

Alpha activity in the insula accompanies the urge to neutralize in sub-clinical obsessive–compulsive participants

RHIANNON JONES* and JOYDEEP BHATTACHARYA

Department of Psychology, Goldsmiths, University of London, London, UK

(Received: May 2, 2012; revised manuscript received: July 3, 2012; accepted: July 14, 2012)

Background and aims: The behavioural addiction model of obsessive–compulsive disorder (OCD) proposes that as compulsions successfully reduce obsession-provoked anxiety in the early stages of the disorder, their performance is rewarding and therefore potentially addictive. According to this theory, the urge to perform a compulsion or neutralization resembles craving in addiction, and ventral fronto-striatal reward circuitry is activated during compulsive or neutralizing behaviour, resembling substance addiction disorders. The current study used EEG source localisation to test this hypothesis by examining brain activity accompanying the urge to neutralize and covert neutralization. **Methods:** Two groups of non-clinical participants (15 Low-OC, 15 High-OC) performed a task in which the urge to neutralize was induced by supplying participants with an obsessive–compulsive-like thought. Source localised EEG activity was compared between a negative condition with high urge to neutralize, and a positive condition with low urge to neutralize, and correlations between brain activity and self-reported urge to neutralize were examined. **Results:** High-OC participants reported a significantly greater urge to neutralize than Low-OC participants, and the majority of participants reported performing covert neutralization during the experiment. Between-condition comparisons in the High-OC group revealed significantly greater alpha activity in the insula and vIPFC in the negative than the positive condition, which was significantly correlated with both urge to neutralize and later decrease in negative affect. **Conclusions:** The current results support the proposal that the urge to neutralize in OCD is neurally similar to craving in substance addiction, in agreement with the behavioural addiction model of OCD.

Keywords: behavioural addiction, insula, LORETA, neutralization, obsessive–compulsive disorder

INTRODUCTION

Obsessive–compulsive disorder (OCD) is a chronic and severely debilitating psychiatric disorder which is believed to affect approximately 1–3% of the population (Rasmussen & Eisen, 1994; Torres et al., 2006). OCD is characterised by the presence of obsessions and compulsions. Obsessions take the form of intrusive, repetitive and distressing thoughts, images or urges, which are ego-dystonic in nature. Compulsions take the form of repetitive behaviours or mental rituals which are performed in order to decrease the distress caused by the obsessions (American Psychiatric Association, 2000).

The most widely accepted model of neural circuitry underlying the symptoms of OCD proposes an imbalance between ventral and dorsal fronto-striatal networks, specifically relating to hyperactivity and hypoactivity of the direct and indirect basal ganglia pathways, respectively (Mataix-Cols & van den Heuvel, 2006; Saxena & Rauch, 2000). It is suggested that this imbalance may be mediated by the dopamine system, whereby hyperactivity of the ventral pathway is the result of stronger D₁ receptor expression, and hypoactivity of the dorsal pathway is the result of stronger D₂ receptor expression (see Van den Heuvel et al., 2010). Support for the fronto-striatal model includes set-shifting deficits in OCD populations (Chamberlain et al., 2008) and abnormal activation of ventral prefrontal-striatal circuitry during response inhibition (Roth et al., 2007).

An alternative, although not mutually exclusive, model considers OCD as a form of behavioural addiction with its basis in dysfunctional reward circuitry and the dopaminer-

gic system (Denys, Zohar & Westenberg, 2004; Holden, 2001; Marks, 1990). This model suggests that compulsions evolve over time in a way similar to a substance-use addiction; initially a compulsion is freely chosen as a method of decreasing the anxiety provoked by an obsessive thought, is successful in relieving anxiety, and is relatively limited in terms of the time and effort which is required to perform it. As time goes on, however, the compulsion is considered essential, has lost its effectiveness, and increases in length and effort of performance. This progression seems comparable to the pattern of addiction, in which a drug is initially taken freely in order to experience its rewarding effects, but eventually is considered essential, the rewarding effects decrease, and the individual feels it necessary to take ever increasing amounts (Denys, 2011).

This model is supported by neurobiological similarities between OCD and addiction disorders, such as increased dopamine overactivity in ascending pathways involving D_{2/3} receptors (Denys et al., 2004; Hesse et al., 2005; Van der Wee et al., 2004; Volkow & Fowler, 2000; Volkov et al., 1993, 2001) and defective processing of natural rewards (Figeo et al., 2011; Nielen, den Boer & Smid, 2009). The similarity of OCD and addictive circuitry is also shown in a review by Van den Heuvel et al. (2010), who illustrates that a similar disinhibition of ventral and inhibition of dorsal

* Corresponding author; Rhiannon Jones, Department of Psychology, Goldsmiths, University of London, Lewisham Way, New Cross SE14 6NW; Phone: +44-2070785128; E-mail: rhiannon.jones@gold.ac.uk

fronto-striatal pathways is present in cocaine dependency and impulse control in Parkinson's disease as is present in OCD. Furthermore a review of similarities and distinctions in neural circuitry, neurobiology, and endophenotypes across OCD and other compulsive and impulsive disorders suggests that the impulsive-compulsive spectrum involves "a complicated interaction of multiple, orthogonally related diatheses" (Fineberg et al., 2010, p. 600).

According to the behavioural addiction model of OCD one would expect the urge to carry out a compulsion to activate similar circuitry as the urge to engage in addictive behaviour. However, while reward-related structures are activated during OCD symptom provocation (Liu, Hairston, Schrier & Fan, 2011; Rotge et al., 2008), no study to date has shown a specific relationship between this activation and the subjective urge to perform a compulsion or neutralize an obsessive thought.

The current experiment investigated whether activation of reward circuitry accompanies the urge to neutralize during obsessive-compulsive cognitions. Neutralization refers to a covert mental process which is functionally similar to a compulsion in that it is performed to 'cancel out' the effects of an intrusive obsessive thought; for example by following a negative thought with a positive thought (Salkovskis, 1985). This is believed to reduce the probability of misfortune occurring as a result of the thought, and reduce one's feeling of responsibility for any such misfortune (Salkovskis, 1996).

