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

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Thomas, Susan; Gonsalvez, Craig J.; and Johnstone, Stuart, "How specific are inhibitory deficits to obsessive-compulsive disorder? A neurophysiological comparison with panic disorder" (2014). *Faculty of Science, Medicine and Health - Papers: part A*. 1578.
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How specific are inhibitory deficits to obsessive-compulsive disorder? A neurophysiological comparison with panic disorder

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.

Keywords

Obsessive-compulsive disorder, anxiety, ERPs, inhibition, N2, P3, panic disorder

Disciplines

Medicine and Health Sciences | Social and Behavioral Sciences

Publication Details

Thomas, S. J., Gonsalvez, C. J. & Johnstone, S. J. (2014). How specific are inhibitory deficits to obsessive-compulsive disorder? A neurophysiological comparison with panic disorder. *Clinical Neurophysiology*, 125 (3), 463-475.

Title Page

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

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Highlights

- We conducted the first event-related potential study of inhibitory processes in OCD to include an anxious comparison group, in the search for OCD-specific deficits.
- As in previous studies of inhibition, participants with OCD showed RT impairment, and ERP anomalies during several (P2, N2, P3) information-processing stages, compared to healthy controls.
- Surprisingly, deficits and ERP anomalies did not differ qualitatively between OCD and panic disorder, precluding OCD-specific interpretations and illustrating the importance of including clinical comparison groups in future research, to advance neurobiological models of OCD.

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 versus 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.

Keywords: *Obsessive-compulsive disorder; anxiety; ERPs; inhibition; N2; P3; panic disorder*

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 versus other psychiatric conditions (Stein et al. 2010; Bienvenu et al. 2012). While ERP studies have 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. 1996; 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; Bannon et al. 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, Hohagen 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) versus 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; Towey et al. 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. 1996) 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).

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 (Ruchow 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, Hermann 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; Ruchow 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; 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, (Durstun 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).

In our previous study, increasing the numbers of preceding Go stimuli resulted in incremental increases in N1, P2 and N2 latencies, interpreted as an indication of greater inhibitory difficulty to NoGo stimuli as a function of preceding Go stimuli. ERP amplitudes showed more complex higher-order effects with indications of inhibition which reversed towards the end of longer stimulus trains, possibly due to anticipatory effects (Thomas et al. 2009). Thus we established a means of comparing ERPs to stimuli associated with differing difficulty of inhibition, independent of motor confounds. Additionally, when we conducted the standard Go/NoGo comparison, well established Go-NoGo effects were replicated, suggesting that the modified task was comparable with previous Go/NoGo studies.

1.3 Panic disorder

Panic disorder is a common anxiety disorder which, like OCD, results in significant impairment in functioning. The neurobiology of panic disorder is not yet fully understood, however dominant models implicate both excessive activation, and impaired cortical inhibition, of anxiety-related caudal limbic neural circuits (Coplan and Lydiard 1998). The prefrontal cortex is also implicated in the core pathophysiology of panic disorder, with hypofrontality in imaging studies being interpreted to indicate executive dysfunction and impaired prefrontal cortical inhibition of hyperactivity of anxiety-related neural circuitry (Ohta et al. 2008). Individuals with panic disorder therefore constitute a suitable comparison group in the search for OCD-specific inhibitory deficits.

1.4 The current study

The current study used ERP and behavioural data to examine sensorimotor inhibition in

OCD, to establish the nature of inhibitory anomalies, and the extent to which they are OCD-specific or shared with an anxiety disorder (PD). We used the experimental approach established earlier with a healthy sample (Thomas et al. 2009). ERP measures, RT and accuracy of responses were analysed to Go and NoGo stimuli in a standard Go/ NoGo comparison. Additionally, we manipulated the difficulty of inhibition by varying the number of Go stimuli which preceded NoGo stimuli. Forty clinical participants were recruited (20 with diagnoses of OCD and 20 with PD) for comparison with the ERP and performance data for the HCs previously reported (Thomas et al. 2009).

We predicted atypical activation and/or topography of N2 and P3 components, and of the NoGo versus Go N2 and P3 components in OCD relative to HC. To support OCD-specific inhibitory deficits, the OCD group should differ from both the healthy and anxious control groups. Additionally, we predicted that comparison of NoGo stimuli differentially negatively primed by preceding Go stimuli would provide further insight into inhibitory processes and that the OCD group would show atypical ERP latencies with increasing difficulty of inhibition in comparison to HC and anxious controls.

2. Method

2.1 Participants

Forty individuals participated in the current study: 20 with OCD and 20 with PD with or without agoraphobia. Their data were compared with those of 20 HCs reported in our previous study (Thomas et al. 2009). The data for the clinical groups were collected contemporaneously with those for the healthy controls, in the same lab with identical testing procedures and recording instrumentation. Because the clinical participants took longer to recruit, as is often the case, we finished recruitment for the healthy controls earlier than the clinical groups. Because of the novel nature of the methodology, we considered that it was important to first publish a report which considered performance and neural correlates during this task in healthy

participants, as a foundation for later interpreting the complex between-group analysis.

No individuals in the PD group had a personal or known family history of OCD or obsessive-compulsive symptoms. Clinical participants were recruited through local clinics. Diagnoses were confirmed using the Composite International Diagnostic Interview for DSM-IV (World Health Organisation 1997). While some participants were prescribed occasional benzodiazepines (Table 1), none had taken benzodiazepines in the preceding 48 hours. HCs were free from past or present psychiatric disorders. Exclusion criteria across groups were head injuries, neurological disorders, substance abuse and psychoses. The University of Wollongong Ethics Committee approved the research protocol beforehand and participants gave written informed consent.

2.2 Materials

Symptom types and severity were assessed using the Padua Inventory-Washington State University Revision (PI-WSUR (Burns et al. 1996), the Yale-Brown Obsessive Compulsive Scale (Goodman et al. 1989), the Brief Symptom Inventory (BSI; Derogatis and Melisaratos 1983) and Obsessional Beliefs Questionnaire (OBQ-44; Obsessive Compulsive Cognitions Working Group 1997; 2001; 2005).

2.3 Stimuli

Stimuli were presented individually on a computer screen in white on a black background. They comprised a baseline stimulus (!), a Go stimulus (✓), and a NoGo stimulus (X). Two further stimuli were included for future comparisons of task-switching performance and are not examined here (X-Go and dedicated NoGo), following at the end of stimulus trains. Stimuli occurred in sequences or trains of 4-8 (See Figure 1.). Trains commenced with the baseline stimulus, followed by between 1-4 Go stimuli (✓), followed by a NoGo stimulus (X). The X-NoGo stimulus was followed on 50% of trials by a repetition of the X-stimulus (because participants were required to respond to X-repetitions, this stimulus is termed X-Go) and on

50% of trials by a square (dedicated NoGo stimulus). Thus a NoGo (N) stimulus occurred in each train, but because N was preceded by one or more Go-stimuli, the overall ratio of Go: NoGo stimuli presented to participants was 14:4 or 69%: 31%. Train types were equiprobable and presented randomly. Stimulus duration was 200 ms. ISI varied randomly between 1-3 s (mean 2 s) and inter train interval varied randomly between 4-6 s. Overall, 635 stimuli were presented to participants in 70 trains.

2.4 Procedure

After completing interviews and questionnaires, participants were fitted with the electrode cap. During the experiment participants were comfortably seated in a dimly lit sound-attenuated room, 1m from the computer screen, with a button-press device fixed to a chair arm next to their dominant hand.

2.5 Electrophysiological recording

The EEG was recorded from 19 scalp electrodes (F1, F2, F3, Fz, F4, F7, F8, T3, T4, T5, T6, C3, Cz, C4, P3, Pz, P4, O1, O2) and referenced to linked ears according to the international 10 – 20 system (Jasper, 1958) using tin electrodes in an electrode cap. The participant was grounded by a cap electrode located midway between Fpz and Fz. Vertical EOG was recorded from electrodes placed 1 cm above and below the left eye, and electrodes placed beyond the outer canthus of each eye recorded horizontal EOG. Electrode impedances were below 5k Ω .

