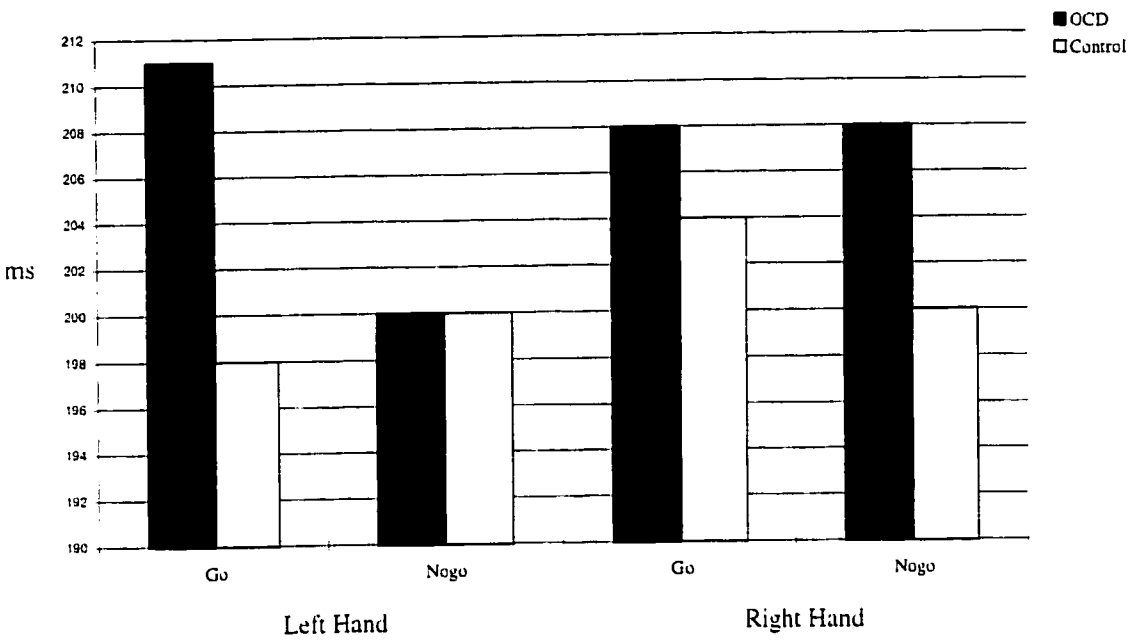
Effects involving Group factor: No significant main or interaction effect involving the group factor was observed. Reanalysis following exclusion of medicated patients also failed to reveal any significant effects involving the Group factor.

N200 latency at lateral electrodes.

Effects not involving Group factor: A significant Hand X Hemisphere X Anterior/Posterior Axis X Stimulus interaction was obtained for N200 latency [$F(2, 34) = 5.58$, $p = .007$, $\epsilon = 0.934$]. This finding was due to the latency being shorter at F3 than C3, P3 and F4 when participants were responding to the nogo stimuli with their left hand.

Effects involving Group factor: A significant Group X Hand X Stimulus interaction [$F(1, 17) = 4.38$, $p = .052$] revealed shorter N200 latency for the OCD but not the control group when responding with the left hand to the nogo (200 ms) than go (211 ms) stimulus (Figure 5). This finding was unaffected by covariance of BDI or STAI-S. Exclusion of the two medicated patients also did not eliminate the result [$F(1, 15) = 4.71$, $p = .046$]. There were an insufficient number of patients to form groups of those with and without secondary diagnoses to permit comparison with the control group. Comparison of the two patient subgroups ($n = 5$ for each) was not significant, although the limited sample sizes indicate that this finding must be interpreted with caution.

Figure 5. Mean N200 latency (in milliseconds) at lateral electrodes for OCD and control groups as a function of response hand and stimulus.

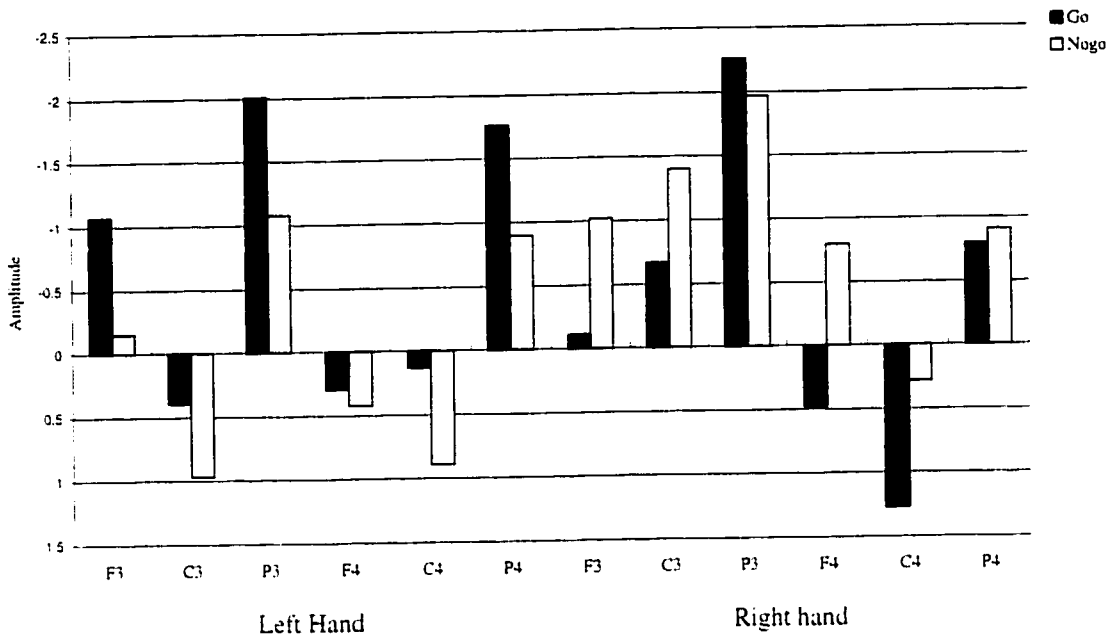

OCD
Control
ms
212
210
208
206
204
202
200
198
196
194
192
190
Go
Nogo
Go
Nogo
Left Hand
Right Hand

N200 amplitude at lateral electrodes.

Effects not involving Group factor: A significant Hand X Hemisphere X Anterior/Posterior Axis X Stimulus interaction was obtained for N200 amplitude [$F(2, 36) = 3.92$, $p = .039$, $\epsilon = 0.814$]. This finding was due to the N2 amplitude being larger at C4 when responding to the go stimulus with the left (0.37 μV) than right (1.27 μV) hand. N200 amplitude was also larger amplitude at C3 when responding to the go stimulus with the right (-0.67 μV) than left (0.38 μV) hand. Further analyses revealed that go stimulus N2 amplitude was larger at P3 (-2.01 μV) than C3 (0.38 μV) when responding with the left hand, and at P4 (-0.80 μV) than C4 (1.27 μV) when responding with the right hand. In contrast, nogo N2 amplitude was larger at F3 (-0.15 μV) and P3 (-1.08 μV) than C3 (0.97 μV) when responding with the left hand. This interaction was illustrated in Figure 6.

Effects involving Group factor: A significant Group X Hand X Hemisphere X Anterior/Posterior Axis X Stimulus interaction was obtained for N200 amplitude [$F(2, 36) = 3.54$, $p = .041$, $\epsilon = 0.974$]. This finding was due to the OCD but not control group having larger amplitude at P3 (-1.89 μV) than C3 (1.37 μV) when responding with the left hand. Although ANCOVA using BDI and STAI-S did not effect these findings, exclusion of the two medicated patients rendered the interaction non-significant [$F(2, 32) = 2.78$, $p = .079$, $\epsilon = 0.975$]. No differences were noted between patients ($n = 5$ each group) with and without a secondary diagnosis.

Figure 6. Mean N200 amplitude (μV) at lateral electrodes as a function of response hand, laterality, anterior/posterior axis and stimulus.


Go
Nogo
Amplitude
-2.5
-2
-1.5
-1
-0.5
0
0.5
1
1.5
F3
C3
P3
F4
C4
P4
F3
C3
P3
F4
C4
P4
Left Hand
Right hand

N200 latency at midline electrodes.

Effects not involving Group factor: A significant main effect of Stimulus [$F(1, 21) = 4.29$, $p = .051$] indicated shorter N200 latency for the nogo (197 ms) than go (203 ms) stimulus.

Effects involving Group factor: No significant main or interaction effect involving the Group factor was obtained. Reanalysis following exclusion of medicated patients also failed to reveal any significant effects involving the Group factor.

N200 amplitude at midline electrodes.

Effects not involving Group factor: A significant Anterior/Posterior Axis X Stimulus interaction was obtained for N200 amplitude [$F(2, 42) = 4.92$, $p = .013$, $\epsilon = 0.965$]. This finding was due to N2 amplitude being larger for the nogo stimulus at Fz (-0.43 μV) than Cz (0.27 μV).

Effects involving Group factor: No significant main or interaction effect involving the Group factor was obtained. Reanalysis following exclusion of medicated patients also failed to reveal any significant effects involving the Group factor.

P300 latency at lateral electrodes.

Effects not involving Group factor: A Hand X Hemisphere interaction revealed shorter P300 latency over the left (381 ms) than right (393 ms) hemisphere when responding with the left hand, and shorter latency over the right hemisphere when responding with the

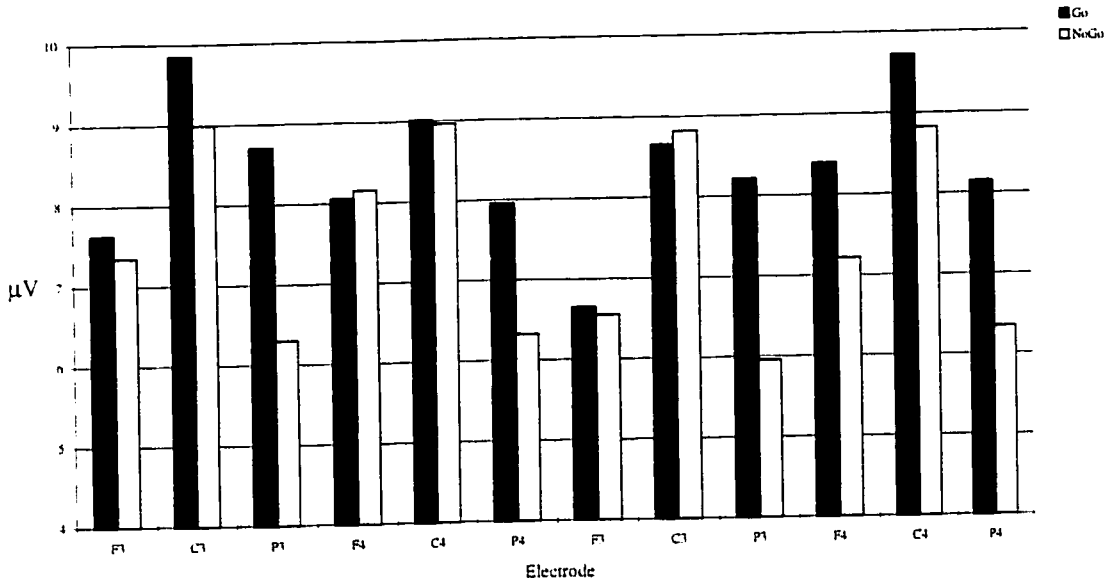
right (376 ms) as opposed to left (393 ms) hand [$F(1, 32) = 9.09$, $p = .005$]. A Hemisphere X Stimulus interaction indicated shorter P300 latency for go (375 ms) than nogo (393 ms) stimuli across right hemisphere electrode sites.