We used a modification of Rachman, Shafran, Mitchell, Trant and Teachmann's (1996) thought-action fusion (TAF) paradigm which has been widely used to induce an urge to neutralize in non-clinical participants (Bocci & Gordon, 2007; Marcks & Woods, 2007; Rassin, 2001; Van den Hout, van Pol & Peters, 2001; Van den Hout, Kindt, Weiland & Peters, 2002; Zucker, Craske, Barrios & Holguin, 2002) and used low resolution brain electromagnetic tomography (LORETA) to localise the sources of neutralization-related electrical brain activity (electroencephalogram, EEG). In this paradigm, participants are given a sentence to copy, containing a blank space in which they insert the name of a loved one (e.g. "I hope that _____ has a car accident."). This results in the participant believing that they have increased the likelihood of harm befalling their loved one in reality – a concept known as likelihood-thought-action fusion (TAF-Likelihood: Shafran, Thordardson & Rachman, 1996), and is accompanied by feelings of guilt, anxiety, and the urge to neutralize the potential harm. Following previous replications of this paradigm (Bocci & Gordon, 2007; Marcks & Woods, 2007; Rassin, 2001; Van den Hout et al., 2001; Van den Hout et al., 2002; Zucker et al., 2002) we predicted that participants' anxiety, guilt, urge to neutralize and estimated likelihood of harm occurring would decrease significantly over the course of a trial, and that participants would report using spontaneous neutralization techniques (Bocci & Gordon, 2007; Van den Hout et al., 2002). We also predicted that participants with higher levels of OC traits would report higher levels of anxiety, guilt, likelihood and urge to neutralize. Finally, on the basis of the reduced insula activation in OCD patients during natural reward (Figeet et al., 2011) and the strong link between the insula and craving in addiction (Naqvi & Bechara, 2008; Paulus, 2007), we predicted that the main generator of urge-related neural activity to be the insula.

METHODS

Participants

Fifteen individuals with high (High-OC) and 15 age-matched individuals with low obsessive-compulsive traits (Low-OC) were selected to participate based on their scores on the Obsessive-Compulsive Inventory – Revised (OCI-R; Foa, Huppert, Leiberg, Langner & Kichic et al., 2002). The OCI-R score of the High-OC group was significantly higher ($t(28) = 13.02, p < .0001$) than that of the Low-OC group. Participant demographics are shown in Table 1. Participants completed a visual analogue scale for self-reported anxiety before the experiment began, which showed no difference between the High-OC (2.2 ± 1.7) and Low-OC (1.9 ± 1.7) groups ($t = .434, p = .67$). The study protocol was approved by the local Ethics Committee at Goldsmiths, University of London.

Table 1. Participant demographics according to OC-group

	Low-OC	High-OC
	<i>N</i> = 15	<i>N</i> = 15
Sex: M/F	5/10	6/9
Age:	25.7 ± 2.5	25.7 ± 4.3
OCI-R Total:	5.2 ± 3.3	28.9 ± 6.2
OCI-R Subscales:		
Hoarding	2.0 ± 1.8	5.3 ± 3.9
Checking	0.9 ± 1.6	5.7 ± 2.3
Ordering	1.1 ± 1.3	6.2 ± 3.4
Neutralizing	0.1 ± 0.4	3.3 ± 3.4
Washing	0.4 ± 1.1	3.0 ± 3.2
Obsessing	0.6 ± 0.8	5.5 ± 3.7

Stimuli

Stimuli were four positive and four negative sentences written in the first person, with a blank space for name insertion, e.g. "I hope that _____ wins the lottery soon", and "I hope that _____ becomes seriously ill soon." The events used in these stimuli were closely matched for relative positive and negative valence as rated by an independent sample of 25 undergraduates (21 females, mean age = 19.36 ± 1.78 years).

Visual analogue scales

At three points during each experimental trial participants completed visual analogue scales (VAS) to indicate their emotions at that particular time. Four VAS were used, with a scale ranging from 0 (not at all) to 10 (very much). The VAS assessed: Anxiety, Guilt, Likelihood (estimated likelihood of the event occurring), and Urge to Neutralize (urge to 'cancel out' what they had done).

Use of spontaneous neutralization strategies:

Post experiment

Following experiment completion, participants were given the instructions:

"Please write in the space below any strategies you used to make yourself feel better about reading out the negative sentences, e.g. reminding yourself that you did not mean what you said, or any 'mental ritual'. Please go into as much detail as you are able."

Task and procedure

Before the experiment, participants wrote a list of close family and friends, and were restricted to using these names for insertion into the sentence stimuli.

Participants were seated in a dark room with an intercom connection to the experimenters. All instructions and stimuli were presented on a computer monitor located approximately 90 cm from the participants. Participants completed an on screen VAS for their current level of anxiety before performing a practice trial which was identical to the experimental trials, but with a neutral sentence.

Each trial was composed of three phases: Reading phase, Visualisation phase, and Suppression phase (Figure 1). The reading phase began with presentation of the sentence stimulus on screen. Participants were required to close their eyes and to repeat the sentence aloud, inserting their chosen name. Participants then completed the four on-screen VAS of anxiety, guilt, likelihood and urge to neutralize.

The visualisation phase followed, in which the participants were instructed to close their eyes and visualise the stimulus event in as much detail as possible. This phase lasted 1 min, after which a beep prompted participants to open their eyes and complete the four VAS for a second time. Then in the suppression phase participants were instructed to think about anything except for the stimulus event for a further 1 min, and to press a button every time a thought of the event came to mind. The four VAS were again completed. Participants were then given the option to neutralize. A short Go/NoGo task was then performed and participants were given a short break before beginning the following trial. The order of positive and negative trials was randomised.