2.6 Data analysis

One-way analyses of variance (ANOVAs) were used to compare groups on age and psychometric variables. Significant differences between groups were followed by simple effects comparisons to investigate which group differences were driving the effects. Fisher's exact test was used to compare group categorical variables.

Mean RTs for correct responses by stimulus type were calculated for each participant in each task. Extreme scores (± 2 SDs from the participant's condition mean) were excluded

(Ratcliff, 1993; Thomas et al. 2009). A one-way ANOVA was used to compare groups on RTs to Go stimuli. Effects of the number of preceding Go stimuli upon commission errors to NoGo stimuli were analysed using a 3 Group (HC, PD, OCD) x 4 Stimulus sequence position (GN, GGN, GGGN, GGGGN) ANOVA. As described above, planned contrasts assessed linear and quadratic effects for the Stimulus sequence position factor.

The ERP epoch was defined as 100 ms pre- to 800 ms post-stimulus. ERP data were amplified with EEG and EOG gains of 20,000 and 5,000 respectively, digitized at a sampling rate of 512 Hz with a bandpass down 3 dB at 0.01 and 35 Hz, and filtered offline with a low pass zero phase shift filter at 30 Hz, 48dB/octave. Data were accepted after artifact rejection ($\pm 100\mu\text{V}$) and eye-movement correction (Semlitsch et al. 1986).

Five components were quantified, with amplitudes determined relative to the 100 ms pre-stimulus baseline. Peaks were automatically detected in specified channels where they generally showed maximal amplitude in the grand mean waveforms: O1 for P1 (50–140ms); O2 for N1 (90–160 ms); Pz for P2 (150 - 210 ms); Fz for N2 (180 - 400 ms), and Pz for P3 (290 - 600 ms). Search windows were based on visual inspection of the grand mean waveforms. Following automatic detection, individual peaks were visually inspected and manually confirmed or corrected. Eleven sites were the focus of data analysis (F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, O1, O2). ERP latencies were recorded as the time during the search window of maximal amplitude at the index channel, and the component amplitudes for all 11 electrodes were taken at the same post-stimulus latency (Picton et al. 2000).

Within the lateral plane, two planned contrasts were computed: left versus right hemispheres, and the midline region versus the mean of the left and right hemispheres. The contrasts for the Sagittal factor were: (i) frontal vs. parietal electrodes and (ii) central vs. the mean of the frontal and parietal electrodes. As the contrasts were planned and there were no more of them than the degrees of freedom for an effect, no Bonferroni-type adjustment was

necessary (Tabachnick et al. 2001). Greenhouse–Geisser corrections were applied where appropriate. ERP data were normalised using the vector scaling procedure (McCarthy and Wood 1985), and interactions involving topography are reported only if they remained significant after normalisation.

To assess whether any Group effects or interactions may have been related to medication status, for each clinical group separately, analyses were repeated as above with a between group factor of Medication, with 2 levels (no medication, current medication). Interactions and effects are only reported if no involved factor interacted with Medication.

3. Results

3.1 Group characteristics and psychometric variables

Tables 1 shows that there were no significant differences between groups for demographic variables. Table 2 shows psychometric results, with the OCD group having higher scores than the HC group on all measures of psychopathology. There were no significant differences between the OCD and PD groups on measures of psychological symptoms, except that the OCD group scored significantly higher on OCD symptoms (measured by the Padua Inventory). The PD group scored higher than the HC group on all measures of psychopathology, except in OCD symptoms.

3.2 Behavioural results

Table 3 shows behavioural data across groups. There were no interactions between Medication and performance. There was an effect of Group on RT, $F(2, 57) = 4.27, p = .02$, with both clinical groups having longer RTs than the HC group (OCD vs. HC: $F(1, 38) = 5.48, p = .025$; PD vs. HC: $F(1, 38) = 8.72, p = .005$; PD vs. OCD: $F(1, 38) = 1.5, p = .7$). Accuracy of responses to NoGo stimuli (NoGo-X) was high (99.9%) and did not differ by Group or as a function of Go preceding NoGo stimuli.

3.3 ERPs to Go versus NoGo stimuli

Table 4 shows all significant ERP effects and interactions involving Group, and accompanying two-group comparisons. Grand mean waveforms to Go and NoGo stimuli are shown in Figure 2. Mean ERPs to Go stimuli and NoGo (NoGo-X) stimuli were compared in a Stimulus (Go, NoGo) x Sagittal (frontal, central, parietal) x Lateral (left, midline, right) x Group (HC, PD, OCD) ANOVA. For N1 amplitude, an additional ANOVA was conducted at occipital electrodes (O1, O2) with factors of Group (as above) x Stimulus type (as above) x Lateral (left, right).

P1 amplitude was larger to NoGo than Go stimuli, $F(1, 57) = 18.6, p < .001$, and had a greater central (versus fronto-parietal) effect to NoGo than Go stimuli, $F(1, 57) = 11.27, p < .01$.

N1 amplitude was greater fronto-parietally (versus centrally) to NoGo than Go stimuli, $F(1, 57) = 7.78, p < .01$. N1 amplitude was greater at lateral (vs. midline) sites, with this effect being greater for NoGo compared to Go stimuli, $F(1, 57) = 20.04, p < .01$. N1 latency was faster to Go than NoGo stimuli, $F(1, 57) = 4.3, p < .05$.

P2 amplitude was larger, $F(1, 57) = 7.18, p < .01$, and showed a stronger parietal > frontal effect, $F(1, 57) = 6.92, p < .05$, to NoGo than Go stimuli. P2 latency was faster to Go than NoGo stimuli, $F(1, 57) = 9.39, p < .01$.

For N2, the Group by Sagittal interaction was significant, $F(2, 57) = 3.28, p < .05$, with both clinical groups having the same atypical topography of N2 amplitude across Go and NoGo stimuli, and an absence of the frontal > parietal topography seen in the HCs. N2 amplitude was greater centrally (versus fronto-parietally) to NoGo than Go stimuli, $F(1, 57) = 6.81, p < .05$. N2 latency was faster to Go than NoGo stimuli, $F(1, 57) = 8.54, p < .01$.

P3 amplitude was larger to NoGo than Go stimuli, $F(1, 57) = 4.04, p < .05$. P3 amplitude showed a stronger frontal (vs. parietal) effect to NoGo than Go stimuli (i.e. a NoGo anteriorisation effect), $F(1, 57) = 5.35, p < .05$ and a greater central (versus fronto-parietal)

effect to NoGo than Go stimuli, $F(1, 57) = 28.57, p < .001$. P3 latency was faster to Go than NoGo stimuli, $F(1, 57) = 5.94, p < .05$.

3.4 ERPs to NoGo stimuli as a function of preceding sequence

Mean ERPs to NoGo stimuli as a function of the number of preceding Go stimuli are shown in Figure 4. ERPs to NoGo stimuli were analysed using an ANOVA with Group x Stimulus sequence (GN, GGN, GGGN, GGGGN) x Sagittal x Lateral factors as above. For N1 amplitude, an additional ANOVA was conducted at occipital electrodes (as before). Because the focus of the current study is between-group differences, only interactions involving Group are reported here. A detailed consideration of sequence effects in the current experimental approach appears elsewhere (Thomas et al. 2009). Mean ERP amplitudes to NoGo stimuli for significant Group effects and interactions are plotted in Figure 5, and latencies in Figure 6.

P1 amplitude showed a Group by Laterality (linear) interaction, $F(2, 57) = 4.4, p < .05$, driven by increased right versus left hemisphere amplitude for P1 to NoGo stimuli in the PD versus OCD and HC groups.

N1 amplitude showed a Group by Laterality (linear) interaction, $F(2, 57) = 3.3, p < .05$, driven by reduced N1 amplitude in the left versus right hemisphere to NoGo stimuli in PD relative to HCs (Table 4). Table 4 shows a main effect of Group for N1 latency, $F(2, 57) = 6.84, p < .01$, driven by significantly longer N1 latencies to NoGo stimuli in the OCD than HC group (Figure 6).