Effects involving Group factor: A significant Group X Hand X Hemisphere X Anterior/Posterior Axis [$F(2, 64) = 4.19$, $p = .020$, $\epsilon = 0.981$] was obtained. This finding was due the OCD group having shorter P300 latency at P4 when responding with the right (369 ms) as compared to the left (414 ms). This finding remained significant after covarying the influence of BDI and STAI-S, as well as when only unmedicated patients where included in the analysis [$F(2, 56) = 3.48$, $p = .040$, $\epsilon = 0.959$]. Comparison of patients with (n = 10) and without (n = 6) a secondary diagnosis was not significant.

P300 amplitude at lateral electrodes.

Effects not involving Group factor: A significant Hand X Hemisphere X Anterior/Posterior Axis X Stimulus interaction was found for the lateral electrodes [$F(2, 64) = 3.35$, $p = .051$, $\epsilon = 0.825$]. Further analyses revealed that the go P300 had a centroparietal scalp distribution over the left hemisphere and a more central distribution over the right hemisphere. Furthermore, go P300 was larger at F4 and C4 than F3 and C3 when participants responded with their right hand. Go P300 amplitude was not significantly smaller over the hemisphere contralateral than ipsilateral to the response hand. Nogo P300 was frontocentrally distributed over both hemispheres irrespective of response hand. This pattern of findings was illustrated in Figure 7.

Figure 7. Mean P300 amplitude (μV) at lateral electrodes as a function of response hand, laterality, anterior/posterior axis and stimulus.



Left Hand

Right Hand

Effects involving Group factor: No significant main or interaction effect involving the Group factor was obtained for P300 amplitude at lateral electrodes. Reanalysis following exclusion of medicated patients also did not reveal any significant group effect [$F(2, 56) = 2.46$, $p = .067$, $\epsilon = 0.651$].

P300 latency at midline electrodes.

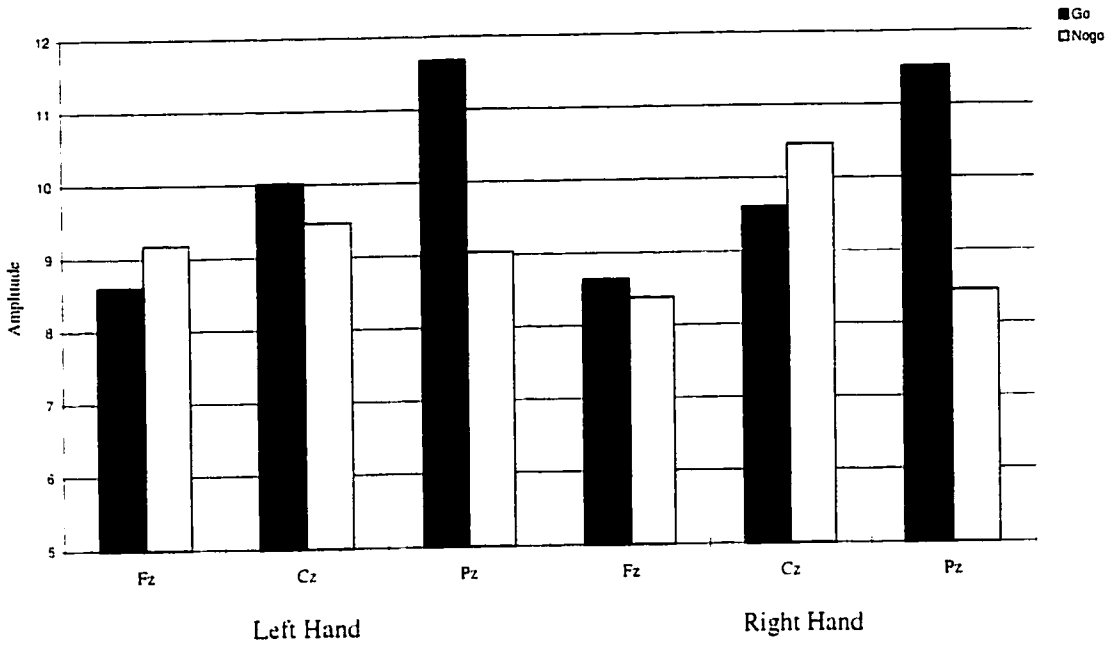
Effects not involving Group factor: No significant main or interaction effect was observed for P300 latency at midline electrodes.

Effects involving Group factor: No significant main or interaction effect was observed for the Group factor. Reanalysis following exclusion of medicated patients also failed to reveal any significant effects involving the Group factor.

P300 amplitude at midline electrodes.

Effects not involving Group factor: A significant Hand X Anterior/Posterior Axis X Stimulus interaction was found for the midline electrodes [$F(2, 64) = 4.35$, $p = .024$, $\epsilon = 0.831$]. Further analyses revealed that this interaction was due to P300 amplitude being significantly larger for the nogo stimulus at Cz (10.33 μV) than at Fz (8.29 μV) and Pz (8.41 μV) when participants responded with the right but not left hand. Go P300 amplitude was noted to decline significantly in amplitude from parietal to central to frontal electrodes for both hands. This effect was illustrated in Figure 8.

Figure 8. Mean P300 amplitude (μV) at midline electrodes as a function of response hand, anterior/posterior axis and stimulus.


Go
Nogo
Amplitude
12
11
10
9
8
7
6
5
Fz
Cz
Pz
Fz
Cz
Pz
Left Hand
Right Hand

Effects involving Group factor: No significant main or interaction effect involving the Group factor was obtained. Reanalysis following exclusion of medicated patients did revealed a significant Group X Stimulus interaction [$F(1, 28) = 4.53$, $p = .042$]. This effect was due to the unmedicated patient but not control group having larger go than nogo amplitudes.

Discussion of Experiment II

Experiment II sought to evaluate response inhibition in OCD as measured by the P300 ERP during the performance of a visual go/nogo task. In contrast to the findings of Malloy et al. (1989) the present results indicated that the OCD group did not differ from the control group in the extent of shift towards a frontocentral nogo P300 amplitude scalp distribution. The OCD group also did not have smaller P300 amplitude at frontal electrode sites than controls. The OCD group was observed to differ from the control group with respect to the latency of N100 and N200. The patient group also demonstrated shorter P300 latency when responding with the right than left hand, a pattern that was not observed for the normal controls. ERP findings could not be accounted for by depression, state anxiety or the presence of secondary diagnoses. Medication status could not account for the findings with the exception of a subgroup of the patients that were unmedicated but not controls having larger go than nogo P300 amplitude at midline electrodes. The present pattern of results did not support previous

observations suggesting that OCD is characterized by general cortical hyperarousal (Beech et al., 1983; Shagass et al., 1984; Towey et al., 1990) or a selective disturbance of the left or right hemisphere (Flor-Henry, 1979; Otto, 1992).

Slow Potential Overlap

A number of findings suggested that the present ERP latency and amplitude data could not be fully accounted for by the influence of overlapping CNV or motor potentials. Nogo latency has been argued to be shorter than go P300 latency because participants can discontinue ongoing response preparation processes reflected in later components of the CNV (Simson et al., 1977). In addition, other negative movement-related potentials have usually been observed to be larger over the hemisphere contralateral to the response hand at frontal and central electrode locations (Brunia & Damen, 1988; Damen & Brunia, 1994; Rohrbaugh & Gaillard, 1983) suggesting that shorter nogo than go latency may be more pronounced over the hemisphere contralateral to the response hand.

A number of observations with respect to the latency data in the present experiment were inconsistent with the motor potential overlap hypothesis. First, P300 latency was shorter for the go than nogo stimulus over the left hemisphere and did not significantly differ over the right hemisphere, irrespective of response hand; Second, P300 latency was observed to be shorter over the hemisphere ipsilateral to the response hand irrespective of stimulus type; Third, although CNV tends to be largest over central scalp sites no interaction was observed between stimulus type and the midline electrodes for P300 amplitude; Fourth, N100 and N200 latency were also not consistently shorter for nogo than go stimuli at electrode sites contralateral to response hand.

A number of observations with respect to the amplitude data also did not appear to be consistent with a significant influence of negative slow waves on N100 and N200: First, no significant effect of response hand was obtained for N100 amplitude at midline electrodes; Second, N100 amplitude increased from frontal to central to parietal electrodes over both hemispheres, regardless of response hand; Third, N100 amplitude was larger for nogo than go stimuli at lateral frontal sites, while the opposite was found at lateral parietal sites. The latter finding argues against CNV overlap since N100 would be expected to be larger for go than nogo stimuli at frontal electrodes given continuance of CNV activity; Fourth, although N200 amplitude was found to be larger at central electrode sites contralateral to the response hand, the within-hemisphere topography indicated significantly larger amplitude for parietal than central electrodes. The parietal maximum for the N100 and N200 is inconsistent with the more central and frontal distribution of the CNV and negative movement-related potentials; Fifth, N100 and N200 amplitudes were not consistently larger for the go than the nogo stimulus.

N200 amplitude was, however, observed to be larger for the go stimulus at central electrodes contralateral to both response hands. This finding suggested the presence of CNV or movement-related negativity could not be completely excluded. Nevertheless, the more parietal than frontocentral distribution of the go N200 over both hemispheres irrespective of response hand and the failure to observe reduced N200 amplitude for the go as compared to nogo stimulus at the central midline electrode, are both inconsistent with the motor overlap hypothesis. It must be reiterated, however, that the reduction in sample size for N100 and N200 engendered by the failure to observe these components for many participants indicated that these conclusions must be tempered.

A number of observations have indicated that CNV and negative movement-related potentials are unlikely to have significantly influenced P300 amplitude: First, P300 amplitude to the go stimulus was not significantly reduced over the hemisphere contralateral as compared to ipsilateral to the response hand; Second, Nogo P300 was not larger over the hemisphere contralateral to the response hand, as would be expected if there were negative movement-related potential overlap (Robert et al., 1994). It should be noted that the present analyses did not permit the possible influence of negative slow waves to be completely discounted. Concurrent recording of negative slow potentials and the ERP components elicited during go/nogo tasks will be required in order to determine their precise relationship in OCD. The required instrumentation for such concurrent recording were not available for the present investigation (Bauer, 1998). Further research comparing OCD and control participants during go/nogo task performance using with appropriate instrumentation is therefore recommended.