EEG Data. Sixty-four channel EEG was continuously recorded by active scalp electrodes according to the extended 10–20 international system of electrode placement

(Jasper, 1958). Electrodes were placed above, below and at the outer canthus of each eye, to record vertical and horizontal eye movements. The EEG signals were amplified by BioSemi Active Two® amplifiers and filtered between 0.6–100 Hz. The sampling frequency was 512 Hz.

EEG data were re-referenced offline to an average reference montage (excluding T7 and T8 due to noisy recordings). Power line noise was removed by a notch filter at 50 Hz with a bandwidth of 2 Hz. In the case of bad channels nearest neighbour interpolation was used (< 1 channel per participant on average). As suppression phase data was contaminated with motor activity relating to button presses indicating intrusive thoughts, only visualisation phase EEG data was used in the current analysis.

Four positive and negative visualisation epochs of one minute each were divided into 2-second non-overlapping epochs. Epochs containing muscle or eye-movement artefacts were rejected visually, leaving an average of 100.1 ± 13.0 and 98.2 ± 17.4 epochs for the Low-OC group, and 85.6 ± 17.6 and 92.9 ± 15.5 for the High-OC group, in the positive and negative conditions, respectively.

These epochs were also separated into the first and second half (30 seconds) of visualisation for both conditions, providing a mean of 48.9 ± 7.1 and 51.2 ± 7.3 epochs for the first and second half of the positive visualisation period for the Low-OC group and 42.1 ± 9.5 and 43.5 ± 8.8 epochs for the High-OC group, and 45.5 ± 10.6 and 50.9 ± 9.8 epochs for the first and second half of the negative visualisation for the Low-OC group, and 44.0 ± 8.8 and 48.9 ± 9.2 epochs for the High-OC group.

LORETA analysis. Standardized low resolution brain electromagnetic tomography (sLORETA) was used to compute the cortical three-dimensional distribution of current density. This method uses a linear, minimum norm inverse solution to give images of standardized current density with exact localisation and no localisation bias. While perfect to-

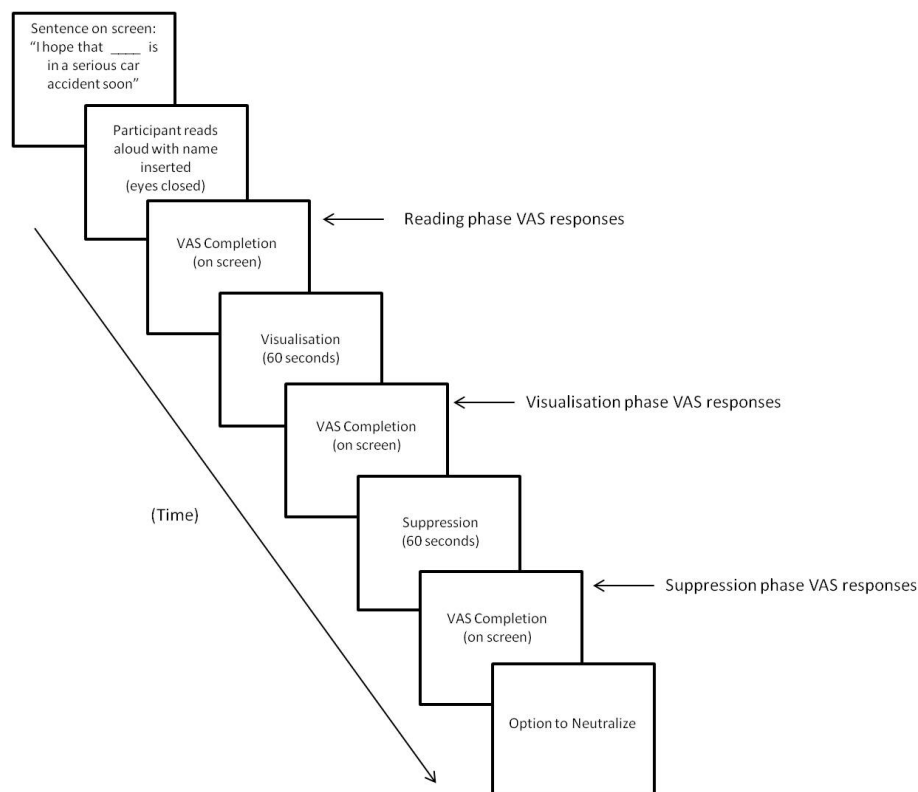


Figure 1. Schematic diagram of one experimental trial from the negative condition

mography cannot be achieved for the EEG, LORETA has the lowest level of localisation error of all published 3D, discrete, distributed, linear EEG/MEG tomographies, which is consistent even when sources are localised deep in the brain (Pascual-Marqui, 1999, 2002). In the current implementation of sLORETA, computations were made in a realistic head model (Fuchs, Kastner, Wagner, Hawes & Ebersole, 2002), using the MNI152 template (Mazziotta et al., 2001), with the three-dimensional solution space restricted to cortical gray matter, as determined by the probabilistic Talairach atlas (Lancaster et al., 2000). The LORETA-KEY software package (Pascual-Marqui, 2002) was used to compute average cross-spectral matrices for 8 EEG bands (Delta: 1.5–6 Hz, Theta: 6.5–8 Hz, Alpha1: 8.5–10 Hz, Alpha2: 10.5–12 Hz, Beta1: 12.5–18 Hz, Beta2: 18.5–21 Hz, Beta3: 21.5–30 Hz, and the total spectral power: 1.5–30 Hz), providing a single cross-spectral matrix for each participant, frequency band and condition, from which current source density was calculated.

Current source density values were log-transformed and normalised to reduce the effects of individual difference in skull thickness, etc. Non-parametric statistical analysis was performed for between group differences within valence conditions, and within group differences between conditions. This is based on estimating the empirical probability distribution of the maximum *t* statistic under the null hypothesis, via 5000 randomisations, and corrects for multiple comparisons of all 2394 voxels and all discrete frequencies, as is standard for LORETA analysis (see Nichols & Holmes,

2002 for information regarding this permutation procedure), with a significance level of $p < .05$.