For P2, a main effect of Group, $F(2, 57) = 3.97, p < .05$, and simple effects showed that the OCD group had significantly smaller P2 amplitude to NoGo stimuli than HCs. A Group by Sagittal interaction, $F(2, 57) = 12.08, p < .01$, and simple effects showed that the OCD group had significantly reduced parietal versus frontal P2 amplitude to NoGo stimuli compared to HC and PD groups. This effect was also present in the PD group relative to HCs.

For N2, a Group by Sagittal (frontal vs. parietal) interaction for N2 amplitude to NoGo

stimuli, $F(2, 57) = 5.21, p < .01$, and simple effects showed a stronger frontal > parietal effect for N2 amplitude to NoGo stimuli in HCs than OCD and PD groups. N2 latency showed a main effect of Group, $F(2, 57) = 3.51, p < .05$, with the PD group having shorter N2 latencies than the OCD and HC groups. The Stimulus (linear) by Group interaction, $F(2, 57) = 4.41, p < .05$, was significant, driven by both clinical groups failing to show the increase in N2 latency as a function of Go preceding NoGo stimuli evidenced by the HCs.

P3 amplitude showed a significant Group by Sagittal (frontal vs. parietal) interaction, $F(2, 57) = 5.51, p < .01$. Simple effects analyses indicated atypical topography of P3 amplitude in both clinical groups, with reduced parietal versus frontal P3 compared to HCs.

3.5 Relationships between experimental effects and symptoms

We conducted selective Pearson correlations to examine relationships between the above significant effects and symptom severity as measured by the Y-BOCS, the BSI (Anxiety, Obsessive-compulsive and Depression subscales, Global Severity Index and Positive Symptom Distress Index), the PI-WSUR, and the OBQ-44.

RT to Go stimuli was positively correlated with Y-BOCS Obsessions, $r(20) = .50, p < .05$, and Compulsions, $r(20) = .49, p < .05$. For ERPs, only correlations significant at the 0.01 level are reported. N2: Right parietal amplitude to NoGo stimuli was negatively correlated to BSI Anxiety, $r(60) = -.34$. Left parietal amplitude to Go stimuli negatively correlated to OBQ total, Responsibility/Threat, Importance/Control of Thoughts, Thoughts of harm, BSI OC, Anxiety, Global Severity Index, Positive Symptom Total and Positive Symptom Distress Index, $r(60)$ between $-.34$ and $-.43$. Midline parietal amplitude to Go stimuli negatively correlated to OBQ total, $r(60) = -.34$, and Importance/Control of Thoughts, $r(60) = -.41$. Right parietal amplitude to Go stimuli negatively correlated to OBQ Importance/Control of Thoughts, $r(60) = -.41$, BSI Anxiety, $r(60) = -.37$ and BSI Positive Symptom Total, $r(60) = -.34$. For P3, latency to Go stimuli correlated positively with BSI Anxiety, $r(60) = -.35$.

4. Discussion

Current models of OCD implicate additional neurobiological processes compared to other anxiety-related disorders (e.g., Kuelz et al. 2004). While numerous ERP studies have attempted to identify neuropsychological factors which may increase understanding of the pathophysiology of OCD, very few have included clinical comparison groups, thus limiting conclusions about OCD-specific deficits. The current study addressed these limitations by including an anxious comparison group with PD, having similar levels of symptom severity but without any personal or family history of OCD. Although there have been several previous studies of neural activity accompanying response inhibition in OCD, to our knowledge this was the first to include an anxious comparison group. Additionally, we employed a specially modified Go/NoGo task (Thomas et al. 2009) which included an additional examination of inhibitory processes which avoided some of the interpretive limitations when comparing Go with NoGo stimuli. This task allowed the comparison of different groups of NoGo stimuli with each other which were differentially primed by preceding Go stimuli, and therefore differed in inhibitory difficulty while not having the response requirement differences inherent in Go/NoGo comparisons.

4.1 Go/NoGo Comparison

When we followed the well-established method of comparing ERPs to Go versus NoGo stimuli, P3 amplitude was larger and showed a stronger frontal (vs. parietal) effect to NoGo than Go stimuli (i.e. a classic NoGo anteriorisation effect), across groups. This is consistent with previous OCD studies (e.g. Kim et al. 2007), and indicates that the task was comparable to existing Go/NoGo studies, with NoGo stimuli being associated with ERP responses typically interpreted as indexing brain inhibitory mechanisms (Roberts et al. 1994; Fallgatter and Strik 1999) in both the clinical and healthy groups.

Both clinical groups, however, showed remarkably similar atypical topography of N2 across stimuli, with more posteriorly distributed N2 amplitudes and an absence of the strong frontally maximal topography seen in the HC group. Additionally, greater negativity of N2 in parietal regions was related to several measures of psychopathology including obsessional beliefs, obsessive-compulsive symptoms, anxiety, and overall severity of psychological symptoms and distress. This was localised to the right hemisphere for NoGo stimuli but occurred across left, midline and right parietal sites to Go stimuli.

Previously, Kim et al. (2007) also reported a more posteriorly distributed NoGo N2 in OCD compared to controls, correlated with symptom severity, which they interpreted as indicating inhibitory deficits in OCD, possibly induced by dysfunctions of the inferior prefrontal cortex and contributing to the pathophysiology of OCD. Also, a more posteriorly distributed NoGo N2 has been reported in children relative to adults, interpreted to indicate the effortful recruitment of more primitive brain regions, such as the striatum, for inhibitory control before the prefrontal brain regions are fully mature (Ciesielski et al. 2004; Jonkman et al. 2007). In the current study this posteriorly distributed N2 negativity occurred across Go and NoGo stimuli, suggesting a general processing anomaly such as a misallocation of cognitive resources noted in previous OCD studies (Di Russo et al. 2000), rather than purely an inhibitory deficit. Posterior shifts in N2 topography have been linked to the effects of noradrenaline release on cortical processing (Warren et al. 2011). It is possible that the atypical N2 topography reflects recruitment of additional cortical areas in task performance in the clinical groups, linked to catecholamine release, however further research is needed. Occurrence of the same pattern of topographical abnormalities in participants with panic disorder and no history of OCD militates against an OCD-specific interpretation.

Consistent with previous research, N1, P2, N2 and P3 latencies were prolonged to NoGo compared to Go stimuli across groups, likely indicating the higher processing demands

involved in inhibiting, compared to executing, anticipated actions (Fallgatter and Strik 1999). Both clinical groups had general RT slowing to Go stimuli. RT impairment in participants with OCD was positively related to (Y-BOCS) symptom severity. Longer RTs to Go stimuli have been reported previously in OCD relative to HCs (Aycicegi et al. 2003), however many studies find no impairment (Di Russo et al. 2000; Johannes et al. 2001; Herrmann et al. 2003; Roth et al. 2007; Bohne et al. 2008). Reviews of neuropsychological performance in OCD (Kuelz et al. 2004; Olley, Malhi et al. 2007) conclude that task performance is often at a similar overall level to controls, but is accompanied by longer RTs in about half the studies, indicating that accuracy may be accomplished at a cost to speed. Medication status did not interact with RTs in the current study, and it is therefore concluded that both anxious groups showed general RT slowness associated with clinical status. This interpretation was supported by the correlation between P3 latency to Go stimuli and BSI Anxiety severity, suggesting that clinical anxiety was associated both with slower cognitive as well as motor responses to Go stimuli. In summary of the Go versus NoGo results, this is to our knowledge the first ERP Go/NoGo study which included an anxious comparison group, and no OCD-specific inhibitory or general deficits were detected.