Topography

Consistent with previous studies, nogo P300 amplitude was observed to have a frontocentral and go P300 amplitude a centroparietal scalp distribution. This distribution was seen at both midline and lateral electrodes (Figures 3, 7 and 8). The observation of frontocentral distribution for the nogo P300 over both hemispheres irrespective of response hand was consistent with neuropsychological data implicating the frontal lobes in response inhibition during go/nogo tasks (Lezak, 1995). The lack of differences in the

topographical distribution of P300 between the OCD and control groups therefore suggested that OCD was not characterized by a frontal lobe-related inhibitory control deficit, at least as manifested in the frontocentral nogo P300.

In the present experiment, the frontocentral nogo P300 distribution appeared somewhat more pronounced at lateral than midline electrode sites. Nogo amplitude tended to be maximal at central rather than frontal electrode sites. Several studies have observed that nogo P300 is maximal in amplitude at central rather than frontal electrode sites (Falkenstein et al., 1995; Kopp et al., 1996; Pfefferbaum et al., 1985; Schupp et al., 1994). This finding has been interpreted as suggesting that nogo P300 may reflect activation of prefrontal cortex in the interruption of response activation processes but that there may also be other contributions to P300 during response inhibition (DeJong, Coles, Logan & Gratton, 1990; Robert et al., 1994).

Naito and Matsumata (1996) observed nogo P300 that was maximal at FCz, an electrode roughly midway between the frontal and central electrodes. These authors proposed that nogo P300 may also reflect activity of motor-related frontal cortical regions such as the supplementary motor cortex. Consistent with this proposal, impoverished ability to inhibit motor responses has been observed in patients with lesions to the left or right supplementary motor cortex (Verfaellie & Heilman, 1987). Supplementary motor cortex involvement in response inhibition has also recently been observed in a study in which disruption of the activity of this region through transcranial magnetic stimulation in patients with Tourette's syndrome, a tic disorder that is closely related neurobiologically to OCD (Pauls, Raymond, & Robertson, 1991), resulted in a diminished ability to inhibit tics (Peterson et al., 1998).

In the present experiment no consistent evidence for hemispheric asymmetries between the groups for P300 amplitude was obtained. This finding was not consistent with theories arguing for either left (Flor-Henry, 1979) or right hemisphere (Otto, 1992) dysfunction in OCD. Neuropsychological data have, however, indicated involvement of bilateral frontal regions in response inhibition (Lezak, 1995).

It is plausible that the failure to observe nogo P300 amplitude topographic/hemispheric differences between the groups may have been related to the selection of electrodes. Malloy and colleagues (1989) observed that the maximal group difference in nogo amplitude was at electrodes located more inferior (F7, FTC) to those employed in the present investigation. Thus although a robust frontocentral distribution for the nogo P300 was found over both hemispheres, for both the control and OCD group, the failure to use more inferior electrodes located in closer proximity to the orbitofrontal cortex may have contributed to the present lack of group differences. It should be noted, however, that three-dimensional mapping of the nogo P300 yielded maximal differentiation from the go stimulus over the right frontal lobe over an area that clearly extended superior to the most inferior electrodes employed by Malloy et al. (Strik et al., 1998). Nevertheless, replication of the present findings using more extensive electrode arrays over both hemispheres is required prior to reaching any firm conclusions with respect to topographic ERP disturbances in OCD.

Amplitude

Few group differences in P300 amplitude emerged in the present experiment. This contrasts with the study by Malloy et al. (1989) in which significantly smaller nogo P300 amplitude at frontal electrode sites was observed for the OCD group. A subgroup of the OCD patients in the present experiment that were unmedicated did however have larger P300 amplitude to go than nogo stimuli across the midline electrodes. This effect was not observed for the normal control group. This finding was unlikely to have been related to the amplitude of the earlier ERP components. No group difference was observed for the N100. In addition, although the OCD group as a whole demonstrated larger N200 amplitude over the left parietal region than controls this finding was rendered non-significant when only unmedicated patients were included in the analysis.

The failure to find P300 amplitude differences between go and nogo stimuli in normal control participants at midline as well as lateral electrodes has been previously reported, albeit inconsistently. Some studies have reported larger P300 amplitude to go stimuli (Pfefferbaum et al., 1980, 1984; Pfefferbaum & Ford, 1988), some to nogo stimuli (Simson et al., 1977; Roberts et al., 1994) and others have found no significant difference (Podlesny et al., 1984; Jodo & Inoue, 1990). Several authors have suggested that the inconsistency may be in part due to the influence of experimental design on the degree of response preparation required by participants (Pfefferbaum et al., 1985; Roberts et al., 1994). When response preparation is high nogo amplitudes have usually been observed to be larger than go amplitudes. The reverse has been more common when response preparation is low. For example, nogo amplitudes have tended to be larger than go amplitudes in studies that have used a warning stimulus (S1-S2 paradigms) that informed

participants to prepare for a target stimulus indicating whether a response is required or not (Jodo & Inoue, 1990; Robert et al., 1994; Simson et al., 1977). The reverse has been observed when no warning stimulus was provided (Cohen, Porjesz, Begleiter, & Wang, 1997).

These observations suggested that the unmedicated OCD patients may have a lower level of response preparation than normal controls (Pfefferbaum et al., 1985; Roberts et al., 1994). Although consistent with the view of P300 amplitude differences for go and nogo stimuli, this interpretation has run counter to the frequent finding of hyperattentiveness or hyperarousal in OCD (Beech et al., 1993; Morault et al., 1998; Towey et al., 1990). Furthermore, studies of unmedicated OCD patients have reported either a reduced P300 amplitude for the patients (Miyata et al., 1998) or no group differences (Morault et al., 1997; Towey et al., 1990; Towey et al., 1993) at midline electrodes for target stimuli. In contrast, Morault et al. (1997) reported larger P300 amplitude to target stimuli in OCD patients who were observed on follow-up evaluation to have experienced a significant reduction in the severity of their OCD symptoms (minimum 50% decrease in YBOCS score) following treatment with either Fluoxetine or Chlomiprimine, as compared to poor responders and normal controls. No other study has addressed the relationship between P300 amplitude and treatment response. It is thus plausible that the present group of unmedicated OCD patients were composed largely of individuals who may demonstrate a positive response to treatment with selective serotonin reuptake inhibitors. Follow-up evaluation of these patients, a subgroup of which have been randomized to receive treatment with Fluoxetine, should help address this issue.

Latency

In the present experiment, the OCD group was observed to have shorter P300 latency over the right parietal region when responding with the right than left hand. This effect was not observed for the normal controls. The finding of shorter P300 latency in OCD has been observed in most of the previous investigations (Miyata, Matsunaga, Kirike, Iwasaki, Takei, & Yamagami, 1998; Morault, Bourgeois, Laville, Bensch, & Paty, 1997; Towey et al., 1990). The relative consistency with which P300 latency is found to be decreased in OCD has been particularly significant given that other psychiatric populations such as schizophrenia, major depressive disorder and agoraphobia, usually demonstrate either no difference or longer latencies than controls (Osada, Sasaki, & Muraoka, 1996; Regan, 1989).

The present experiment was consistent with previous studies in observing shorter P300 latency in OCD to be a within-group effect related to task conditions rather than a between-group effect. Specifically, shorter latency in OCD has usually been observed when the difficulty of discriminating between stimuli was increased or the stimuli themselves were made more complex (Beech et al., 1983; Ciesielski, Beech, & Gordon, 1981; Towey et al., 1990). In contrast, normal controls have showed either no effect of these task parameters or an increase in P300 latency (Pfefferbaum et al., 1983; Towey et al., 1990). The latter finding has been interpreted as reflecting an increase in stimulus evaluation time that is independent of response selection and execution processes (Kutas, McCarthy, & Donchin, 1977; McCarthy & Donchin, 1981).

Shorter P300 latency in OCD patients has usually been interpreted as reflecting cortical overarousal resulting in the speeding of cognitive processes, although differences in reaction and hit rate have usually not been observed (Beech, Ciesielski, & Gordon, 1983; Shagass, Roemer, Straumanis, & Josiassen, 1984). A general state of cortical hyperarousal is also likely to result in increased amplitudes of ERP negativities such as the N100 and N200 and shorter latencies across task parameters (Hillyard & Picton, 1987). This pattern of ERP findings was not observed in the present sample of patients with OCD. Decreased parietal P300 latency in the OCD group is thus unlikely to have reflected a general state of cortical overarousal.

It is possible that the P300 latency finding may have been due to the OCD group having found the go/nogo task somewhat more difficult when responding with their right hand, as reflected by their significantly lower right hand hit rate than the controls. Several observations have suggested that this explanation could not account for the P300 latency effect: First, both the OCD and control group achieved an almost perfect hit rate (98% and 99%, respectively); Second, reaction time did not differ between the groups or hands and was generally consistent with that observed when participants are required to make a difficult discrimination (Pfefferbaum et al, 1983); Third, no difference was observed within the OCD group between left and right hand hit rates or reaction time as would have been expected if task difficulty were significantly affecting the results. Thus the present parietal P300 latency finding is unlikely to have been fully accounted for by task difficulty.

The P300 latency difference may be argued to have resulted from the emphasis participants placed on speed versus accuracy in responding to the target stimuli. In normal volunteers P300 latency has been noted to become shorter when speed is stressed over accuracy in task performance (Pfefferbaum, Ford, Johnson, Wenegrat, & Kopell, 1983). The studies in which OCD patients were observed to have shorter P300 latency did not provide participants with instructions with regard to speed and accuracy. In contrast, in the present experiment participants were encouraged to respond quickly while trying not to make any errors. This instruction did not preclude individual participants from adopting a particular response strategy emphasizing speed over accuracy or vice-versa. Indeed, ratings made by participants after each test block indicated that both groups placed significantly more emphasis on accuracy than speed. Nevertheless, no group difference in the emphasis on speed versus accuracy was observed. It is thus unlikely that the P300 latency finding could have been accounted for by a differential emphasis on speed versus accuracy between the groups.

Only a single previous study has reported reduced P300 latency over the right parietal region in OCD. This may have been in part due to the failure to test for or report P300 latency data for electrodes over the parietal regions (Malloy et al., 1989; Morault et al., 1997; Towey et al., 1990, 1994), and the use of predominantly auditory rather than visual target detection tasks (Morault et al., 1997, 1998; Oades, Zerbin, Dittmann-Balcar, & Eggers, 1996; Towey et al., 1990). When visual stimuli were used P300 latency was found to be shorter for OCD patients at both P3 and P4 electrodes (Beech et al., 1983).