RESULTS

Visual analogue scale responses

Participants' responses on the VAS (Anxiety, Guilt, Likelihood, Urge to Neutralize) recorded at the three *phases* (Reading, Visualisation, Suppression), for both *valences* (Positive, Negative), were entered into a mixed factorial ANOVA, with *group* (High-OC, Low-OC) as a between-subjects factor.

A main effect of *group* showed that the High-OC group gave significantly higher responses than the Low-OC group ($F(1, 28) = 6.009, p = .021$), and a main effect of *valence* showed that both groups gave higher responses in the negative than the positive condition ($F(1, 28) = 11.976, p = .002$).

The significant group difference remained in the negative condition ($F(1, 28) = 5.756, p = .023$), and a significant effect of *phase* showed that participants' ratings of anxiety, guilt, likelihood and urge to neutralize decreased significantly over the course of a trial ($F(2, 56) = 24.782, p < .001$) as shown in Figure 2.

In the positive condition, anxiety, guilt, and urge to neutralize were examined excluding likelihood as higher estimations of likelihood of the positive event's occurrence would not indicate negative affect. Surprisingly, the main

Negative condition

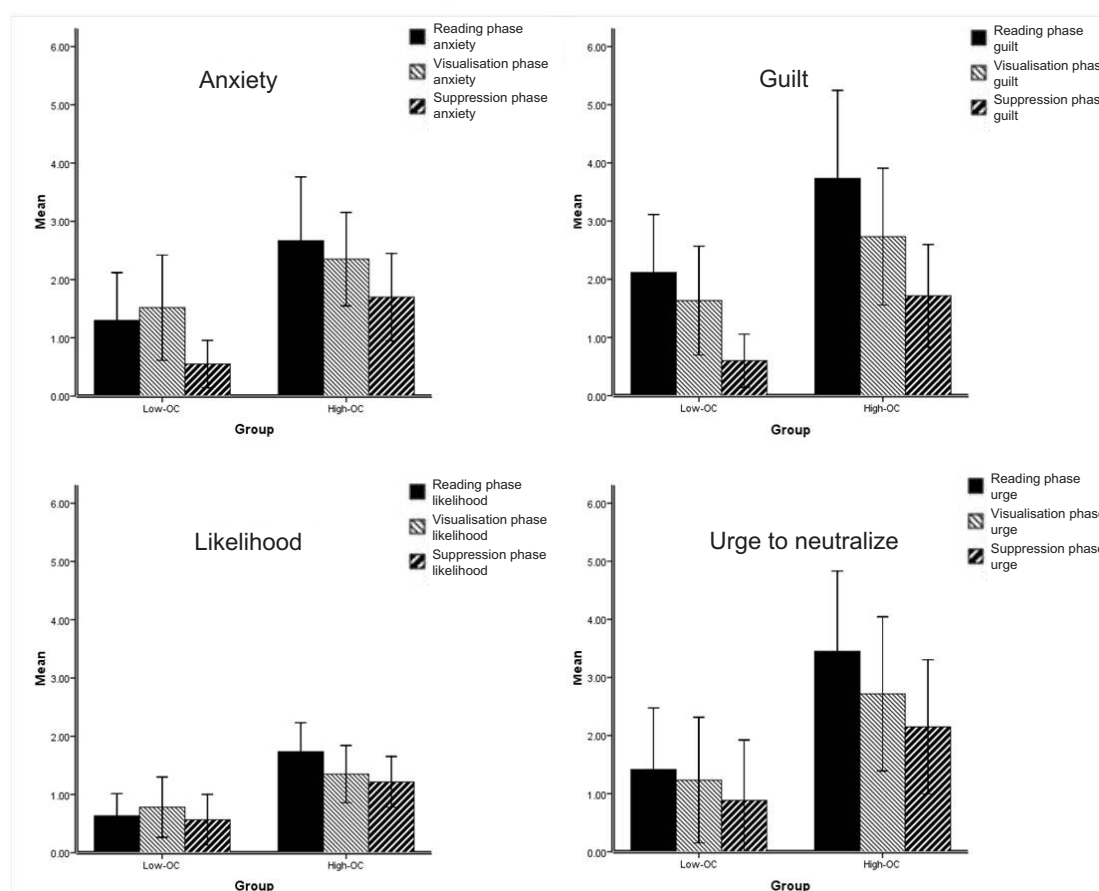


Figure 2. Means and standard errors of VAS responses from the Low-OC and High-OC groups for anxiety, guilt, likelihood, and urge to neutralize during negative trials at the reading, visualisation and suppression phases

effect of group remained significant ($F(1, 28) = 6.640, p = .016$) as the High-OC group reported significantly greater negative affect. No significant effect of *phase* was present ($F(2, 56) = .097, p = .91$) indicating that participants' VAS responses remained relatively stable throughout the trial. No significant effects of *group* or *phase* on likelihood were present.

Use of spontaneous neutralization techniques

Post-experiment reports of neutralization were available for 25 of the 30 participants (11 Low-OC; 14 High-OC). Of the 11 Low-OC participants, six (55%) reported mentally rehearsing that there would be no negative consequences of sentence reading because it was 'just an experiment', compared with 12 of the 14 High-OC participants (85.7%). Five (45.5%) Low-OC participants reported that they did not use any type of emotion regulation strategy, compared to only 2 (14.3%) High-OC participants.

Only one Low-OC participant (9.1%) reported using a strategy more akin to neutralization, in which they put a positive spin on the subject material. In contrast, 7 High-OC participants (50.0%) reported having used neutralization strategies including putting a positive spin on the material, mentally reversing the sentence, or rationalising the name choices and focusing on having 'saved' another of the names on their list.