4.2 Inhibitory load manipulation

The current study also manipulated the difficulty of withholding responses to NoGo stimuli by varying the number of preceding Go stimuli. By comparing NoGo stimuli of varying inhibitory difficulty we could examine the neural correlates of inhibition while avoiding the interpretive difficulties inherent in Go/ NoGo comparisons, such as motor movements overlapping ERPs to a greater extent for Go than NoGo stimuli (Kopp et al. 1996; Falkenstein et al. 1999). We initially trialed this modified Go/NoGo task in healthy participants and found that increasing the number of Go stimuli before NoGo stimuli led to ERP indications of greater inhibitory difficulty including incremental increases in N1, P2 and N2 latencies (Thomas et al.

2009). Because the aim of the current study was to identify OCD-specific inhibitory deficits, we focus here on between-group differences. Further information about sequence effects in this task as a result of experimental manipulations is considered in more detail elsewhere (Thomas et al. 2009).

In the current study, both anxious groups failed to show the increase in N2 latency as a function of the number of Go preceding NoGo stimuli evidenced by the HCs. Towey et al. (1993) reported that increasing task difficulty resulted in longer N2 and P3 latencies in HCs, but not in OCD patients in an auditory oddball task. A defining feature of inhibitory brain processes is a decrement (in speed or accuracy) resulting from previous stimulation (Posner and Snyder 1975; Buckner et al. 1998; Klein 2000), and longer ERP latencies to NoGo than Go stimuli are attributed to higher processing demands when withholding than executing anticipated actions (Fallgatter and Strik 1999; Herrmann et al. 2003; Salisbury et al. 2004). The N2 ERP component is considered a key neurophysiological aspect of response inhibition processes (Kaiser et al. 2006). Failure of both anxious groups to show the increase in N2 latency evidenced by the HCs with increasing inhibitory load may indicate anomalous brain inhibitory mechanisms in both clinical groups.

The OCD group had longer N1 latencies to NoGo stimuli than the HCs. N1 latency increases with increased attention to stimuli, and with effort at processing (Callaway and Halliday 1982). One previous ERP Go/NoGo study reported longer N1 latency to Go stimuli in OCD (Di Russo et al. 2000) while others found no significant differences between control and OCD ERP latencies (Malloy et al. 1989; Schall et al. 1997; Herrmann et al. 2003; Ruchow et al. 2007). Longer N1 latencies in OCD were also reported in an oddball task (Morault et al. 1997). The current findings may indicate slower or more effortful early discriminative processing (Oades et al. 1996) in OCD.

Participants with OCD had smaller P2 amplitude, particularly parietally, to NoGo

stimuli relative to HCs. The P2 is interpreted as representing stimulus discrimination and classification (Dowman 2004) and inhibitory processes (Coburn et al. 2005) and is affected by vigilance and arousal (Oades et al. 1996). Reduced P2 latency has been linked to weakness of inhibition (Muller and Roberts 2005). Smaller P2 amplitudes have previously been reported in participants with OCD, relative to HCs and those with schizophrenia, during an auditory oddball task (Oades, Zerbin et al. 1996). P2 amplitude increases with faster, more accurate performance in Go/NoGo tasks (Johnstone et al. 2001), suggesting that it is related to stimulus evaluation processes underlying optimal performance. Several studies demonstrate a dependence of P2 amplitude on serotonin activity (Norra et al. ; Hegerl and Juckel 1993; Hegerl et al. 2001; Juckel et al. 2003; Senkowski et al. 2003; Juckel et al. 2008). Serotonin dysregulation is implicated in the pathogenesis of OCD (Hesse et al. 2005; Baca-Garcia et al. 2007; Lin 2007; Goddard et al. 2008; Perani et al. 2008; Matsumoto et al. 2010) and anxiety disorders generally, including panic disorder (Coplan and Lydiard 1998; Bandelow et al. 2008). It is therefore notable that the PD group showed intermediate P2 amplitude between the HCs and OCD group, and shared P2 topographical anomalies with OCD relative to the HCs. In a previous study, participants with PD had reduced P2 amplitude to non-targets, compared to healthy controls (Wang et al. 2003). Taken in conjunction with previous research, the current P2 results may indicate shared anomalies in arousal, vigilance or inhibition in OCD and panic disorders.

In the current study, both clinical groups also shared atypical topography of the NoGo P3, with lower parietal relative to frontal amplitude compared to HCs. Lower parietal P3, which improves after treatment with SSRIs, has been previously reported in OCD, interpreted as a sign of general cognitive and inhibitory dysfunction (Sanz et al. 2001). Additionally, higher frontal cortical activation in OCD has been noted in several studies (reviewed in Saxena and Rauch 2000). These patterns are typically interpreted within a model of OCD-specific

posterior cortical under-activation and anterior cortical over-activation of a primary or compensatory nature (Ciesielski et al. 2005; Menzies et al. 2008). The current results, however, indicate that abnormalities in parietal activation are not OCD-specific but common to PD. Additionally, the P3 results must be viewed in the context that in the current study both clinical groups showed increased parietal negativity across several (P2, N2 and P3) information-processing stages. Parietal brain regions are increasingly implicated in both OCD (Ciesielski et al. 2005; Menzies et al. 2008) and PD (Alemayehu et al. 1995; Heller et al. 1997; Bisaga et al. 1998), and the current results support the consideration of their role in information-processing in these disorders.

4.3 Summary and integration

Overall, participants with OCD showed several significant differences from HCs in performance and ERP measures in the Go/NoGo task. Similar anomalies have been reported in previous ERP studies of OCD, including RT impairment (see Kuelz et al. 2004; Olley et al. 2007), more posteriorly distributed N2 amplitude (Kim et al. 2007), a failure to show increasing N2 latency with increasing task difficulty (Towey et al. 1993), longer N1 latencies to NoGo stimuli (Di Russo et al. 2000) and smaller P2 amplitude (Oades, Zerbin et al. 1996).

Surprisingly, however, with the inclusion of an anxious comparison group in the current study, we found that participants with PD showed remarkably similar performance and ERP anomalies to the OCD group. For most effects, the OCD group differed significantly only from the HCs and the PD group showed an intermediate effect. There were only two findings where the OCD group differed significantly from both the HC and PD groups. The first was greater scores on measures of OCD symptoms (e.g. Padua) in the OCD than other groups, as would be predicted. The second was a reduced parietal: frontal topography of P2 to NoGo stimuli, however the PD group showed this same atypical topography and also differed significantly from the HCs for this effect, suggesting that the same underlying processes were present in

both clinical conditions, but were more pronounced in OCD than in PD.

The current pattern of results leads to the suggestion that general and inhibitory anomalies in the current study are not OCD-specific but may represent common abnormalities among these disorders. Additionally, it highlights the need for caution in interpreting the results of studies of OCD without anxious control groups. The only previous ERP study of which we are aware to include an anxious control group found N2 abnormalities in OCD versus HCs in an oddball task for target and non-target stimuli, with N2 negativity for a social phobic comparison group falling halfway between, supporting a similar interpretation.

These findings have implications for understanding the extent to which OCD is associated with unique deficits and psychophysiological activity relative to panic disorder. The extent to which pathological processes in OCD overlap with anxiety disorders such as PD has important nosological and clinical implications. Very few previous studies of brain activity in OCD included anxious control groups, including the majority of neuroimaging studies upon which neurobiological models of OCD (e.g. Saxena and Rauch 2000; Whiteside, Port et al. 2004) have been developed. Inclusion of a PD group showing equivalent levels of symptom severity and medication status led to results which are more consistent with conceptualisations of a considerable overlap in the neural substrates of OCD with PD rather than with models emphasising a unique neural signature in OCD (Mataix-Cols and van den Heuvel 2006). The overlapping ERP and behavioural results during response inhibition in the current study may be related to other shared phenomena between the two disorders. Both OCD and PD share symptoms of anxiety and behavioural avoidance, although with different foci and manifestations (Miyata et al. 1998; Bartz and Hollander 2006). For both conditions, first line treatments include SSRIs and tricyclic antidepressants (TCAs), often with higher doses in OCD, and cognitive behavioural therapy (CBT). Both disorders are characterised by failures to inhibit irrelevant and repetitive stimuli (Amir et al. 2001; Wise et al. 2009).