Research has indicated differential hemispheric asymmetries for the visual and auditory P300 (Gevins, Schaffer, Doyle, Cutillo, Tannehill, & Bressler, 1983; Tenke, Bruder, Towey, Leite, & Sidtis, 1993). Hemispheric asymmetry of P300 latency to either target or non-target stimuli has not been found when normal control participants perform a visual target detection task with their dominant right hand (Alexander et al., 1995). That P300 latency was observed to be shorter over the right parietal region for OCD patients when responding with their right but not left hand may therefore implicate a dysregulation of the cognitive processes underlying the parietal P300 that may be specific to visual stimuli. Although scalp recorded ERPs have not allowed for the localization of this disturbance, evidence from research employing patients with acquired brain lesions has suggested a significant contribution from the parietal cortex to the parietal P300 (Johnson, 1989; Knight, Scabini, Woods, & Clayworth, 1989). Involvement of the parietal lobe in OCD is consistent with neuropsychological evidence for poorer performance of OCD patients on visuospatial than verbal tasks (Otto, 1992). Direct comparison of P300 elicited during auditory and visual go/nogo tasks would be helpful in evaluating whether the present finding is modality specific. Employing functional neuroimaging to evaluate right parietal lobe metabolism during the performance of a visual go/nogo task may be helpful in determining the integrity of this brain region in OCD.

In addition to P300, group differences were observed for N100 and N200 latency. The normal control group was found to have shorter N100 latency at the left parietal than left central or frontal electrode sites across stimulus types. This effect was not observed in the OCD group. The N1 observed in the present experiment was distributed

maximally over the lateral parietal regions. This distribution suggested that the N1 was unlikely to have been the same as the selective attention related N100 given that the latter has a frontocentral distribution (Näätänen, 1992). N100 with a posterior distribution has been observed in a number of studies employing visual stimuli and has been suggested to represent activity in the cortical pathways "projecting from the striate cortex to the parietal lobe and encoding spatial aspects of visual information" (Mangun, 1995). This interpretation appeared to be consistent with the significant amount of visuospatial information contained within the stimuli employed in the present experiment (i.e., direction of motor response indicated by arrows, discrimination between ovals and circles). The present topographic findings therefore suggested that the normal controls may have recruited the posterior cortical pathways more efficiently than the patients in order to encode the visual stimuli. The failure to find group differences in the latency of the N100 at the posterior sites suggested that the groups did not differ in how rapidly the encoding process was carried out. In addition, that the present finding was only observed for the right hand suggested that it could not be accounted for by potential group differences in pupil dilation during task performance.

There are several potential explanations for the failure of other ERP studies of OCD to have observed posterior N100 latency differences: First, the majority of the studies employed auditory target detection tasks, thus not allowing for an evaluation of the posterior N100 related to visuospatial processing; Second, studies that have employed visual stimuli have either not reported data for the N100 (Beech et al., 1983; Ciesielski et al., 1981) or used stimuli that are likely to have placed relatively limited demands on visuospatial processing (Savage, Weilburg, Duffy, Baer, Shera, & Jenike, 1994); Third,

Savage et al. (1994) failed to observe differences in visual N100 to brief high frequency stroboscopic light flashes but the stimuli were administered while the participant's eyes were closed, thus precluding the appearance of the posterior N100; Fourth, Malloy et al.'s (1989) visual go/nogo stimuli consisted of the words "go" and "stop". These stimuli may not have placed sufficient demands on visuospatial information processing in order to yield a posterior N100 effect. That stimulus complexity may be a particularly salient factor in eliciting posterior N100 differences between OCD and normal controls is consistent with the importance on these experimental factors in previous studies of OCD (Beech et al., 1983; Morault et al., 1997; Towey et al., 1990).

The functional significance of the posterior N100 latency finding has remained unclear given the structure of the task and the lack of investigations that may provide supportive or disconfirming evidence. Nevertheless, evidence of poor performance in OCD on behavioral tasks that place significant demands on the processing of visuospatial information (Otto, 1992; Tallis, 1997) indicated that further investigation is warranted. ERP studies of OCD using visual stimuli varying in complexity would likely be useful in determining the replicability and functional significance of the posterior N100 finding in OCD. Nevertheless, the limited sample size available for group comparison on the N100 indicated that any conclusions based on the present findings must be tempered.

In addition to the N100 and P300, N200 latency was observed to be shorter across lateral electrode sites when responding to nogo than go stimuli with the left hand in the OCD. This effect was not observed for the control group. Decreased N200 latency in

OCD has been observed in a number of studies regardless of whether stimuli were presented in the auditory or visual modality (Ciesielski et al., 1981; Miyata et al., 1998; Morault et al., 1997; Tower et al., 1990).

Shorter N200 and P300 latency in OCD have both been observed as an increase in latency with increasing task difficulty or stimulus complexity in normal controls, but no significant change or reduced latency to these task parameters in patient groups (Towey, 1990). Shorter N200 latency for OCD as compared to normal controls and patients with social phobia have also been noted (Beech et al., 1983; Ciesielski et al., 1981; Miyata, 1998). Shorter N200 and P300 latencies has usually been interpreted as reflecting cortical hyperarousal during difficult or complex tasks. This interpretation did not appear to be readily applicable to the present finding in light of the arguments present above for P300 latency.

Shorter N200 latency for the nogo than go stimulus in OCD may have reflected differences in attention processes. Towey et al. (1994) have observed shorter latency and larger amplitude of the processing negativity in OCD, an ERP component enhanced during focused attention. The processing negativity overlapped the latency range of the N200. They therefore argued that previous findings for the N200 may have in part been due to hyperattentivenes. Towey et al. (1994) did not however report data for N200 latency. It thus remains unclear whether shorter N200 latency may have been accounted for by overlap of the processing negativity. Further investigation employing manipulations of selective attention to go and nogo stimuli would be useful in determining the influence of attention focus on N200 go/nogo differences between OCD patients and normal control participants.

Other functional interpretations of the N200 provided alternative explanations for the present findings. Scalp topography of N200 amplitude in the current study demonstrated a more frontal and parietal distribution for the nogo stimulus at both midline and lateral electrode sites. Go N200 had a more parietal distribution. Nogo N200 has been observed to have a widespread distribution over bilateral frontal and parietal regions, irrespective of which hand was used to respond (Sasaki, 1995). The essentially frontal distribution of nogo N200 has led several authors to suggest that the nogo N200 may reflect the inhibition of inappropriate response tendencies (Gemba & Sasaki, 1989; Jodo & Kayama, 1992, Kiefer, Marzinzik, Weisbrod, Scherg, & Spitzer, 1998; Kopp, Mattler, Goaertz, & Rist, 1996; Naito & Matsumura, 1994; Pfefferbaum et al., 1985; Sasaki, Gemba, Nambu, & Matsuzaki, 1993). Shorter nogo than go N200 latency observed for the OCD group in the present experiment may therefore reflect hyperactivation in the speed of mechanisms involved in the inhibition of inappropriate response tendencies of the non-dominant left hand.

It is plausible that such hyperactivation in OCD patients was due to the patients perceiving themselves as having a greater tendency to respond inappropriately with the non-dominant left hand during nogo trials, thus resulting in a more rapid application of inhibitory mechanisms. That the problem may be primarily one of inaccurate monitoring of self-generated actions rather than a deficit in inhibitory control was suggested by the lack of group differences in false alarm rate or amplitude of the N200 and P300. This interpretation is consistent with evidence that OCD patients have difficulty judging the accuracy of their responses during behavioral tasks despite performance that did not differ from normal controls (Foa, Amir, Gershuny, Molnar, & Kozak, 1997; MacDonald,

Antony, MacCleod, & Richter, 1997; McNally & Kohlbeck, 1993). That perceptual influences may have played a role in the present findings is also consistent with evidence suggesting that N200 may reflect decision making processes (Näätänen, 1992).

Further research may evaluate this hypothesis by having participants rate the degree to which they believe they have successfully inhibited any tendency to respond to nogo stimuli to obtain from them a subjective estimate of their perceived accuracy. Such ratings have been used to demonstrate dissociation between task performance and confidence of accuracy in studies of OCD (Foa et al., 1997; MacDonald et al., 1997). If the shorter nogo N200 latency in OCD is related to a misperception of the engagement or actual production of erroneous responses, then a significant correlation should be observed between N200 latency and confidence in inhibitory control with decreasing confidence related to shorter latency. In addition, measuring the activity of forearm flexor muscles during the performance of the go/nogo task would provide evidence of partial responses to the nogo stimulus in the absence of overt failures to inhibit responding (Coles, Scheffers, & Fournier, 1995). Recording such myogenic responses would allow the determination of whether OCD patients actually have a greater tendency to activate incorrect responses. If nogo N200 latency is only shorter when such myogenic activity is present then the component is likely to reflect the rapid initiation of inhibitory control rather than a misperception of a greater tendency towards erroneous responding because an actual incorrect response was in fact initiated. In contrast, if N200 latency is shorter irrespective of myogenic activity then the component is more to likely to be reflecting faulty perception.

In summary, experiment II did not yield any firm conclusions with regard to the status of inhibitory mechanisms in OCD. There is as yet limited understanding of the aspects of inhibitory control reflected by the N200 and P300, although many authors have argued that both components reflect some aspect of response inhibition. It is thus plausible that OCD may be associated with disturbances of some but not other aspects of inhibitory control such as detection of erroneous response tendencies, initiation or termination of response inhibition. Further investigations will therefore be required in order to clarify the integrity of inhibitory control in OCD. Nevertheless, the present ERP findings revealed shorter component latencies related to task parameters within the OCD group is consistent with most of the ERP literature on the disorder. This observation contrasted with research on other psychiatric disorders that have largely observed shorter or no difference from normal controls. Shorter ERP latencies thus appear to have some specificity for OCD and may be considered as a candidate biological marker for the disorder. Research investigating ERP latencies in populations that may be at risk for developing OCD may therefore be fruitful. The possibility that OCD involves inaccurate monitoring of self-generated actions rather than a deficit in inhibitory control was raised in the present experiment. Previous research has observed a relationship between impoverished monitoring of actions and compulsive checking in subclinical populations (Roth & Baribeau, 1996). Studies investigating the relationship between ERPs, neuropsychological test performance or neuroimaging findings and OCD symptom subtypes in patient groups have generally not observed any significant relationships (Miyata et al., 1998; Saxena et al., 1998; Tallis, 1997). These studies, however, have relied largely on correlational analysis with relatively limited participant samples.

Further investigations employing large patient samples will be required before any firm conclusions can be drawn with respect to the salience of symptom subtype to response monitoring and brain integrity in OCD.

General Summary and Discussion

Several authors have hypothesized that OCD is associated with a disturbance of executive functions, and/or the purported frontal lobe systems subserving these functions (Baxter et al., 1987; Flor-Henry et al., 1979; Malloy, 1987; Rosenberg & Keshavan, 1998). The present investigation employed a converging methods approach to evaluate this hypothesis. In experiment I outpatients with OCD and normal controls completed a battery of clinical neuropsychological tests. In experiment II outpatients with OCD and normal control participants completed a visual go/nogo task while ERPs associated with response inhibition were recorded. Attempts were made to address a number of statistical and methodological limitations of previous studies.