LORETA activity during visualisation

High-OC vs. Low-OC group. Whole-brain analysis showed that the High-OC group had greater alpha1 current source density (henceforth to be referred to as 'activity') than the Low-OC group in the right superior frontal gyrus (rSFG) during the full negative visualisation. However, this difference was only present in the first 30s. During this period the High-OC group also showed higher theta activity in the right temporal and parietal regions and the insula (Table 2 and Figure 3). No between-group differences were present in the positive visualisation.

Negative vs. positive. No significant differences were found between the full negative and positive visualisation phases when both groups were combined or in the groups separately. However, comparisons of the first half of the visualisations, which was temporally closest to the reading phase in which the High-OC group reported their greatest levels of negative affect, significant differences were seen within the High-OC group. This contrast revealed significantly greater alpha1 and total spectral activity in a large left-lateralised area covering the vlPFC (BA44, 45 & 47) and insula (BA13) in the negative compared to the positive visualisation (see Table 3 and Figure 4). These differences, however, disappeared in the second half of the visualisations, consistent with the decrease in negative affect seen between the reading and the visualisation phase in this group. The Low-OC group showed no difference in activity between the negative and positive conditions.

The increase of insula activity in the High-OC during negative visualisation was consistent with our prediction that activation of this structure would accompany the urge to neutralize. In order to further clarify this relationship, we examined correlations between negative reading phase urge to neutralize in the entire sample ($N = 30$) and alpha band and total spectral activity of the insula/vlPFC voxels which

Table 2. Summary of whole-brain LORETA comparison (non-parametric unpaired *t*-test) of High-OC ($N = 15$) vs. Low-OC ($N = 15$) participants during the negative visualisation phase

Phase	Lobe	Region	BA	Hemi- sphere	X	Y	Z	Band
<i>Whole visualisation</i>								
	Frontal	SFG	6	R	18	−4	71	$\alpha 1$
		SFG	6	R	18	3	71	$\alpha 1$
<i>1st half of visualisation</i>								
	Temporal	STG	29	R	46	−32	15	θ
		STG	29	R	53	−32	15	θ
	Parietal	IPL	40	R	39	−32	43	θ
		PostCG	40	R	53	−25	15	θ
		PostCG	40	R	53	−25	22	θ
		PostCG	40	R	39	−32	50	θ
	Sub-lobar	Insula	13	R	46	−32	22	θ
		Insula	13	R	53	−32	22	θ
		Insula	13	R	46	−25	22	θ
	Frontal	SFG	6	R	18	−4	71	$\alpha 1$
		SFG	6	R	18	3	71	$\alpha 1$

Table 3. Summary of whole-brain LORETA comparison (non-parametric paired *t*-test) of the first half of the negative compared to the positive visualisation phase in High-OC participants ($N = 15$)

Lobe	Region	BA	Hemi-sphere	X	Y	Z	Band
Frontal	IFG	47	L	-52	17	1	$\alpha 1$
	IFG	47	L	-45	17	1	$\alpha 1$
	IFG	13	L	-38	24	8	$\alpha 1$
	IFG	45	L	-31	24	8	$\alpha 1$
	IFG	44	L	-52	10	8	$\alpha 1 \Omega$
	IFG	44	L	-59	17	15	$\alpha 1 \beta 1 \Omega$
	IFG	44	L	-52	17	15	$\alpha 1 \Omega$
	IFG	47	L	-52	31	-6	Ω
	IFG	45	L	-52	31	1	Ω
	IFG	44	L	-52	38	1	Ω
	IFG	45	L	-52	24	8	Ω
	IFG	45	L	-52	31	8	Ω
	IFG	45	L	-52	38	8	Ω
	PreCG	44	L	-52	17	8	$\alpha 1 \Omega$
	PreCG	44	L	-45	17	8	$\alpha 1 \Omega$
	PreCG	43	L	-52	-11	15	$\alpha 1$
	MFG	9	L	-45	31	36	$\alpha 2$
Sub-lobar	Extra-nuclear	13	L	-38	3	-6	$\alpha 1$
	Extra-nuclear	13	L	-38	10	-6	$\alpha 1$
	Extra-nuclear	47	L	-31	17	1	$\alpha 1$
	Insula	13	L	-45	3	1	$\alpha 1$
	Insula	13	L	-38	3	1	$\alpha 1$
	Insula	13	L	-45	10	1	$\alpha 1$
	Insula	13	L	-38	10	1	$\alpha 1$
	Insula	13	L	-38	17	1	$\alpha 1$
	Insula	13	L	-38	3	8	$\alpha 1$
	Insula	13	L	-38	10	8	$\alpha 1$
	Insula	13	L	-31	10	8	$\alpha 1$
	Insula	13	L	-38	17	8	$\alpha 1$
	Insula	13	L	-31	17	8	$\alpha 1$
	Insula	13	L	-45	-18	15	$\alpha 1$
Temporal	STG	22	L	-52	10	1	$\alpha 1$
	STG	22	L	-52	-18	8	$\alpha 1$

$\alpha 1$ = alpha1 (8.5–10 Hz); $\beta 1$ = Beta1 (12.5–18); Ω = total (0.5–30 Hz)