These results support recent observations that the tendency to study OCD in isolation from other disorders may have been an important barrier to progress in determining OCD-specific versus general (disorder nonspecific) etiologic factors (Taylor 2012). If an inhibitory deficit is not specific to OCD, its importance in aetiological theories declines because it cannot be a necessary and sufficient cause of the disorder (see Nigg 2000).

4.4 Caveats and future directions

Some clinical participants were prescribed medication at the time of testing. Previous ERP studies of OCD include medicated participants (Malloy et al. 1989; Sanz, Molina et al. 2001; Herrmann et al. 2003; Ruchow et al. 2007; Bohné et al. 2008; Hashimoto et al. 2008), which may be due to difficulties in recruiting research participants with OCD (Muller and Roberts 2005) as well as practical and ethical difficulties in finding off-medication patients (Clark et al. 2009). We addressed confounds of comparing a medicated clinical group with drug-naïve healthy controls by the inclusion of a clinical comparison group, taking similar levels and types of medications and differing significantly only on measures of OCD. Data were also reanalysed with medication as a between-subjects factor and found no interaction between medication status and any performance variables or ERP latencies. There were a small number of interactions between ERP amplitude topography or stimulus type and medication, and these results were excluded from reporting, reducing the likelihood of medication effects accounting for the current results. Nonetheless it is possible that medications influenced the results.

As in most OCD ERP research the current study examined inhibitory processes to neutral stimuli only. Because individuals with OCD do not complain of global inhibitory deficits, but struggle to inhibit personally repugnant thoughts (Moritz et al. 2009), there is a need to investigate inhibition in relation to affective stimuli. Indeed there is some evidence of disorder-specific neural activity to affective stimuli between individuals with OCD and those

with panic disorder (van den Heuvel, Veltman et al. 2005; Thomas et al. 2013).

4.5 Conclusions

In the current study, ERP and behavioural anomalies in OCD during a response inhibition task were not qualitatively different to those in PD but were generally more severe. Previous research may have overestimated the specificity of deficits to OCD, due to a lack of clinical comparison groups. Additionally, the extent of inhibitory deficits in PD may have been inadequately explored. The current study highlights the need for further research using anxious comparison groups, to improve neurobiological models of OCD.

References

- Alemayehu S, Bergey GK, Barry E, Krumholz A, Wolf A, Fleming CP, et al. Panic attacks as ictal manifestations of parietal lobe seizures. *Epilepsia*. 1995;36:824-30.
- Amir N, Freshman M, Ramsey B, Neary E, Brigidi B. Thought-action fusion in individuals with OCD symptoms. *Behav Res Ther*. 2001;39:765-76.
- Aycicegi A, Dinn WM, Harris CL, Erkmen H. Neuropsychological function in obsessive-compulsive disorder: effects of comorbid conditions on task performance. *Eur Psychiatry*. 2003;18:241-8.
- Baca-Garcia E, Vaquero-Lorenzo C, Diaz-Hernandez M, Rodriguez-Salgado B, Dolengevich-Segal H, Arrojo-Romero M, et al. Association between obsessive-compulsive disorder and a variable number of tandem repeats polymorphism in intron 2 of the serotonin transporter gene. *Prog Neuropsychopharmacol Biol Psychiatry*. 2007;31:416-20.
- Bandelow B, Zohar J, Hollander E, Kasper S. World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for the Pharmacological Treatment of Anxiety, Obsessive-Compulsive and Post-Traumatic Stress Disorders—First Revision. *World J Biol Psychiatry*. 2008;9:248-312.
- Bannon S, Gonsalvez CJ, Croft RJ. Processing impairments in OCD: It is more than inhibition! *Behav Res Ther*. 2008;46:689-700.
- Bannon S, Gonsalvez CJ, Croft RJ, Boyce PM. Response inhibition deficits in obsessive-compulsive disorder. *Psychiatry Res*. 2002 2002/6/1;110:165-74.
- Bartz JA, Hollander E. Is obsessive-compulsive disorder an anxiety disorder? *Prog Neuropsychopharmacol Biol Psychiatry*. 2006;30:338-52.
- Bekker EM, Kenemans JL, Verbaten MN. Source analysis of the N2 in a cued Go/NoGo task. *Cogn Brain Res*. 2005;22:221-31.
- Bienvenu OJ, Rasmussen SA, Fyer AJ, Pinto A, Rauch SL, Pauls DL, et al. Is obsessive-compulsive disorder an anxiety disorder, and what, if any, are spectrum conditions? A family study perspective. *Psychol Med*. 2012;42:1-13.
- Bisaga A, Katz JL, Antonini A, Wright E, et al. Cerebral glucose metabolism in women with panic disorder. *American J Psychiatry*. 1998;155:1178-83.
- Bjorklund DF, Harnishfeger K. The evolution of inhibition mechanisms and their role in human cognition and behaviour. In: Dempster CJB, editor. *Interference and inhibition in cognition*. London: Academic Press, Inc.; 1995.
- Bohne A, Savage CR, Deckersbach T, Keuthen NJ, Wilhelm S. Motor inhibition in trichotillomania and obsessive-compulsive disorder. *J Psychiatr Res*. 2008;42:141-50.
- Bokura H, Yamaguchi S, Kobayashi S. Electrophysiological correlates for response inhibition in a Go/NoGo task. *Clin Neurophysiol*. 2001;112:2224-32.
- Bokura H, Yamaguchi S, Matsubara M, Kobayashi S, editors. *Frontal lobe contribution to response inhibition process—an ERP study and aging effect*. 2002: Elsevier.
- Braff DL. Information Processing and Attention Dysfunctions in Schizophrenia. *Schizophr Bull*. 1993;19:233-59.
- Buckner RL, Goodman J, Burock M, Rotte M, Koutstaal W, Schacter D, et al. Functional-Anatomic Correlates of Object Priming in Humans Revealed by Rapid Presentation Event-Related fMRI. *Neuron*. 1998;20:285-96.
- Burns GL, Keortge SG, Formea GM, Sternberger LG. Revision of the Padua Inventory of obsessive compulsive disorder symptoms: distinctions between worry, obsessions, and compulsions. *Behav Res Ther*. 1996;34:163-73.
- Callaway E, Halliday R. The effect of attentional effort on visual evoked potential N1 latency. *Psychiatr Res*. 1982;7:299-308.
- Ciesielski KT, Hämäläinen MS, Lesnik PG, Geller DA, Ahlfors SP. Increased MEG activation