Results of experiment I did not reveal any significant difference between the OCD and normal control groups observed on neuropsychological tests that place strong demands on executive functions. Poorer language ability in the OCD group in the context of overall adequate functioning was observed. The latter finding may have been in part due to subtle disturbances in other cognitive functions. This was suggested because partialling out the effects of other domains of functioning from the Language composite using Chapman and Chapman's (1989) standardized residualized score method failed to reveal any differential impairment in the Language composite relative to the other domains.

Evaluation of the P300 ERP associated with response inhibition during performance of a go/nogo task also failed to provide strong support for the executive function hypothesis. In contrast, within-group analyses revealed that only the normal control group had shorter posterior N100 latency. This finding suggested that OCD may be characterized by less efficient recruitment of posterior cortical pathways involved in the encoding of visual stimuli. Consistent with previous research, the OCD group demonstrated shorter N200 and P300 latencies related to task parameters. The functional significance of the N200 and P300 findings remained unclear, but were hypothesized to reflect disturbances in the monitoring of self-generated actions and dysregulation of stimulus evaluation processes, respectively. Finally, unmedicated OCD patients demonstrated larger P300 amplitude to go than nogo stimuli. This finding suggested that the present group of unmedicated patients may have been composed largely of individuals who would show a positive response to treatment with selective serotonin reuptake inhibitors.

Nevertheless, a number of findings indicated that there may be subtle executive dysfunction in OCD. On the individual neuropsychological tests all comparisons were non-significant. A trend was observed, however, for the OCD group to perform worse than controls on a word fluency task. Preventing repetition of words during this task requires expressive speech skills as well as mental flexibility and response monitoring. In the present ERP experiment, the OCD group was observed to have Shorter N200 latency for the nogo than go stimulus in OCD. One plausible interpretation of this finding was that patients with OCD have difficulty monitoring their actions and therefore may hyperactivate response inhibition mechanisms. Thus results of both the

neuropsychological and ERP experiments appear to implicate dysfunctional response monitoring in OCD. It should be noted however that this interpretation is quite speculative as the exact cognitive mechanisms involved in adequate performance of word fluency and go/nogo tasks have yet to be fully elucidated. In addition, the relationship between the present neuropsychological and ERP data could not be statistically evaluated because of the relatively modest sample sizes and the use of somewhat different participants to comprise the patient and control groups in experiment I and II. Further study of larger samples using the convergent methods approach would be helpful in clarifying this relationship.

Neither the neuropsychological nor the ERP findings could readily be accounted for by demographic characteristics, affective variables or the inclusion of patients with secondary affective disorders. Separation of the patient samples based on the presence or absence of a secondary diagnosis resulted in relatively limited sample sizes. Any firm conclusions with regards to the influence of secondary diagnoses on neuropsychological test performance or response inhibition as measures in the present experiment must therefore be tempered. Further investigation of larger samples of OCD patients with and without secondary affective disorders may prove fruitful. Grouping OCD patients based on the presence of specific affective disorders prior to evaluation of executive or other cognitive functions also appears warranted. This suggestion arose given previous research demonstrating impoverished executive functions in patients with primary depression and social phobia but not those with panic disorder. Thus the potential impact of having a secondary diagnosis on cognitive functioning in OCD may be in part related to the specific secondary diagnosis present.

The failure to find strong and consistent evidence for a disturbance of executive functions in OCD may be related to clinical characteristics other than the presence or absence of affective disorder. Previous research has observed poorer performance on an executive function task in OCD patients that were judged to be more psychotic (Malloy, 1987). There is a relatively consistent association between impoverished executive functions and disorders within the schizophrenia-spectrum. It is plausible that the failure to observe convincing evidence of impoverished executive functions in the present investigation may have been due to the exclusion of patients with obvious psychotic symptoms. It is unclear from the Malloy et al. study, however, whether the OCD patients were psychotic or had limited insight into their illness. Distinguishing between poor insight and delusions has been noted to be difficult (Kozak & Foa, 1994). There has been no study to date investigating the relationship between insight or psychotic symptoms and measures of cognitive functioning in OCD. Nevertheless, a growing body of evidence has linked poor insight with impoverished executive functions in disorders such as schizophrenia (Mohamed, Fleming, Penn, & Spaulding, 1999). It is therefore plausible that the patients included in the present investigation had relatively good insight. This may have in part accounted for the failure to observe executive function disturbance. We are currently conducting an investigation to evaluate executive functions in OCD patients with varying levels of insight into their illness.

As with secondary diagnoses, the separation of the OCD groups into medicated and unmedicated subsamples resulted in relatively small sample sizes. Thus any firm conclusions with regards to the effects of medication status on the neuropsychological and ERP findings must be tempered. Evaluating the effects of medication status on

executive functions may, however, be best served by the use of a double-blind placebo controlled design. This design would permit a more valid evaluation of changes in cognitive functioning following the administration of placebo or medication by using each participant as his/her own baseline. Such a study is likely to be limited however by the limited number of neuropsychological tests and lack of ERP tasks/components with good test-retest reliability. Thus until tests with adequate psychometric properties are developed further research comparing larger samples of unmedicated and medicated patients is suggested.

I am currently conducting a meta-analysis of the neuropsychological literature on OCD. Meta-analysis may be conducted in order to address theoretical issues, experiemental issues or both. Meta-analysis will provide a statistical assessment of the strength of differences between OCD patients and normal controls across the large number of neuropsychological studies and tests employed. It is expected that this will aid in the identification of domains of functioning that may be particularly disturbed in OCD. Meta-analytic techniques designed to evaluate the potential impact of moderator variables (e.g., demographics, comorbidity, medication status) on neuropsychological test performance in OCD will also be employed (Hedges & Olkin, 1985). It is expected that this latter use of meta-analysis will help identify variables that may have played a particularly salient role in contributing to inconsistencies in the neuropsychological literature on OCD.

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APPENDIX A

Consent form for patients and normal controls

Consent form for patients:

PROJET SUR LES TROUBLES ANXIEUX

Centre De Recherche Fernand Seguin

FORMULAIRE DE CONSENTEMENT

Dans ce programme de recherche, nous évaluons les fonctions cognitives chez des personnes souffrant de troubles d'anxiété afin de mieux comprendre la ou les causes de ces troubles.

(Nom; S.V.P. imprimé) _____,

J'accepte de participer à un programme de recherche dirigé par Jacinthe Baribeau. Ph.D. et Robert M. Roth, M.A. du Centre Ferand Seguin de l'Hôpital Louis-H. Lafontaine et du département de psychologie de l'Université Concordia. Le programme requiert que je vienne au Centre Fernand Seguin deux fois à l'intérieur d'un période de deux semaines.

Dans la première session je complèterai une série de tests neuropsychologiques. Ces tests sont des évaluations de plusieurs fonctions cognitives telles que la mémoire, l'attention et la capacité de planifier des réponses. Cette rencontre durera 2 1/2 heurs.

La deuxième session d'évaluation inclut l'enregistrement de potentiels évoqués utilisant la technique standardisée de l'électroencéphalogramme (EEG) telle que pratiquée a l'hôpital. Des capteurs métalliques seront attachés sur mon cuir chevelu, sur le nez, et

quatre autour des sourcils et de la joue. Il n'y a aucune douleur associée à cette procédure sinon un léger inconfort. Je complèterai plusieurs tâches, telle que presser un bouton chaque fois qu'un symbole me sera présenté sur un écran d'ordinateur et pendant la pésentation de sons par des écouteurs. Ce rencontre durera 2 1/2 heurs.

Au début de chacune de ces deux recontres je compléterai quelques brefs questionnaires sur mon état émotionnel. Aussi, on me remettra une enveloppe contenant des questionnaires que je compléterai et remettrai au deuxième rencontre. Ces questionnaires concernent: (1) des informations démographiques (e.g., mon âge, mon histoire personelle et familiale de maladie), (2) un questionnaire sur des problemes spécifiques tels que les obsessions-compulsions, et (3) l'inventaire TCI qui contient des questions concernant mes croyances, attitudes et expériences.

Je comprends que je suis libre d'interrompre ma collaboration à n'importe quel moment, quelle que soit la raison, sans conséquence négative, avec l'entente que les données déjà accumulées pourront être utilisées en toute confidentialité, pour des fins de recherche scientifique. De la retroaction sur ma performance pourra être donnée à mes thérapeutes sur demande **seulement et seulement avec ma permission**.

Je vais recevoir $20 pour avoir compléter les questionnaires et les deux sessions d'évaluations.

On me promet que mon dossier sera strictement confidentiel et que seules les personnes impliquées dans ce projet y auront accès. Je suis libre de participer à ce programme.

Je déclare qu'on m'a expliqué, et je comprends la procédure et les raisons de cette étude.

Signature:

Nom du participant: _____

Nom du moniteur: _____

Date: A _____ M _____ J _____

Consent form for normal controls:

PROJET SUR LES TROUBLES ANXIEUX

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FORMULAIRE DE CONSENTEMENT

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Dans la première session je complèterai une série de tests neuropsychologiques. Ces tests sont des évaluations de plusieurs fonctions cognitives telles que la mémoire, l'attention et la capacité de planifier des réponses. Cette rencontre durera 2 1/2 heurs.

La deuxième session d'évaluation inclut l'enregistrement de potentiels évoqués utilisant la technique standardisée de l'électroencéphalogramme (EEG) telle que pratiquée a l'hôpital. Des capteurs métalliques seront attachés sur mon cuir chevelu, sur le nez, et

quatre autour des sourcils et de la joue. Il n'y a aucune douleur associée à cette procédure sinon un léger inconfort. Je complèterai plusieurs tâches, telle que presser un bouton chaque fois qu'un symbole me sera présenté sur un écran d'ordinateur et pendant la pésentation de sons par des écouteurs. Ce rencontre durera 2 1/2 heurs.

Au début de chacune de ces deux recontres je compléterai quelques brefs questionnaires sur mon état émotionnel. Aussi, on me remettra une enveloppe contenant des questionnaires que je compléterai et remettrai au deuxième rencontre. Ces questionnaires concernent: (1) des informations démographiques (e.g., mon âge, mon histoire personelle et familiale de maladie), (2) des questionnaires sur des problemes spécifiques tels que les obsessions-compulsions, et (3) l'inventaire TCI qui contient des questions concernant mes croyances, attitudes et expériences.

Je comprends que je suis libre d'interrompre ma collaboration à n'importe quel moment, quelle que soit la raison, sans conséquence négative, avec l'entente que les données déjà accumulées pourront être utilisées en toute confidentialité, pour des fins de recherche scientifique.

Je vais recevoir $20 pour avoir compléter les questionnaires et les deux sessions d'évaluations.

On me promet que mon dossier sera strictement confidentiel et que seules les personnes impliquées dans ce projet y auront accès. Je suis libre de participer à ce programme.