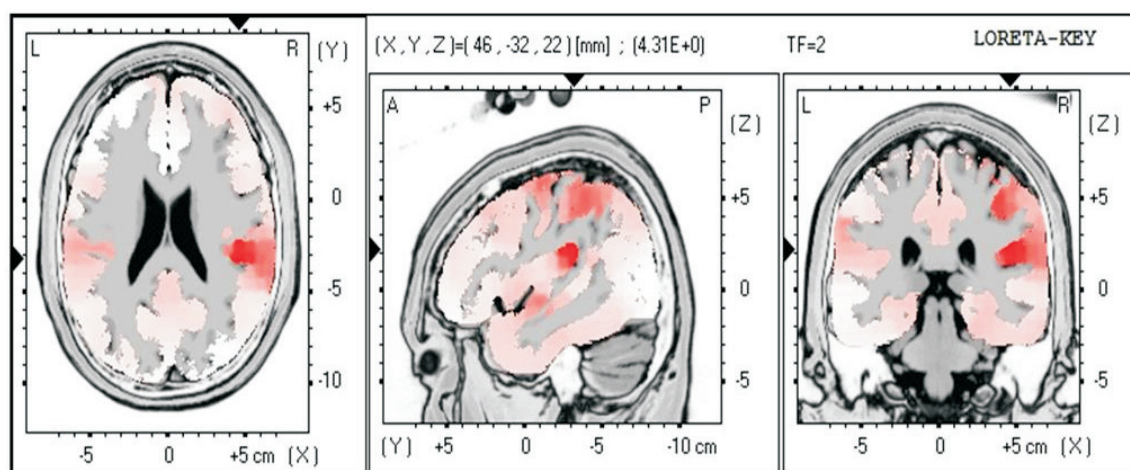


Figure 3. Theta current source density (CSD) difference between the High-OC group and Low-OC group during the first 30 seconds of the negative visualisation. Areas showing a High-OC > Low-OC group difference are indicated in red, with darker colour representing a greater difference

Table 4. Spearman's rho correlations between alpha (α_1) and total spectral (Ω) current source density in vIPFC and insula clusters, and participants' self-reported urge to neutralize at the reading phase ($N = 30$): Full Spearman's correlation, partial Spearman's correlation controlling for reading phase anxiety, and partial Spearman's controlling for initial (pre-experiment) anxiety

Frequency band (voxels)	Region	Hemisphere	Reading urge adjusted for reading anxiety	Reading urge adjusted for initial anxiety	Reading urge
Alpha 1	vIPFC (7)	L	$\rho = .394$ ($p = .031$)	$\rho = .354$ ($p = .060$)	$\rho = .397$ ($p = .033$)
	Insula (11)	L	$\rho = .392$ ($p = .032$)	$\rho = .359$ ($p = .056$)	$\rho = .397$ ($p = .033$)
All frequencies (0.5–30 Hz)	vIPFC (9)	L	$\rho = .394$ ($p = .031$)	$\rho = .352$ ($p = .061$)	$\rho = .398$ ($p = .033$)

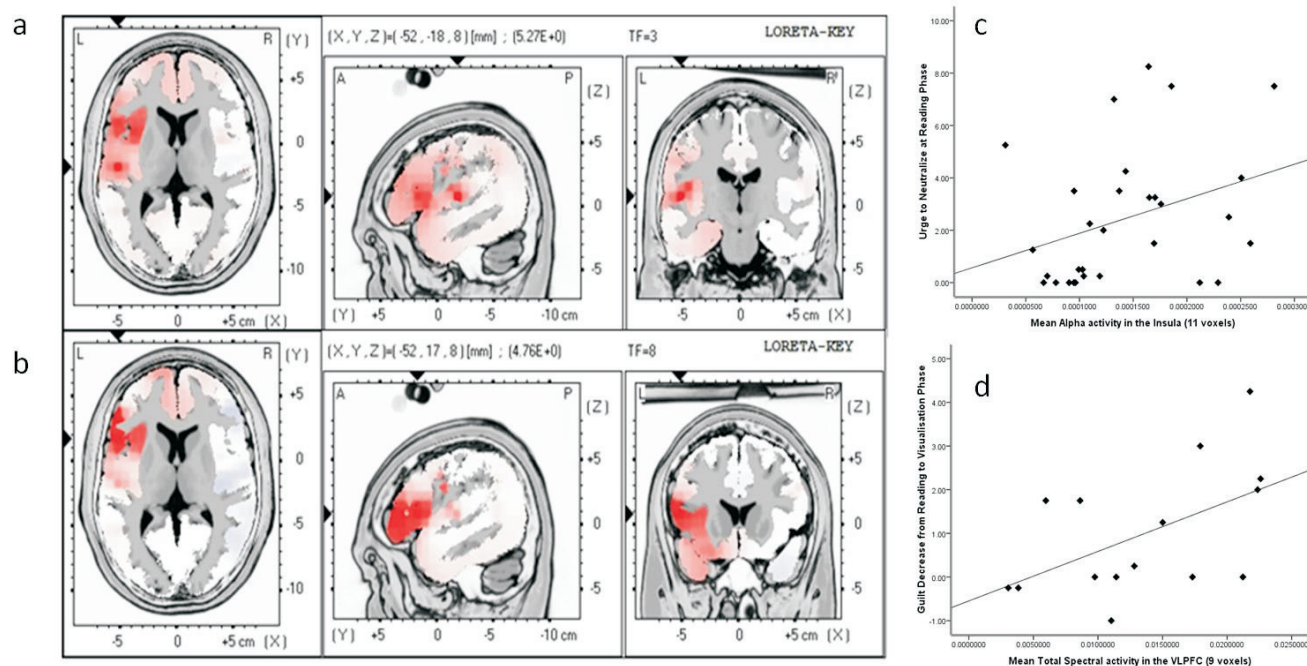


Figure 4. Mean current source density (CSD) in the first 30 seconds of the negative visualisation vs. the first 30 seconds of the positive visualisation in the High-OC group ($N = 15$) in the a) alpha 1 band (8.5–10 Hz); b) total spectrum (0.5–30 Hz). Correlations are shown between c) alpha 1 CSD in the anterior insula cluster (11 voxels) and all participants' urge to neutralize at the reading phase ($N = 30$); d) total spectral CSD with the decrease in High-OC participants' self-reported guilt from the reading to the visualisation phase ($N = 15$)

showed a significant condition effect in the High-OC group. Spearman's rho correlations showed a significant relationship between these variables (Table 4, Figure 4c). We also ran partial correlations between these variables, adjusting for reading phase and pre-experiment anxiety, to ensure that the relationships were not simply due to the insula's role in anxiety in general (see Paulus & Stein, 2006), which gave very similar results.