- in OCD reflects a compensatory mechanism specific to the phase of a visual working memory task. *NeuroImage*. 2005;24:1180-91.
- Ciesielski KT, Harris RJ, Cofer LF. Posterior brain ERP patterns related to the go/no-go task in children. *Psychophysiology*. 2004;41:882-92.
- Clark CR, Galletly CA, Ash DJ, Moores KA, Penrose RA, McFarlane AC. Evidence-based medicine evaluation of electrophysiological studies of the anxiety disorders. *Clin EEG neurosci*. 2009;40:84.
- Coburn KL, Amoss RT, Arruda JE, Kizer LD, Marshall YS. Effects of flash mode and intensity on P2 component latency and amplitude. *Int J Psychophysiol*. 2005;55:323-31.
- Coplan JD, Lydiard RB. Brain circuits in panic disorder. *Biol Psychiatry*. 1998;44:1264-76.
- Derogatis LR, Melisaratos N. The Brief Symptom Inventory- An introductory report. *Psychol Med*. 1983;13:595-605.
- Di Russo F, Zaccara G, Ragazzoni A, Pallanti S. Abnormal visual event-related potentials in obsessive-compulsive disorder without panic disorder or depression comorbidity. *J. Psychiatr Res*. 2000;34:75-82.
- Dowman R. The Pain-Evoked P2 Is Not a P3a Event-Related Potential. *Brain Topogr*. 2004;17:3.
- Durston S, Thomas KM, Worden MS, Yang Y, Casey BJ. The Effect of Preceding Context on Inhibition: An Event-Related fMRI Study. *NeuroImage*. 2002;16:449-53.
- Eimer M. Effects of attention and stimulus probability on ERPs in a Go/Nogo task. *Biol Psychology*. 1993;35:123-38.
- Epstein JN, Johnson DE, Varia IM, Conners CK. Neuropsychological assessment of response inhibition in adults with ADHD. *J Clin Exp Neuropsychol*. 2001;23:362-71.
- Falkenstein M, Hoormann J, Hohnsbein J. ERP components in Go/Nogo tasks and their relation to inhibition. *Acta Psychol. (Amst.)*. 1999;101:267-91.
- Fallgatter AJ, Strik WK. The NoGo-anteriorization as a neurophysiological standard-index for cognitive response control. *Int J Psychophysiol*. 1999;32:233-8.
- Goddard AW, Shekhar A, Whiteman AF, McDougale CJ. Serotonergic mechanisms in the treatment of obsessive-compulsive disorder. *Drug Discov Today*. 2008;13:325-32.
- Gohle D, Juckel G, Mavrogiorgou P, Pogarell O, Mulert C, Rujescu D, et al. Electrophysiological evidence for cortical abnormalities in obsessive-compulsive disorder - A replication study using auditory event-related P300 subcomponents. *J. Psychiatr Res*. 2008;42:297-303.
- Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischmann RL, Hill CL, et al. The Yale-Brown obsessive compulsive scale. *Arch Gen Psychiatry*. 1989;46:1006-11.
- Greisberg S, McKay D. Neuropsychology of obsessive-compulsive disorder: a review and treatment implications. *Clin Psychol Rev* 2003;23:95-117.
- Hashimoto T, Shimizu E, Koike K, Orita Y, Suzuki T, Kanahara N, et al. Deficits in auditory P50 inhibition in obsessive-compulsive disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2008;32:288-96.
- Hegerl U, Gallinat J, Juckel G. Event-related potentials: Do they reflect central serotonergic neurotransmission and do they predict clinical response to serotonin agonists? *J Affect Disord*. 2001;62:93-100.
- Hegerl U, Juckel G. Intensity dependence of auditory evoked potentials as an indicator of central serotonergic neurotransmission: A new hypothesis. *Biol Psychiatry*. 1993;33:173-87.
- Heller W, Nitschke JB, Etienne MA, Miller GA. Patterns of regional brain activity differentiate types of anxiety. *J Abnorm Psychol*. 1997;106:376-85.
- Herrmann MJ, Jacob C, Unterecker S, Fallgatter AJ. Reduced response-inhibition in obsessive-compulsive disorder measured with topographic evoked potential mapping. *Psychiatr*

- Res. 2003;120:265-71.
- Hesse S, Muller U, Lincke T, Barthel H, Villmann T, Angermeyer MC, et al. Serotonin and dopamine transporter imaging in patients with obsessive-compulsive disorder. *Psychiatry Research: Neuroimaging*. 2005;140:63-72.
- Jodo E, Kayama Y. Relation of a negative ERP component to response inhibition in a Go/No-go task. *Electroencephalogr and Clin Neurophysiol*. 1992;82:477-82.
- Johannes S, Wieringa BM, Nager W, Rada D, Dengler R, Emrich HM, et al. Discrepant target detection and action monitoring in obsessive-compulsive disorder. *Psychiatr Res: Neuroimaging*. 2001;108:101-10.
- Johnstone SJ, Barry RJ, Anderson JW. Topographic distribution and developmental timecourse of auditory event-related potentials in two subtypes of attention-deficit hyperactivity disorder. *Int J Psychophysiol*. 2001;42:73-94.
- Jonkman LM, Sniedt FLF, Kemner C. Source localization of the Nogo-N2: A developmental study. *Clin Neurophysiol*. 2007;118:1069-77.
- Juckel G, Gallinat J, Riedel M, Sokullu S, Schulz C, Möller H-J, et al. Serotonergic dysfunction in schizophrenia assessed by the loudness dependence measure of primary auditory cortex evoked activity. *Schizophr Res*. 2003;64:115-24.
- Juckel G, Gudlowski Y, Müller D, Özgürdal S, Brüne M, Gallinat J, et al. Loudness dependence of the auditory evoked N1/P2 component as an indicator of serotonergic dysfunction in patients with schizophrenia - A replication study. *Psychiatr Res*. 2008;158:79-82.
- Kaiser S, Weiss O, Hill H, Markela-Lerenc J, Kiefer M, Weisbrod M. N2 event-related potential correlates of response inhibition in an auditory Go/Nogo task. *Int J Psychophysiol*. 2006;279-82.
- Kim M-S, Kim YY, Yoo SY, Kwon JS. Electrophysiological correlates of behavioral response inhibition in patients with obsessive-compulsive disorder. *Depress Anxiety*. 2007;24:22-31.
- Kivircik BB, Yener GG, Alptekin K, Aydin H. Event-related potentials and neuropsychological tests in obsessive-compulsive disorder. *Prog. Neuropsychopharmacol Biol Psychiatry*. 2003 2003;6;27:601-6.
- Klein RM. Inhibition of return. *Trends Cogn Sci*. 2000;4:138-47.
- Kopp B, Mattler U, Goertz R, Rist F. N2, P3 and the lateralized readiness potential in a nogo task involving selective response priming. *Electroen Clin Neuro*. 1996;99:19-27.
- Kuelz AK, Hohagen F, Voderholzer U. Neuropsychological performance in obsessive-compulsive disorder: a critical review. *Biol Psychol*. 2004;65:185-236.
- Lin P-Y. Meta-analysis of the association of serotonin transporter gene polymorphism with obsessive-compulsive disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2007;31:683-9.
- Ludewig S, Geyer MA, Ramseier M, Vollenweider FX, Rechsteiner E, Cattapan-Ludewig K. Information-processing deficits and cognitive dysfunction in panic disorder. *J Psychiatry Neurosci*. 2005;30:37.
- Ludewig S, Ludewig K, Geyer M, Hell D, Vollenweider F. Prepulse inhibition deficits in patients with panic disorder. *Depress Anxiety*. 2002;15:55-60.
- Malloy P, Rasmussen S, Braden W, Haier RJ. Topographic evoked potential mapping in obsessive-compulsive disorder: Evidence of frontal lobe dysfunction. *Psychiatr Res*. 1989;28:63-71.
- Maltby N, Tolin DF, Worhunsky P, O'Keefe TM, Kiehl KA. Dysfunctional action monitoring hyperactivates frontal-striatal circuits in obsessive-compulsive disorder: an event-related fMRI study. *NeuroImage*. 2005;24:495-503.
- Mataix-Cols D, van den Heuvel OA. Common and distinct neural correlates of obsessive-