Je déclare qu'on m'a expliqué, et je comprends la procédure et les raisons de cette étude.

Signature:

Nom du participant: _____

Nom du moniteur: _____

Date: A _____ M _____ J _____

APPENDIX B

Add for recruitment of normal controls.

Volontaires demandés pour recherche en psychologie

Centre de Recherche Fernand Seguin

Nous recrutons des volontaires ne présentant pas de désordres mentaux ou physiques, âgés entre 20 et 55 ans, pour participer dans un projet de recherche en psychologie. Les évaluations ne comportent aucun risque connu pour la santé physique et mentale. Votre participation sera rémunérée. Pour plus d'information, laissez votre nom et numéro de téléphone au 251-4015 (extension 2341).

APPENDIX C

Telephone Screen.

LABORATOIRE DE NEUROPSYCHOLOGIE

CENTRE FERNARD SEGUIN

QUESTONNAIRE D'INFORMATION POUR SUJET CONTROLE

POUR LE PROJECT TOC

COURT ENTRETIEN TÉLÉPHONIQUE

"Merci d'avoir appelez pour être bénévole dans notre étude. J'aimerais premièrement vous décrire de quoi consistera votre participation, si vous êtes d'accord pour participer. Après, si vous êtes encore intéressés, je vous poserais quelques questions pour vérifier si vous qualifiez pour participer.

Il y a différents types de tâches dans notre étude: compléter des questionnaires. compléter des tâches psychologiques visant à observer des choses comme la mémoire et l'attention. Par exemple, je pourrais vous raconter une courte histoire et ensuite vous demander de vous rappeler de quoi parlait l'histoire. D'autres tâches demanderont l'enregistrement de l'activité du cerveau à l'aide d'un électroencéphalogramme ou EEG. Le EEG est utilisé de façon routinière dans les hôpitaux, et est sans douleur. Pour enregistrer l'activité du cerveau, nous allons placer sur votre tête des capteurs métalliques remplis d'une pâte à base d'eau et de sel. Il n'y a aucune aiguille ou risque pour la santé impliqué. Les tâches neuropsychologiques et le EEG sont complétés en deux rencontres d'environ 3 heures chacunes, séparées en temps de pas plus que deux semaines. De plus,

on vous demandera de donner un échantillon de sang avant chacune des deux rencontres, ceci pris par une infirmière de l'hôpital. Vous recevrez une rémunération de $20 pour avoir compléter tout ce qu'on vous demande, à la fin de la deuxième rencontre.

Est-ce-que vous êtes intéressés? **OUI** **NON**

⇓

NON: Si l'individu indique qu'il (qu'elle) **n'est pas intéressé**, demande la question suivante:

"Comme vous n'êtes pas intéressé à participer, j'aimerais seulement vous demandez, pour nos dossiers, pour quelle raison vous n'êtes pas intéressés?" (écris mot-à-mot la réponse):

SI INTÉRESSÉS, complétez ce qui suit:

"J'ai juste besoin de vous demander quelques questions pour déterminer si vous êtes éligible pour notre étude. L'information que vous fournirez sera gardée strictement confidentielle par notre équipe de recherche."

Date d'aujourd'hui J____ M____ A_____

Nom de famille:_____

Prénom: _____

Genre: M F Main utilisée pour écrire: Droite____ Gauche____

Les deux____

Numéros de téléphone: Travail ( ) _____

Maison ( )_____

Meilleurs temps pour vous atteindre: _____.

1. Souffrez-vous présentement de n'importe quelle maladie médicale (e.g., diabète, cancer?)

Oui_____ Non_____

2. Avez-vous, dans le passé souffert de telles maladies (e.g., diabète, cancer?)

Oui_____ Non_____

3. Souffrez-vous présentement de n'importe quel problème psychologique qui nuit significativement à votre habileté à poursuivre vos activités quotidiennes, ou pour lequel vous prenez des médicaments ou voyez un thérapeute? Oui_____ Non_____

4. Avez-vous, dans le passé souffert de n'importe quel problème psychologique qui a significativement nuit à votre habileté à poursuivre vos activités quotidiennes, ou pour lequel vous avez pris des médicaments ou avez vu un thérapeute? Oui_____ Non_____

5. Avez-vous déjà eu un coup à la tête qui a résulté dans une perte de conscience?

Oui_____Non_____

6. Est-ce que vous prenez présentement, ou avez vous consommé dans la dernière année des drogues telles que la marijuana, le cocaine, ou LSD? Oui_____ Non_____

7. Est-ce que vous avez déja eu des problèmes reliés à votre consommation d'alcool, tel qu'une visite à un hôpital, conduire saoûl, être dans une bagarre après avoir bu?

Oui ____ Non____

8. Membres de famille avec problèmes psychologiques? Oui____Non____

9. Prenez-vous présentement n'importe quelle médicament Oui____Non____

10. Intéresser à participer dans autres études Oui____Non____

Si la personne a répondu NON à toutes les questions précédentes:

"D'après ce que vous m'avez dit, vous semblez qualifiés pour participer à l'étude. Un membre de notre équipe de recherche vous appelera aussi tôt que possible pour schéduler la première rencontre, qui va comprendre une prise de sang, et des tâches neuropsychologiques. Toutes les rencontres se tiendront au Centre Fernand Seguin, 7331 rue Hochelaga.

Si la personne a répondu OUI à n'importe quelle des questions précédentes:

"D'après ce que vous m'avez dit, vous ne remplissez pas les conditions nécessaires pour participer à l'étude que nous sommes en train de faire. Néanmoins, nous allons conserver votre nom au cas où il y aurait une étude pour laquelle votre participation serait grandement appréciée. Merci tout de même d'avoir appelé."

Si il y a détresse exprimée, la ressource à contacter est Kieron O'Connor.

APPENDIX D

Description of neuropsychological tests.

Executive functions

Wisconsin Card Sorting Task (WCST; Heaton, Chelune, Talley, Kay, & Curtis, 1993). Four stimulus cards are used, the first with a red triangle, the second with two green stars, the third with three yellow crosses, and the fourth with four blue circles. Participants are given two packs of sixty-four response cards with designs similar to the stimulus cards, and varying in color, geometric form, and number of forms. Participants are required to match each of the response cards to one of the four stimulus cards. Feedback is provided each time as to whether the participant is right or wrong. No other information is provided. The category (color, form, number) to which sorting cards is correct is changes after each series of ten consecutive correct sorts. The participant is not informed of the change in the category he/she must sort to. A persevertive error is scored when sorting to the previously correct category persists.

Self-Ordered Pointing task (Petrides & Milner, 1982). In the self-ordered pointing test a set of twelve designs are arranged in different layouts on twelve pages. Participants are required to point to a different design on each page and avoid selecting any of the designs more than once. Participants must also avoid selecting designs at a specific location on the 4 X 3 design grid more than two pages in a row. The abstract designs version of the task was employed. Perseverative errors occurred when participants selected an item more than once on a given trial or selected designs at the same location more than two pages in a row.

Trail Making Test trial B (Reitan & Wolfson, 1985). Participants are first required to connect, using a pen, in ascending order twenty-five encircled numbers randomly arranged on a page (trial A). They must then encircle twenty-five numbers and twenty-five letters in alternating order (trial B). Participants must complete these tasks as quickly as possible while avoiding making mistakes. The time taken to complete part B is employed as a measure of mental flexibility.

Verbal memory

Logical Memory subtest of the Wechsler Memory Scale-Revised (Wechsler, 1987). Participants are read two prose passages and are subsequently required to recall as many details of the story as possible. Recall is assessed immediately after presentation and again after a thirty-minute delay.

Rey Auditory-Verbal Learning Test (RAVLT; Lezak, 1995). Participants are read a list of fifteen unrelated words which they must recall in any order. The list is repeated a total of five times with recall being assessed after each presentation of the list. Participants are then asked to recall a new list of words, followed a recall of the first word list. Recall of the first list is again assessed after a twenty-minute delay.

Nonverbal memory

WMS-R Visual Reproduction thirty minute delayed recall score (Wechsler, 1987). Participants are presented with four stimulus cards on each of which are abstract geometric designs. Participants are given ten seconds to observe each stimulus card after which they must immediately reproduce the designs from memory. Recall of the designs is also assessed after a thirty-minute delay.

Rey-Osterreith Complex Figure thirty minute delayed recall score (Osterreith, 1944). Participants are presented with a complex geometric design and are required to reproduce it. The stimulus remains in view while it is copied. Recall of the design is again assessed after a thirty-minute delay.

Language

Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983). Participants are presented with a series of sixty pages on each of which is one representational design (e.g., a beaver). Participants must name each of the designs. If after twenty-seconds they are unable to name the design a phonetic cue is provided (e.g., "bea" for beaver). If the participant produces a response that appears to suggest a misperception of the object (e.g., wig for beaver) a stimulus cue is provided (e.g., "its an animal"). The total score is calculated as the total number of spontaneously produced correct responses plus the correct responses following a phonetic cue.

Controlled Oral Word Fluency (Spreen & Strauss, 1998). Participants are asked to generate orally as many words as they can that begins with a given letter in one minute. The most commonly employed letters (F, A, S) were used in the present study.

Participants are instructed that proper names, repetition of words, and production of multiple words with the same root (e.g., walks, walk, walking) are not permitted. The total score is the number of correct words produced for the three letters.

Visuospatial

Hooper Visual Organization Test (VOT; Hooper, 1958). Participants are presented with thirty drawings of common objects. Each object is cut into two or more pieces and randomly arranged on the stimulus page. Participants must conceptually rearrange the pieces in order to name the object. Performance on the task is, however, relatively independent of confrontational naming ability (Ricker & Axelrod, 1995). The total score is the number of objects correctly identified.

Block Design subtest of the WAIS-R (WAIS-R; Wechsler, 1981). Participants are presented with either four or nine red and white blocks. The blocks are used to construct replicas of a model design made either by the examiner or printed on stimulus cards. The task is timed with bonus points being awarded for correct designs produced within pre-specified time intervals.

Motor Abilities

Hand Dynamometer (Reitan & Davison, 1974). Participants are required to squeeze a strain gauge alternately with their left and right hands. A practice trial is followed by two test trials for each hand. A third trial is administered if the scores for the two test trials for a given hand exceeds 5 kg. The total score is the average of the two test trials.

Purdue Pegboard (Tiffin, 1968). Participants are required to place as many pegs as they can, one at a time, into a column of holes, first with their preferred then non-preferred hand. Three trials, each lasting thirty-seconds, are conducted with each hand. The total score is the average across the three trials for each hand.

APPENDIX E

Time and Group X Time Interactions.

