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How specific are inhibitory deficits to obsessive-compulsive disorder? A neurophysiological comparison with panic disorder

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HIGHLIGHTS

- We conducted the first ERP study of inhibition in obsessive-compulsive disorder (OCD) to include an anxious comparison group.
- Surprisingly, inhibitory deficits and ERP anomalies were very similar in OCD and panic disorder, although more severe in OCD.
- Neurobiological models of OCD may overestimate the presence of OCD-specific inhibitory deficits, due to the lack of clinical comparison groups in previous studies.

ABSTRACT

Objective: Impaired inhibition may perpetuate repetitive symptoms in obsessive-compulsive disorder (OCD), however OCD-specific deficits have yet to be established. We investigated neural correlates of inhibition in OCD vs. healthy and anxious controls.
Methods: ERPs and reaction times (RTs) were compared between participants with OCD ($n = 20$), panic disorder (PD; $n = 20$) and healthy controls (HCs; $n = 20$) during an adapted Go/NoGo task, which manipulated inhibitory difficulty.
Results: A classic P3 NoGo anteriorisation effect occurred across groups. Both clinical groups showed RT impairment, and similar topographical anomalies of several (P2, N2 and P3) ERP components. Notably, both clinical groups lacked the strong frontally maximal N2 component topography seen in the HCs, across stimuli. Additionally, with increasing inhibitory difficulty, N2 latency increased in HCs but not in the clinical groups.
Conclusions: Unexpectedly, ERP and behavioural anomalies during inhibition in OCD were not qualitatively different to those in PD, but were generally more severe. Common general and inhibitory deficits may underlie intrusive mental phenomena in both conditions.
Significance: This first ERP response inhibition study in OCD to include anxious controls disconfirmed hypotheses regarding OCD-specific inhibitory deficits, indicating the importance of comparing OCD to other conditions, to evaluate neurobiological models.

1. Introduction

Current approaches to OCD implicate additional neurobiological processes in its aetiology compared to other anxiety disorders (Kuelz et al., 2004). Consequently, much research has focused on identifying OCD-specific neuropsychological deficits which may increase understanding of the pathophysiology underlying the disorder. While OCD has been linked to a wide variety of neuropsychological deficits, particularly in executive processing and inhibition, results are frequently inconsistent or are not replicated, and OCD-specific impairments have yet to be clearly established (Greisberg and McKay, 2003; Kuelz et al., 2004; Simpson et al., 2006; Olley et al., 2007). The extent to which information-processing anomalies in OCD overlap with those in other anxiety disorders is central to ongoing considerations of the classification of OCD and its relationship to anxiety disorders vs. other psychiatric conditions (Stein et al., 2010; Bienvenu et al., 2012). While ERP studies have

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allowed the nuanced study of inhibition in OCD, as with brain imaging studies (Rauch et al., 1997; van den Heuvel et al., 2005; Radua et al., 2010), ERP studies comparing OCD with other disorders are extremely rare (Oades et al. 1996a; Schall et al., 1997; Miyata et al. 1998), limiting conclusions regarding OCD-specific deficits.

Impaired sensorimotor inhibition, that is the ability to suppress task-irrelevant information and to restrain prepotent behavioural responses when they are inappropriate (Bjorklund and Harnishfeger, 1995), has long been hypothesised to underlie repetitive symptoms in OCD and has been widely investigated. The Go/NoGo task is commonly used to investigate inhibitory processes, and requires withholding responses to infrequent "NoGo" stimuli presented amongst frequent "Go" stimuli requiring a motor response. Some Go/NoGo studies report impaired performance in OCD in the form of higher commission errors (Bannon et al., 2002, 2008) or slower reaction times (RTs; Aycicegi et al., 2003), however most report no behavioural impairment in participants with OCD (Di Russo et al., 2000; Johannes et al., 2001; Herrmann et al., 2003; Maltby et al., 2005; Roth et al., 2007; Bohne et al., 2008). Studies using standard measures of inhibition have yet to build a consistent picture of deficits in OCD, possibly due to the use of non-specific experimental tasks and test batteries designed to indicate gross neuropsychological deficits which may not be sensitive to more subtle anomalies seen in psychiatric disorders such as OCD (Sanz et al., 2001; Kuelz et al., 2004). ERPs allow the study of subtle psychophysiological anomalies including those which are not accompanied by behavioural deficits.

1.1. ERP studies of OCD

ERP studies of OCD have usually employed auditory oddball tasks, which measure attention to standard (i.e. non-target) vs. infrequent (i.e. target) stimuli. Differences between OCD and healthy controls are usually reported, however specific findings differ considerably. Differences in OCD relative to HCs include both larger (Towey et al., 1990, 1993) and smaller N2 amplitudes (Morault et al., 1997), and both larger P3a amplitude (Gohle et al., 2008), and smaller P3 amplitude (Oades et al. 1996a) have been reported. The inconsistent direction of findings may be due to differing task and stimulus complexity and may indicate a dysregulation (Morault et al., 1997) of N2 and P3 inhibitory processes rather than consistent under- or over-activation of specific components. Additionally, increased N1 latency has been reported in OCD, possibly indicating anomalies in stimulus discrimination (Morault et al., 1997). Reduced N2 and P3 latencies are reported in several studies (Towey et al., 1990, 1993; Morault et al. 1997; Sanz et al., 2001; Kivircik et al., 2003), interpreted as a sign of cortical over-arousal in OCD which may be linked to inhibitory deficits and intrusive symptoms (Morault et al., 1997).