- compulsive and related disorders. *Psychiatr Clin North Am.* 2006;29:391.
- Matsumoto R, Ichise M, Ito H, Ando T, Takahashi H, Ikoma Y, et al. Reduced serotonin transporter binding in the insular cortex in patients with obsessive-compulsive disorder: A DASB PET study. *Neuroimage.* 2010;49:121-6.
- McCarthy G, Wood CC. Scalp distributions of event-related potentials: an ambiguity associated with analysis of variance models. *Electroencephalogr Clin Neurophysiol.* 1985;62:203.
- Menzies L, Chamberlain SR, Laird AR, Thelen SM, Sahakian BJ, Bullmore ET. Integrating evidence from neuroimaging and neuropsychological studies of obsessive-compulsive disorder: The orbitofronto-striatal model revisited. *Neurosci Biobehav Rev* 2008;32:525-49.
- Miyata, Matsunaga, Kiriike, Iwasaki, Takei, Yamagami. Event-related potentials in patients with obsessive-compulsive disorder. *Psychiatry Clin Neurosci.* 1998;52:513-8.
- Miyata, Matsunaga, Kiriike, Iwasaki, Takei, Yamagami. Event-related potentials in patients with obsessive-compulsive disorder. *Psychiatry Clin Neurosci.* 1998;52:513-8.
- Morault P, Bourgeois M, Laville J, Bensch C, Paty J. Psychophysiological and Clinical Value of Event-Related Potentials in Obsessive-Compulsive Disorder. *Biol Psychiatry.* 1997 1997/7/1;42:46-56.
- Muller J, Roberts J. Memory and attention in Obsessive-Compulsive Disorder: a review. *J Anxiety Disord.* 2005;19:1-28.
- Murphy F, Sahakian B, Rubinsztein J, Michael A, Rogers R, Robbins T, et al. Emotional bias and inhibitory control processes in mania and depression. *Psychol Med.* 1999;29:1307-21.
- Nigg JT. On inhibition/disinhibition in developmental psychopathology: Views from cognitive and personality psychology and a working inhibition taxonomy. *Psychol. Bull.* 2000;126:220-46.
- Norra C, Mrazek M, Tuchtenhagen F, Gobbelé R, Buchner H, Saß H, et al. Enhanced intensity dependence as a marker of low serotonergic neurotransmission in borderline personality disorder. *J Psychiatr Res.* 2003;37:23-33.
- Oades RD, Dittmann-Balcar A, Schepker R, Eggers C, Zerbin D. Auditory event-related potentials (ERPs) and mismatch negativity (MMN) in healthy children and those with attention-deficit or tourette/tic symptoms. *Biol Psychol.* 1996;43:163-85.
- Oades RD, Zerbin D, Dittmann-Balcar A, Eggers C. Auditory event-related potential (ERP) and difference-wave topography in schizophrenic patients with/without active hallucinations and delusions: a comparison with young obsessive-compulsive disorder (OCD) and healthy subjects. *Int J Psychophysiol.* 1996;22:185-214.
- Obsessive compulsive cognitions working g. Development and initial validation of the obsessive beliefs questionnaire and the interpretation of intrusions inventory. *Behav Res Ther.* 2001;39:987-1006.
- Obsessive Compulsive Cognitions Working Group. Psychometric validation of the obsessive belief questionnaire and interpretation of intrusions inventory--Part 2: Factor analyses and testing of a brief version. *Behav Res Ther.* 2005;43:1527-42.
- Obsessive Compulsive Cognitions Working Group. Cognitive assessment of obsessive-compulsive disorder. *Behav Res Ther.* 1997 1997/7;35:667-81.
- Ohta H, Yamagata B, Tomioka H, Takahashi T, Yano M, Nakagome K, et al. Hypofrontality in panic disorder and major depressive disorder assessed by multi-channel near-infrared spectroscopy. *Depress Anxiety.* 2008;25:1053-9.
- Olley A, Malhi G, Sachdev P. Memory and executive functioning in obsessive-compulsive disorder: A selective review. *J Affect Disord.* 2007;104:15-23.
- Paradiso S, Lamberty GJ, Garvey MJ, Robinson RG. Cognitive impairment in the euthymic phase of chronic unipolar depression. *J Nerv Mental Dis.* 1997;185:748-54.

- Perani D, Garibotto V, Gorini A, Moresco RM, Henin M, Panzacchi A, et al. In vivo PET study of 5HT_{2A} serotonin and D₂ dopamine dysfunction in drug-naïve obsessive-compulsive disorder. *NeuroImage*. 2008;42:306-14.
- Picton TW, Bentin S, Berg P, Donchin E, Hillyard R, Johnson RJ, et al. Guidelines for using human event-related potentials to study cognition: recording standards and publication criteria. *Psychophysiology*. 2000.
- Posner MI, Snyder CR. Facilitation and inhibition in the processing of signals. In: Rabbitt PMA, Dornic S, editors. *Attention and Performance* London: Academic Press; 1975. p. 669-81.
- Radua J, van den Heuvel OA, Surguladze S, Mataix-Cols D. Meta-analytical comparison of voxel-based morphometry studies in obsessive-compulsive disorder vs other anxiety disorders. *Arch Gen Psychiatry*. 2010;67:701.
- Ratcliff R. Methods for dealing with reaction time outliers. *Psychol Bull*. 1993;114: 510.
- Rauch SL, Savage CR, Alpert NM, Fischman AJ, Jenike MA. The Functional Neuroanatomy of Anxiety: A Study of Three Disorders Using Positron Emission Tomography and Symptom Provocation. *Biol Psychiatry*. 1997;42:446-52.
- Roberts LE, Rau H, Lutzenberger W, Birbaumer N. Mapping P300 waves onto inhibition: Go/No---Go discrimination. *Electroencephal Clin Neurophysiol*. 1994;92:44-55.
- Roche RAP, Garavan H, Foxe JJ, O'Mara SM. Individual differences discriminate event-related potentials but not performance during response inhibition. *Exp Brain Res*. 2005;160:60-70.
- Roth RM, Saykin AJ, Flashman LA, Pixley HS, West JD, Mamourian AC. Event-Related Functional Magnetic Resonance Imaging of Response Inhibition in Obsessive-Compulsive Disorder. *Biol Psychiatry*. 2007;62:901-9.
- Ruchow M, Reuter K, Hermle L, Ebert D, Kiefer M, Falkenstein M. Executive control in obsessive-compulsive disorder: event-related potentials in a Go/Nogo task. *J Neural Transm*. 2007;114:1595-601.
- Salisbury DF, Griggs CB, Shenton ME, McCarley RW. The NoGo P300 'anteriorization' effect and response inhibition. *Clin Neurophysiol*. 2004;115:1550-8.
- Salisbury DF, Griggs CB, Shenton ME, McCarley RW. The NoGo P300anteriorization'effect and response inhibition. *Clin neurophysiol*. 2004;115:1550.
- Sanz M, Molina V, Martin-Loeches M, Calcedo A, Rubia FJ. Auditory P300 event related potential and serotonin reuptake inhibitor treatment in obsessive-compulsive disorder patients. *Psychiatr Res*. 2001;101:75-81.
- Saxena S, Rauch SL. Functional Neuroimaging and the anatomy of obsessive-compulsive disorder. *Psychiatr Clin North Am*. 2000;23:563-86.
- Schall U, Schon A, Zerbin D, Bender S, Eggers C, Oades RD. A left temporal lobe impairment of auditory information processing in schizophrenia: an event-related potential study. *Neurosci Lett*. 1997;229:25-8.
- Semlitsch HV, Anderer P, Schuster P, Presslich O. A solution for reliable and valid reduction of ocular artifacts, applied to the P300 ERP. *Psychophysiology*. 1986;23:695-703.
- Senkowski D, Linden M, Zubrägel D, Bär T, Gallinat J. Evidence for disturbed cortical signal processing and altered serotonergic neurotransmission in generalized anxiety disorder. *Biol Psychiatry*. 2003;53:304-14.
- Simpson HB, Rosen W, Huppert JD, Lin SH, Foa EB, Liebowitz MR. Are there reliable neuropsychological deficits in obsessive-compulsive disorder? *J Psychiatr Res*. 2006;40:247-57.
- Stein DJ, Fineberg NA, Bienvenu OJ, Denys D, Lochner C, Nestadt G, et al. Should OCD be classified as an anxiety disorder in DSM-V? *Depress Anxiety*. 2010;27:495-506.
- Tabachnick BG, Fidell LS, Osterlind SJ. *Using Multivariate Statistics*. 2001. Allyn and Bacon

Boston.