Effect	F	df	p
N100 latency at lateral electrodes			
Time	0.02	1, 17	.888
Group X Time	0.23	1, 17	.635
N100 amplitude at lateral electrodes			
Time	0.87	1, 17	.363
Group X Time	10.80	1, 17	.004
N100 latency at midline electrodes			
Time	0.03	1, 16	.872
Group X Time	0.12	1, 16	.737
N100 amplitude at midline electrodes			
Time	0.15	1, 16	.700
Group X Time	3.31	1, 16	.087
N200 latency at lateral electrodes			
Time	0.64	1, 15	.437
Group X Time	0.19	1, 15	.187
N200 amplitude at lateral electrodes			
Time	0.89	1, 15	.361
Group X Time	0.03	1, 15	.606
N200 latency at midline electrodes			
Time	1.07	1, 19	.314
Group X Time	2.21	1, 19	.154
N200 amplitude at midline electrodes			
Time	1.31	1, 19	.267
Group X Time	0.20	1, 19	.661
P300 latency at lateral electrodes			
Time	12.67	1, 30	.001
Group X Time	0.03	1, 30	.858
P300 amplitude at lateral electrodes			
Time	31.63	1, 30	.001
Group X Time	0.55	1, 30	.463
P300 latency at midline electrodes			
Time	12.41	1, 30	.001
Group X Time	0.19	1, 30	.669
P300 amplitude at midline electrodes			
Time	32.36	1, 30	.001
Group X Time	0.66	1, 30	.422

APPENDIX F

ANOVA tables for ERPs.

ANOVA table for N100 Latency at Lateral Electrodes

Effect	F	df	p
One-Way:			
Stimulus	0.57	1, 19	.460
Hand	0.00	1, 19	.967
Anterior/Posterior Axis	11.89	2, 38	.001
Laterality	0.72	1, 19	.408
Group	0.00	1, 19	.955
Two-Way:			
Stimulus X Hand	0.40	1, 19	.534
Stimulus X Anterior/Posterior Axis	4.48	2, 38	.022
Stimulus X Laterality	0.61	1, 19	.443
Stimulus X Group	0.48	1, 19	.497
Hand X Anterior/Posterior Axis	0.82	2, 38	.437
Hand X Laterality	0.68	1, 19	.420
Hand X Group	0.67	1, 19	.423
Anterior/Posterior Axis X Laterality	0.07	2, 38	.914
Anterior/Posterior Axis X Group	0.69	2, 38	.458
Laterality X Group	1.24	1, 19	.279
Three-Way:			
Stimulus X Hand X Anterior/Posterior Axis	0.12	2, 38	.878
Stimulus X Hand X Laterality	1.27	1, 19	.274
Stimulus X Hand X Group	1.78	1, 19	.199
Stimulus X Anterior/Posterior Axis X Laterality	0.99	2, 38	.382
Stimulus X Anterior/Posterior Axis X Group	2.32	2, 38	.119
Stimulus X Laterality X Group	1.84	1, 19	.191
Hand X Anterior/Posterior Axis X Laterality	1.64	2, 38	.208
Hand X Anterior/Posterior Axis X Group	1.11	2, 38	.337
Hand X Laterality X Group	0.80	1, 19	.383
Anterior/Posterior Axis X Laterality X Group	1.35	2, 38	.272
Four-Way:			
Stimulus X Hand X Anterior/Posterior Axis X Laterality	0.34	2, 38	.695
Stimulus X Hand X Anterior/Posterior Axis X Group	0.03	2, 38	.967
Stimulus X Hand X Laterality X Group	4.61	1, 19	.045
Stimulus X Anterior/Posterior Axis X Laterality X Group	0.27	2, 38	.763
Hand X Anterior/Posterior Axis X Laterality X Group	5.67	2, 38	.007
Five-Way:			
Stimulus X Hand X Ant./Posterior X Laterality X Group	1.18	2, 38	.315

ANOVA table for N100 Amplitude at Lateral Electrodes

Effect	F	df	p
One-Way:			
Stimulus	0.15	1, 19	.703
Hand	0.10	1, 19	.754
Anterior/Posterior Axis	34.89	2, 38	.001
Laterality	2.02	1, 19	.172
Group	1.46	1, 19	.241
Two-Way:			
Stimulus X Hand	0.04	1, 19	.852
Stimulus X Anterior/Posterior Axis	3.62	2, 38	.046
Stimulus X Laterality	0.01	1, 19	.917
Stimulus X Group	0.81	1, 19	.379
Hand X Anterior/Posterior Axis	3.92	2, 38	.041
Hand X Laterality	1.10	1, 19	.308
Hand X Group	0.79	1, 19	.384
Anterior/Posterior Axis X Laterality	1.53	2, 38	.631
Anterior/Posterior Axis X Group	2.81	2, 38	.100
Laterality X Group	2.35	1, 19	.142
Three-Way:			
Stimulus X Hand X Anterior/Posterior Axis	0.04	2, 38	.928
Stimulus X Hand X Laterality	1.95	1, 19	.179
Stimulus X Hand X Group	0.10	1, 19	.752
Stimulus X Anterior/Posterior Axis X Laterality	2.27	2, 38	.126
Stimulus X Anterior/Posterior Axis X Group	0.64	2, 38	.507
Stimulus X Laterality X Group	0.03	1, 19	.876
Hand X Anterior/Posterior Axis X Laterality	3.55	2, 38	.042
Hand X Anterior/Posterior Axis X Group	1.11	2, 38	.329
Hand X Laterality X Group	0.00	1, 19	.996
Anterior/Posterior Axis X Laterality X Group			
Four-Way:			
Stimulus X Hand X Anterior/Posterior Axis X Laterality	1.15	2, 38	.328
Stimulus X Hand X Anterior/Posterior Axis X Group	1.04	2, 38	.349
Stimulus X Hand X Laterality X Group	0.02	1, 19	.877
Stimulus X Anterior/Posterior Axis X Laterality X Group	0.24	2, 38	.759
Hand X Anterior/Posterior Axis X Laterality X Group	2.13	2, 38	.137
Five-Way:			
Stimulus X Hand X Ant./Post. Axis X Laterality X Group	0.34	2, 38	.711

ANOVA table for N200 Latency at Lateral Electrodes

Effect	F	df	p
One-Way:			
Stimulus	0.88	1, 17	.361
Hand	0.71	1, 17	.412
Anterior/Posterior Axis	0.21	2, 34	.724
Laterality	2.93	1, 17	.105
Group	1.01	1, 17	.329
Two-Way:			
Stimulus X Hand	0.37	1, 17	.551
Stimulus X Anterior/Posterior Axis	1.55	2, 34	.232
Stimulus X Laterality	1.24	1, 17	.282
Stimulus X Group	0.75	1, 17	.398
Hand X Anterior/Posterior Axis	2.77	2, 34	.083
Hand X Laterality	1.64	1, 17	.218
Hand X Group	0.01	1, 17	.923
Anterior/Posterior Axis X Laterality	4.63	2, 34	.027
Anterior/Posterior Axis X Group	1.31	2, 34	.277
Laterality X Group	0.49	1, 17	.494
Three-Way:			
Stimulus X Hand X Anterior/Posterior Axis	0.19	2, 34	.768
Stimulus X Hand X Laterality	3.13	1, 17	.095
Stimulus X Hand X Group	4.38	1, 17	.052
Stimulus X Anterior/Posterior Axis X Laterality	3.15	2, 34	.059
Stimulus X Anterior/Posterior Axis X Group	0.22	2, 34	.745
Stimulus X Laterality X Group	0.05	1, 17	.821
Hand X Anterior/Posterior Axis X Laterality	0.70	2, 34	.456
Hand X Anterior/Posterior Axis X Group	1.88	2, 34	.173
Hand X Laterality X Group	0.98	1, 17	.336
Anterior/Posterior Axis X Laterality X Group	0.48	2, 34	.573
Four-Way:			
Stimulus X Hand X Anterior/Posterior Axis X Laterality	5.58	2, 34	.010
Stimulus X Hand X Anterior/Posterior Axis X Group	1.43	2, 34	.254
Stimulus X Hand X Laterality X Group	1.74	1, 17	.204
Stimulus X Anterior/Posterior Axis X Laterality X Group	0.13	2, 34	.863
Hand X Anterior/Posterior Axis X Laterality X Group	0.26	2, 34	.693
Five-Way:			
Stimulus X Hand X Ant./Post. Axis X Laterality X Group	1.88	2, 34	.171

ANOVA table for N200 Amplitude at Lateral Electrodes

Effect	F	df	p
One-Way:			
Stimulus	0.00	1, 18	.952
Hand	1.11	1, 18	.306
Anterior/Posterior Axis	4.35	2, 36	.043
Laterality	2.61	1, 18	.123
Group	0.10	1, 18	.759
Two-Way:			
Stimulus X Hand	2.30	1, 18	.146
Stimulus X Anterior/Posterior Axis	7.07	2, 36	.010
Stimulus X Laterality	1.45	1, 18	.244
Stimulus X Group	0.05	1, 18	.820
Hand X Anterior/Posterior Axis	3.72	2, 36	.055
Hand X Laterality	8.48	1, 18	.009
Hand X Group	0.40	1, 18	.535
Anterior/Posterior Axis X Laterality	0.72	2, 36	.453
Anterior/Posterior Axis X Group	1.52	2, 36	.235
Laterality X Group	0.00	1, 18	.998
Three-Way:			
Stimulus X Hand X Anterior/Posterior Axis	0.05	2, 36	.898
Stimulus X Hand X Laterality	2.81	1, 18	.111
Stimulus X Hand X Group	0.10	1, 18	.755
Stimulus X Anterior/Posterior Axis X Laterality	3.42	2, 36	.062
Stimulus X Anterior/Posterior Axis X Group	0.61	2, 36	.477
Stimulus X Laterality X Group	0.14	1, 18	.713
Hand X Anterior/Posterior Axis X Laterality	8.48	2, 36	.001
Hand X Anterior/Posterior Axis X Group	0.02	2, 36	.942
Hand X Laterality X Group	0.44	1, 18	.517
Anterior/Posterior Axis X Laterality X Group	0.05	2, 36	.896
Four-Way:			
Stimulus X Hand X Anterior/Posterior Axis X Laterality	3.92	2, 36	.039
Stimulus X Hand X Anterior/Posterior Axis X Group	0.84	2, 36	.410
Stimulus X Hand X Laterality X Group	0.26	1, 18	.616
Stimulus X Anterior/Posterior Axis X Laterality X Group	0.42	2, 36	.594
Hand X Anterior/Posterior Axis X Laterality X Group	3.54	2, 36	.041
Five-Way:			
Stimulus X Hand X Ant./Post. Axis X Laterality X Group	0.27	2, 36	.717