Similar reduced Go/NoGo tasks are considered better measures of inhibitory processes (Falkenstein et al., 1999; Di Russo et al., 2000) because they establish pre-potent responding to Go stimuli, and therefore greater difficulty inhibiting responses to NoGo stimuli. When healthy individuals withhold responses to NoGo stimuli, the N2 component is typically larger (Jodo and Kayama, 1992; Eimer, 1993; Falkenstein et al., 1999), and the P3 component is generally larger and more frontally distributed (Roberts et al., 1994; Fallgatter and Strik, 1999) than when they are responding to Go stimuli, interpreted as neurophysiological correlates of inhibitory processes. ERP latencies in Go/NoGo tasks are also related to inhibition. Longer P3 latency has been reported in NoGo compared to Go conditions, interpreted as a sign of higher processing demands in the NoGo condition (Fallgatter and Strik, 1999; Salisbury et al., 2004). While studies primarily focus on the N2/P3 complex in the Go/NoGo task, modulations in earlier waveform components such as the P1, N1 or P2 may play major roles in determining inhibition success (Roche et al., 2005).

Source analyses of ERP components during the Go/NoGo task indicate that the Go-P3 originates in the bilateral parietal lobes, the NoGo-P3 sources are mainly in the inferior anterior cingulate cortex and lateral orbitofrontal area (Bokura et al., 2001), and the N2 component originates in medial orbitofrontal and cingulate cortices (Bokura et al., 2001, 2002; Bekker et al., 2005). Because these regions are also implicated in the pathophysiology of OCD (Whiteside et al., 2004), the Go/NoGo task seems particularly suitable for the study of OCD.

Two visual Go/NoGo studies (Malloy et al., 1989; Kim et al., 2007) report reduced anteriorisation of the N2 during the NoGo condition in OCD compared to controls. In one study this correlated negatively with Y-BOCS symptom severity, interpreted as a sign of inhibitory deficits (Kim et al., 2007). Another study, however, reported increased NoGo N2 amplitudes in OCD compared to healthy controls (Ruchsow et al., 2007). As with the oddball findings, the inconsistencies may be due to differing task and stimulus complexity and may indicate a dysregulation of N2 inhibitory processes which varies in direction (Morault et al., 1997). For the P3, Herrmann et al. (2003) found reduced frontal NoGo amplitude and reduced NoGo anteriorisation in OCD, correlated negatively with YBOCs symptoms scores, again interpreted as indicating inhibitory deficits. Di Russo et al. (2000) found increased frontal P3 amplitude in OCD patients to Go stimuli, relative to controls, with the OCD group having the same large P3 activation to both Go and NoGo stimuli, interpreted as a misallocation of cognitive resources in OCD. With regard to latencies, one study found reduced N2 latencies to Go stimuli in OCD relative to healthy controls (Herrmann et al., 2003).

Previous studies had small sample sizes of 8–13 OCD participants (Schall et al., 1997; Di Russo et al., 2000; Herrmann et al., 2003; Ruchsow et al., 2007). Malloy et al. (1989) had a larger sample of 18 OCD participants, however they analysed left side electrodes only. Only one study we located (Schall et al., 1997) used a clinical comparison group (schizophrenia), and there are apparently no studies in this area comparing OCD with an anxious control group, limiting conclusions about OCD-specific deficits. Sensorimotor inhibitory deficits occur in several psychiatric conditions, including attention-deficit hyperactivity disorder (Epstein et al., 2001), bipolar disorder (Murphy et al., 1999), depression (Paradiso et al., 1997), schizophrenia (Braff, 1993) and panic disorder (Ludewig et al., 2002; Ludewig et al., 2005), and further research is needed to investigate the specificity of effects to OCD.

1.2. Additional methodological issues

One interpretive difficulty which arises in traditional Go/NoGo tasks is that ERP differences may reflect the differential overlap of movement-related activity between Go and NoGo stimuli, rather than purely variations in cognitive inhibitory activity (Kopp et al., 1996; Falkenstein et al., 1999). We previously described a modified Go/NoGo task (Thomas et al., 2009) which addressed the issue of differential Go/NoGo movement overlap by establishing four distinct categories of NoGo stimuli which had been differentially primed by preceding Go stimuli and varied in inhibitory difficulty but not in response requirements. Different categories of NoGo stimuli could therefore be compared as a function of inhibitory load, avoiding the necessity for Go/NoGo comparisons. Following an fMRI study, (Durston et al., 2002), we predicted that inhibitory difficulty would be greater to NoGo stimuli preceded by larger numbers of Go stimuli. As predicted, ERP effects varied systematically according to the preceding context of stimuli. The traditional Go/NoGo analysis was also conducted, for comparison with a large body of previous literature (Thomas et al., 2009).