- Taylor S. Endophenotypes of obsessive–compulsive disorder: Current status and future directions. *J Obsessive Compuls Relat Disord*. 2012;1:258-62.
- Thomas SJ, Gonsalvez CJ, Johnstone SJ. Neural time course of threat-related attentional bias and interference in panic and obsessive-compulsive disorders. *Biol Psychol*. 2013;94:116-129.
- Thomas SJ, Gonsalvez CJ, Johnstone SJ. Sequence effects in the Go/NoGo task: Inhibition and facilitation. *Int J Psychophysiol*. 2009;74:209-219.
- Towey J, Bruder G, Hollander E, Friedman D, Erhan H, Liebowitz M, et al. Endogenous event-related potentials in obsessive-compulsive disorder. *Biol Psychiatry*. 1990;28:92-8.
- Towey J, Bruder G, Tenke C, Leite P, DeCaria C, Friedman D, et al. Event-related potential and clinical correlates of neurodysfunction in obsessive-compulsive disorder. *Psychiatr Res*. 1993;49:167-81.
- van den Heuvel OA, Veltman DJ, Groenewegen HJ, Witter MP, Merkelbach J, Cath DC, et al. Disorder-specific neuroanatomical correlates of attentional bias in obsessive-compulsive disorder, panic disorder, and hypochondriasis. *Arch Gen Psychiatry*. 2005;62:922-33.
- Wang J, Miyazato H, Randall M, Hokama H, Hiramatsu K, Ogura C. The N200 abnormalities of auditory event-related potentials in patients with panic disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2003;27:1013-21.
- Warren CM, Tanaka JW, Holroyd CB. What can topology changes in the oddball N2 reveal about underlying processes? *Neuroreport*. 2011;22:870-4.
- Whiteside SP, Port JD, Abramowitz JS. A meta-analysis of functional neuroimaging in obsessive–compulsive disorder. *Psychiatr Res Neuroimag*. 2004;132:69-79.
- World Health Organization. Composite International Diagnostic Interview: Administrator's guide and reference. Geneva, World Health Organization; 1997.
- Wise V, McFarlane AC, Clark CR, Battersby M. Event-related potential and autonomic signs of maladaptive information processing during an auditory oddball task in panic disorder. *Int J Psychophysiol*. 2009;74:34-44.

Legend of figures

Figure 1. Example of a stimulus train with four Go stimuli. A baseline stimulus (!) is followed by 1-4 go stimuli, and a NoGo stimulus (X-NoGo). These stimuli were followed by either another Go stimulus (X-Go) or dedicated NoGo stimulus (square), which are not examined here.

Figure 2. Grand mean waveforms to Go versus NoGo stimuli, by group.

Figure 3. Mean N2 amplitude across Go and NoGo stimuli, by Sagittal plane and Group.

Figure 4. Grand mean waveforms to NoGo stimuli as a function of the number of immediately preceding Go stimuli in trains (GN-GGGGN), by Group. Note: x axis ticks = 100ms; y axis indicates stimulus onset.

Figure 5. Mean ERP amplitudes to NoGo stimuli for significant Group effects and interactions. Top left: P1 amplitude by lateral plane and Group: Top right: N1 amplitude by Lateral plane and Group: Middle left: P2 amplitude by Group: Middle right: P2 amplitude by Sagittal plane and Group: Bottom right. N2 amplitude by Sagittal plane and Group: Bottom right: P3 amplitude by Sagittal plane and group.

Figure 6. Mean ERP latencies (ms) to NoGo stimuli for significant Group effects and interactions. Left: N1 latency by Group. Right: N2 latency to NoGo stimuli by number of preceding Go stimuli (GN-GGGGN) and Group.

Figure 1
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Figure 2a
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Obsessive-compulsive disorder

Figure 3
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Figure 4
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Table1. Participant demographic characteristics

Variable		HC (n = 20)	PD (n = 20)	OCD (n = 20)	OCD vs. HC	OCD vs. PD	PD vs. HC
Mean age		33 (± 13)	38 (± 12)	39 (± 14)	Ns	Ns	Ns
Gender	Female	13	17	11	Ns	Ns	Ns
Handedness	Right handed	18	17	16	Ns	Ns	Ns
Medication	SSRI	0	6	8	-	-	-
	SNRI	0	0	2	-	-	-
	RIMA	0	0	1	-	-	-
	TCA	0	1	0	-	-	-
	Occasional benzodiazepine	0	1	1	-	-	-
	Combined SSRI and occasional benzodiazepine	0	2	0	-	-	-
	Total on psychotropic medication	0	10	12	***	Ns	***

* $p < .05$, ** $p < .01$, *** $p < .001$. SSRI – selective serotonin reuptake inhibitors; SNRI- Serotonin-norepinephrine reuptake inhibitors; RIMA- Reversible Inhibitor of Monoamine-Oxidase-A.

Table 2

Table 2. Scores in psychometric questionnaires, by group.

Variable		HC (n = 20)	PD (n = 20)	OCD (n = 20)	OCD vs. HC	OCD vs. PD	PD vs. HC
		M (±)	M (±)	M (±)	-	-	-
Yale Brown Obsessive-Compulsive Scale (Y-BOCS)	Obsessions	-	-	14 (6)	-	-	-
	Compulsions	-	-	12 (6)	-	-	-
	Y-BOCS Total	-	-	26 (12)	-	-	-
Brief symptom inventory (BSI)	Depression subscale	.59 (1)	1.41 (1)	1.61 (1)	**	Ns	*
	Phobic anxiety subscale	.3 (1)	1.86 (2)	1.57 (1)	***	Ns	***
	Obsessive-Compulsive subscale	1.01 (1)	1.7 (1)	1.87 (1)	*	Ns	Ns
	Anxiety subscale	.53 (1)	1.9 (1)	2.1 (1)	***	Ns	***
	BSI Global Severity Index	.6 (1)	1.46 (1)	1.6 (1)	**	Ns	**
Padua Inventory	Total Padua score	13 (11)	20 (14)	49 (33)	***	***	Ns
Obsessional Beliefs Questionnaire (OBQ-44)	Responsibility/ threat	50 (16)	64 (22)	72 (21)	**	Ns	Ns
	Perfectionism/ certainty	55 (20)	67 (23)	74 (23)	*	Ns	Ns
	Importance/ control of thoughts	28 (10)	39 (19)	49 (13)	***	Ns	Ns
	OBQ-44 Total score	133 (43)	170 (56)	195 (53)	***	Ns	Ns

* $p < .05$, ** $p < .01$, *** $p < .001$. Note: the Y-BOCS, a measure of OCD severity, was only administered to the OCD group.

Table 3. Mean RT (Ms) and percentage of errors by stimulus type, serial position and group. GN-GGGN indicates NoGo stimuli preceded by one-four Go stimuli respectively.

Stimulus		Healthy control (HC)	Panic disorder (PD)	Obsessive-compulsive disorder (OCD)
Go	RT (SD)	394 (63)	458 (85)	448 (90)
	% Errors (SD)	.03 (.1)	.03 (.05)	.01 (.02)
NoGo	Errors (SD)	.03 (.1)	.03 (.05)	.01 (.02)
GN	Errors (SD)	.09 (.1)	.12 (.3)	.01 (.01)
GGN	Errors (SD)	.09 (.09)	.15 (.29)	.08 (.1)
GGGN	Errors (SD)	.07 (.08)	.11 (.29)	.05 (.09)
GGGGN	Errors (SD)	.05 (.07)	.12 (.3)	.03 (.06)
Baseline stimulus	Errors (SD)	0.2 (.4)	0.25 (.8)	0.3 (.7)

Table 4

Table 4. ANOVA probabilities for significant overall Group effects and interactions and two-group comparisons.

Analysis	Measure		Contrast	ANOVA (<i>P</i> -value)	Simple effects contrasts (<i>P</i> -value)		
Go versus NoGo				Overall Group effect	OCD vs. HC	PD vs. HC	OCD vs. PD
	N2	amplitude	Group x sagittal (linear)	0.045	0.046	0.051	0.959
Inhibition as a function of sequence	P1	amplitude	Group by Laterality (linear)	0.017	0.621	0.021	0.024
	N1	amplitude	Group by Laterality (linear)	0.044	0.104	0.023	0.414
	N1	latency	Group main effect	0.002	0.001	0.002	0.436
	P2	amplitude	Group main effect	0.000	0.000	0.015	0.019
	N2	amplitude	Group by Sagittal (linear)	0.008	0.013	0.017	0.871
		latency	Group by stimulus	0.019	0.025	0.007	0.678
		latency	Group main effect	0.017	0.655	0.008	0.041
	P3	amplitude	Group by Sagittal (linear)	0.006	0.004	0.019	0.711