ANOVA table for P300 Latency at Lateral Electrodes

Effect	F	df	p
One-Way:			
Stimulus	0.93	1, 32	.343
Hand	2.01	1, 32	.166
Anterior/Posterior Axis	1.08	2, 64	.319
Laterality	0.11	1, 32	.746
Group	0.20	1, 32	.659
Two-Way:			
Stimulus X Hand	0.19	1, 32	.662
Stimulus X Anterior/Posterior Axis	0.56	2, 64	.571
Stimulus X Laterality	5.40	1, 32	.027
Stimulus X Group	0.96	1, 32	.336
Hand X Anterior/Posterior Axis	0.11	2, 64	.890
Hand X Laterality	9.09	1, 32	.005
Hand X Group	2.15	1, 32	.152
Anterior/Posterior Axis X Laterality	1.37	2, 64	.260
Anterior/Posterior Axis X Group	0.08	2, 64	.828
Laterality X Group	0.03	1, 32	.855
Three-Way:			
Stimulus X Hand X Anterior/Posterior Axis	0.48	1, 32	.576
Stimulus X Hand X Laterality	0.04	1, 32	.845
Stimulus X Hand X Group	1.57	1, 32	.219
Stimulus X Anterior/Posterior Axis X Laterality	0.03	2, 64	.959
Stimulus X Anterior/Posterior Axis X Group	0.64	2, 64	.527
Stimulus X Laterality X Group	0.38	1, 32	.542
Hand X Anterior/Posterior Axis X Laterality	1.45	2, 64	.241
Hand X Anterior/Posterior Axis X Group	0.98	2, 64	.379
Hand X Laterality X Group	0.00	1, 32	.963
Anterior/Posterior Axis X Laterality X Group	0.14	2, 64	.842
Four-Way:			
Stimulus X Hand X Anterior/Posterior Axis X Laterality	2.30	2, 64	.119
Stimulus X Hand X Anterior/Posterior Axis X Group	0.80	2, 64	.428
Stimulus X Hand X Laterality X Group	1.47	1, 32	.235
Stimulus X Anterior/Posterior Axis X Laterality X Group	0.40	2, 64	.639
Hand X Anterior/Posterior Axis X Laterality X Group	4.19	2, 64	.020
Five-Way:			
Stimulus X Hand X Ant./Post. Axis X Laterality X Group	1.70	2, 64	.197

ANOVA table for P300 Amplitude at Lateral Electrodes

Effect	F	df	p
One-Way:			
Stimulus	9.89	1, 32	.004
Hand	1.59	1, 32	.216
Anterior/Posterior Axis	6.64	2, 64	.006
Laterality	2.24	1, 32	.144
Group	1.41	1, 32	.244
Two-Way:			
Stimulus X Hand	0.20	1, 32	.656
Stimulus X Anterior/Posterior Axis	12.39	2, 64	.001
Stimulus X Laterality	0.00	1, 32	.995
Stimulus X Group	1.85	1, 32	.183
Hand X Anterior/Posterior Axis	2.40	2, 64	.118
Hand X Laterality	11.32	1, 32	.002
Hand X Group	0.65	1, 32	.426
Anterior/Posterior Axis X Laterality	5.10	2, 64	.019
Anterior/Posterior Axis X Group	0.37	2, 64	.629
Laterality X Group	0.01	1, 32	.934
Three-Way:			
Stimulus X Hand X Anterior/Posterior Axis	0.62	2, 64	.472
Stimulus X Hand X Laterality	12.01	1, 32	.002
Stimulus X Hand X Group	0.48	1, 32	.495
Stimulus X Anterior/Posterior Axis X Laterality	3.91	2, 64	.033
Stimulus X Anterior/Posterior Axis X Group	0.66	2, 64	.467
Stimulus X Laterality X Group	0.38	1, 32	.543
Hand X Anterior/Posterior Axis X Laterality	1.86	2, 64	.176
Hand X Anterior/Posterior Axis X Group	0.95	2, 64	.365
Hand X Laterality X Group	0.20	1, 32	.660
Anterior/Posterior Axis X Laterality X Group	2.16	2, 64	.141
Four-Way:			
Stimulus X Hand X Anterior/Posterior Axis X Laterality	3.35	2, 64	.051
Stimulus X Hand X Anterior/Posterior Axis X Group	3.43	2, 64	.062
Stimulus X Hand X Laterality X Group	0.32	1, 32	.574
Stimulus X Anterior/Posterior Axis X Laterality X Group	1.73	2, 64	.191
Hand X Anterior/Posterior Axis X Laterality X Group	0.06	2, 64	.892
Five-Way:			
Stimulus X Hand X Ant./Post. Axis X Laterality X Group	0.16	2, 64	.815

ANOVA table for N100 Latency at Midline Electrodes

Effect	F	df	p
One-Way:			
Stimulus	0.63	1, 18	.436
Hand	0.19	1, 18	.669
Anterior/Posterior Axis	0.21	2, 36	.746
Group	0.02	1, 18	.895
Two-Way:			
Stimulus X Hand	0.35	1, 18	.564
Stimulus X Anterior/Posterior Axis	0.55	2, 36	.539
Stimulus X Group	0.11	1, 18	.747
Hand X Anterior/Posterior Axis	2.89	2, 36	.081
Hand X Group	0.48	1, 18	.498
Anterior/Posterior Axis X Group	0.57	2, 36	.524
Three-Way:			
Stimulus X Hand X Anterior/Posterior Axis	2.05	2, 36	.149
Stimulus X Hand X Group	0.35	1, 18	.564
Stimulus X Anterior/Posterior Axis X Group	0.82	2, 36	.424
Hand X Anterior/Posterior Axis X Group	0.83	2, 36	.425
Four-Way:			
Stimulus X Hand X Anterior/Posterior Axis X Group	0.92	2, 36	.401

ANOVA table for N100 Amplitude at Midline Electrodes

Effect	F	df	p
One-Way:			
Stimulus	0.00	1, 18	.967
Hand	0.53	1, 18	.475
Anterior/Posterior Axis	9.07	2, 36	.005
Group	0.18	1, 18	.678
Two-Way:			
Stimulus X Hand	0.93	1, 18	.347
Stimulus X Anterior/Posterior Axis	1.59	2, 36	.224
Stimulus X Group	1.73	1, 18	.205
Hand X Anterior/Posterior Axis	2.60	2, 36	.090
Hand X Group	0.46	1, 18	.506
Anterior/Posterior Axis X Group	1.09	2, 36	.321
Three-Way:			
Stimulus X Hand X Anterior/Posterior Axis	0.05	2, 36	.930
Stimulus X Hand X Group	0.73	1, 18	.404
Stimulus X Anterior/Posterior Axis X Group	0.48	2, 36	.558
Hand X Anterior/Posterior Axis X Group	0.30	2, 36	.731
Four-Way:			
Stimulus X Hand X Anterior/Posterior Axis X Group	1.04	2, 36	.354

ANOVA table for N200 Latency at Midline Electrodes

Effect	F	df	p
One-Way:			
Stimulus	4.29	1, 21	0.51
Hand	1.40	1, 21	.250
Anterior/Posterior Axis	0.21	2, 42	.718
Group	0.84	1, 21	.368
Two-Way:			
Stimulus X Hand	0.00	1, 21	.963
Stimulus X Anterior/Posterior Axis	1.31	2, 42	.276
Stimulus X Group	1.75	1, 21	.201
Hand X Anterior/Posterior Axis	0.00	2, 42	.990
Hand X Group	0.30	1, 21	.591
Anterior/Posterior Axis X Group	0.06	2, 42	.866
Three-Way:			
Stimulus X Hand X Anterior/Posterior Axis	2.21	2, 42	.132
Stimulus X Hand X Group	0.27	1, 21	.606
Stimulus X Anterior/Posterior Axis X Group	0.15	2, 42	.785
Hand X Anterior/Posterior Axis X Group	0.42	2, 42	.577
Four-Way:			
Stimulus X Hand X Anterior/Posterior Axis X Group	0.15	2, 42	.824

ANOVA table for N200 Amplitude at Midline Electrodes

Effect	F	df	p
One-Way:			
Stimulus	0.01	1, 21	.933
Hand	0.84	1, 21	.369
Anterior/Posterior Axis	0.19	2, 42	.703
Group	0.70	1, 21	.411
Two-Way:			
Stimulus X Hand	1.32	1, 21	.263
Stimulus X Anterior/Posterior Axis	4.92	2, 42	.013
Stimulus X Group	0.02	1, 21	.902
Hand X Anterior/Posterior Axis	1.47	2, 42	.244
Hand X Group	0.04	1, 21	.836
Anterior/Posterior Axis X Group	1.30	2, 42	.271
Three-Way:			
Stimulus X Hand X Anterior/Posterior Axis	1.21	2, 42	.296
Stimulus X Hand X Group	0.10	1, 21	.752
Stimulus X Anterior/Posterior Axis X Group	0.25	2, 42	.771
Hand X Anterior/Posterior Axis X Group	0.97	2, 42	.362
Four-Way:			
Stimulus X Hand X Anterior/Posterior Axis X Group	0.07	2, 42	.861

ANOVA table for P300 Latency at Midline Electrodes

Effect	F	df	p
One-Way:			
Stimulus	0.01	1, 32	.911
Hand	0.16	1, 32	.691
Anterior/Posterior Axis	0.20	2, 64	.491
Group	0.09	1, 32	.770
Two-Way:			
Stimulus X Hand	0.71	1, 32	.404
Stimulus X Anterior/Posterior Axis	2.23	2, 64	.116
Stimulus X Group	0.92	1, 32	.345
Hand X Anterior/Posterior Axis	0.51	2, 64	.601
Hand X Group	0.25	1, 32	.619
Anterior/Posterior Axis X Group	0.72	2, 64	.491
Three-Way:			
Stimulus X Hand X Anterior/Posterior Axis	0.05	2, 64	.947
Stimulus X Hand X Group	0.70	1, 32	.411
Stimulus X Anterior/Posterior Axis X Group	0.33	2, 64	.723
Hand X Anterior/Posterior Axis X Group	0.35	2, 64	.704
Four-Way:			
Stimulus X Hand X Anterior/Posterior Axis X Group	0.04	2, 64	.962

ANOVA table for P300 Amplitude at Midline Electrodes

Effect	F	df	p
One-Way:			
Stimulus	4.87	1, 32	.035
Hand	0.24	1, 32	.629
Anterior/Posterior Axis	2.59	2, 64	.089
Group	1.78	1, 32	.191
Two-Way:			
Stimulus X Hand	0.01	1, 32	.939
Stimulus X Anterior/Posterior Axis	16.63	2, 64	.001
Stimulus X Group	1.27	1, 32	.268
Hand X Anterior/Posterior Axis	1.89	2, 64	.172
Hand X Group	0.14	1, 32	.714
Anterior/Posterior Axis X Group	0.73	2, 64	.475
Three-Way:			
Stimulus X Hand X Anterior/Posterior Axis	4.35	2, 64	.021
Stimulus X Hand X Group	0.05	1, 32	.821
Stimulus X Anterior/Posterior Axis X Group	0.67	2, 64	.485
Hand X Anterior/Posterior Axis X Group	1.87	2, 64	.175
Four-Way:			
Stimulus X Hand X Anterior/Posterior Axis X Group	0.86	2, 64	.411