As mentioned previously, the behavioural responses of the High-OC group decreased significantly from the reading to the visualisation phase, and the majority reported performing covert neutralization. Therefore the insula/vlPFC activity may also reflect covert neutralization processes.

To test this possibility, correlations were examined between the insula/vlPFC activity and the decrease in High-OC participants' VAS responses from reading to visualisation ($N = 15$). This revealed significant correlations between these activities and the decrease in anxiety and guilt from reading to visualisation (see Table 5, Figure 4d).

Table 5. Spearman's rho correlations between alpha1 ($\alpha 1$) and total spectral (Ω) current source density in vlPFC and insula clusters, and the decrease in anxiety and guilt from the reading to the visualisation phase ($N = 15$) in the High-OC group

Frequency band	Region (voxels)	Hemi-sphere	Decrease in anxiety between reading and visualisation phases	Decrease in guilt between reading and visualisation phases
Alpha 1	vlPFC (7)	L	$\rho = .573$ ($p = .025$)	$\rho = .594$ ($p = .02$)
	Insula (11)	L	$\rho = .552$ ($p = .033$)	$\rho = .579$ ($p = .014$)
All frequencies (0.5–30 Hz)	vlPFC (9)	L	$\rho = .555$ ($p = .032$)	$\rho = .617$ ($p = .014$)

Repeated measures ANOVAs of High-OC VAS responses before and after visualisation were run with the mean insula alpha, vlPFC alpha, and vlPFC total spectral activity as covariates. The main effect of *phase* which had previously shown a significant decrease in anxiety, guilt, likelihood, and urge to neutralize between reading and visualisation in the High-OC group ($F(1, 13) = 6.701, p = .021$), was no longer significant with the inclusion of insula alpha ($F(1, 13) = 0.82, p = .382$), vlPFC alpha ($F(1, 13) = 0.86, p = .369$), or vlPFC total spectral activity ($F(1, 13) = 0.19, p = .668$). This suggests that this activation was related to the decrease in negative affect, possibly via covert neutralization.

DISCUSSION

Participants' VAS responses during our thought-action-fusion experiment showed that reading the negative sentence induced anxiety, guilt, and the urge to neutralize, and these negative emotions were significantly greater in the High-OC than in the Low-OC group. The High-OC group also estimated the likelihood of the event occurring as significantly greater than the Low-OC group. Anxiety, guilt, likelihood and urge to neutralize decreased significantly over the course of the trial, as predicted following previous replications of this paradigm (Bocci & Gordon, 2007; Marcks &

Woods, 2007; Rassin, 2001; Van den Hout et al., 2001; Van den Hout et al., 2002; Zucker et al., 2002).

Also in line with our prediction and previous replications (Bocci & Gordon, 2007; Van den Hout et al., 2002), the majority of our participants reported having used some form of cognitive reappraisal to reduce negative affect, and half of the High-OC participants reported using strategies more akin to neutralization such as reversing the negative sentence or imagining positive endings to the scenarios.

Between-group comparisons of neural activity during the visualisation phase revealed greater theta in the High-OC than the Low-OC group in right frontal, temporal and parietal lobes and the insula. Increased theta in OCD is a robust finding (Karadag et al., 2003; Perros, Young, Ritson, Price & Mann, 1992; Velikova et al., 2010) and the regions of activation are consistent with OCD imaging studies (Rotge et al., 2008), suggesting the activation of OCD-related circuitry. However, a more parsimonious explanation may be that this reflects greater anxiety (Aftanas & Pavlov, 2005) or more vivid imagery (Addis, Wong & Schacter et al., 2007; Weiler, Suchan & Daum, 2010).

In the High-OC group alone, significantly greater alpha1 and mean total spectral activity was seen in the negative than the positive condition in a large left-lateralised area covering the insula and vlPFC. This was present in the first half of the visualisation phase, corresponding to the time at which this group had reported their highest levels of anxiety, guilt, likelihood and urge to neutralize, and disappeared in the second half, consistent with the significant decrease in these self-reported emotions. This insula/vlPFC activity was found to correlate with all participants' self-reported reading phase urge to neutralize, consistent with our hypothesis. Furthermore, these correlations remained largely unchanged after adjusting for reading phase or pre-experiment/baseline anxiety. Significant correlations were also present between insula/vlPFC activity and the reduction in High-OC's self-reported anxiety and guilt from the beginning to the end of the visualisation phase – a reduction which was no longer significant when adjusting for this activity.

One explanation for the observed insula/vlPFC activity is that it reflects feelings of anticipated failure to resolve emotional conflict. This experiment induced very strong emotions in participants, and insula activation has previously been linked to anticipated failure or loss in gambling tasks (Paulus, Rogalsky, Simmons, Feinstein & Stein, 2003), particularly when accompanied by a sense of urgency (Jones, Minati, Harrison, Ward & Critchley, 2011). However, if conflict or conflict resolution were the primary source of this activity we may expect to see greater activation of the anterior cingulate, due to its central role in conflict monitoring (Botvinick, Cohen & Carter, 2004; Etkin, Egner, Peraza, Kandel & Hirsch, 2006), which was not present in the current experiment.

A more suitable explanation of these findings suggests the involvement of the insula/vlPFC activity in the urge to neutralize and the performance of covert neutralization, which is consistent with the behavioural addiction model of OCD. This model proposes that reward circuitry is hyperactive during OC compulsions and hypoactive during natural reward processing, as is reported in substance addiction disorders (Martin-Soelch, Missimer, Leenders & Schultz, 2003; Van Hell et al., 2010). Figee et al. (2011) reported that during reward anticipation OCD patients showed attenuated activation of the left insula, left vlPFC and nucleus ac-

cumbens (NAcc), which are all critical constituents of the reward circuit.

Additionally, a significant relationship between participants' urge to neutralize and insula activity in the current experiment is not only in agreement with the behavioural addiction model of OCD, but is also consistent with the fronto-striatal models following the proposal that craving-related insula activity can lead to activation of the direct (ventral) basal ganglia pathway through an increase of mesolimbic dopamine via the ventral tegmental area (Verdejo-García & Bechara, 2009).

Only a small functional distinction is present between the activation of the insula and the vIPFC in the current study, however, the results suggest a marginally stronger relationship between the insula and the urge to neutralize, as shown by the greater volume of activity in this structure, and between the vIPFC and neutralization itself, evidenced by the greater decrease in the reduction of anxiety and guilt when adjusting for this activity. This slight separation in function is consistent with previous research, as the insula is proposed to be important in the conscious feeling of urge and craving (see Naqvi & Bechara, 2008), and the vIPFC has been associated with cognitive reappraisal (Opitz, Rauch, Terry & Urry, 2012; Wager, Davidson, Hughes, Lindquist & Ochsner, 2008).

The finding that insula/vIPFC activity in the current study was mainly found in the alpha band is also consistent with a behavioural-addiction perspective. The alpha frequency has often been associated with addiction (see Parvas, Alia-Klein, Woicik, Volkow & Goldstein, 2011), including findings of increased alpha activity during withdrawal from both heroin (Shufman et al., 1996) and cocaine (Alper, Chabot, Kim, Prichep & John, 1990). The exact functional nature of alpha frequency in these processes is uncertain; for example Reid, Flammino, Howard, Nilsen and Prichep (2008) report findings that suggest increased frontal cortical alpha power to be positively associated with cocaine-induced nervousness, but frontal cortical alpha coherence to be negatively associated with cue-induced cocaine-like high. The role of alpha activity within thalamo-cortical circuitry is itself complex, as the typical inverse relationship between alpha power and cortical excitation appears to be reversed in thalamic and sub-cortical structures such as the insula (see Schreckenberger et al., 2004).

There are a few limitations in the present study, for example the relatively small sample size, and the use of a non-clinical analogue sample. Additionally the source localisation method did not allow for visualisation of deeper ventral-striatal structures, such as the nucleus accumbens, which are likely to be involved in neutralization processes (Figuee et al., 2011; Verdejo-García & Bechara, 2009).

Lateralization differences of insula activation in the current experiment should also be discussed, as the between-group difference in theta activity presented in the right hemisphere, and the between-condition difference in alpha activity presented in the left hemisphere. As previously mentioned, greater theta activity in the High-OC than the Low-OC group may be related to greater anxiety. The right hemispheric lateralization of this effect would be consistent with this hypothesis, particularly in the insula, as greater right insula volume has been associated with higher trait anxiety sensitivity (Rosso et al., 2010). The left hemispheric lateralization of greater alpha activity in the insula/vIPFC during negative compared to positive visuali-

sation is unlikely to be specifically associated with feelings of urge or craving *per se*, as previous studies have not suggested lateralization of these processes (Naqvi & Bechara, 2008; Naqvi, Rudrauf, Damasio & Bechara, 2007). A more apposite explanation is that the observed left lateralization is related to language processing, for which the left hemisphere is dominant (Knecht et al., 2000), and the participants' conscious experience of their urge to neutralize. The forms of cognitive reappraisal which were endorsed by participants are likely to have involved sub-vocalisation, which is consistent with the role of left lateralized insula, and particularly vIPFC, in 'inner speech' (Morin, 2009; Riecker, Ackermann, Wildgruber, Dogil & Grodd, 2000) which appears to be crucial to the experience of self-conscious emotions (Jones & Fernyhough, 2007; Morin, 2009; Morin & Michaud, 2007).

In conclusion, the current findings provide preliminary evidence of a direct link between reward circuitry and neutralization, thereby further clarifying the relationship between neural activity and obsessive-compulsive phenomenology and providing support for the behavioural-addiction perspective.

REFERENCES

- Addis, D. R., Wong, A. T. & Schacter, D. L. (2007). Remembering the past and imagining the future: Common and distinct neural substrates during event construction and elaboration. *Neuropsychologia*, 45, 1363–1377.
- Aftanas, L. & Pavlov, S. V. (2005). Trait anxiety impact on posterior activation asymmetries at rest and during evoked negative emotions: EEG investigation. *International Journal of Psychophysiology*, 55, 85–94.
- Alper, K. R., Chabot, R. J., Kim, A. H., Prichep, L. S. & John, E. R. (1990). Quantitative EEG correlates of crack cocaine dependence. *Psychiatry Research*, 35, 95–105.
- American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders* (4th edition (DSM-IV), text revision). Washington, DC: American Psychiatric Association.
- Bocci, L. & Gordon, P. K. (2007). Does magical thinking produce neutralising behaviour? An experimental investigation. *Behaviour Research and Therapy*, 45, 1823–1833.
- Botvinick, M. M., Cohen, J. D. & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: An update. *Trends in Cognitive Sciences*, 8, 539–546.
- Chamberlain, S. R., Menzies, L., Hampshire, A., Suckling, J., Fineberg, N. A., del Campo, N. et al. (2008). Orbitofrontal dysfunction in patients with obsessive-compulsive disorder and their unaffected relatives. *Science*, 321, 421–422.
- Denys, D. (2011). Obsessionality & compulsivity: A phenomenology of obsessive-compulsive disorder. *Philosophy, Ethics, and Humanities in Medicine*, 6, 3. doi:10.1186/1747-5341-6-3
- Denys, D., Zohar, J. & Westenberg, H. G. (2004). The role of dopamine in obsessive-compulsive disorder: Preclinical and clinical evidence. *Journal of Clinical Psychiatry* 65(Suppl 14), 11–17.
- Etkin, A., Egner, T., Peraza, D. M., Kandel, E. R. & Hirsch, J. (2006). Resolving emotional conflict: A role for the rostral anterior cingulate cortex in modulating activity in the amygdala. *Neuron*, 51, 1–12.
- Figuee, M., Vink, M., de Geus, F., Vulink, N., Veltman, D.J., Westenberg, H. & Denys, D. (2011). Dysfunctional reward circuitry in obsessive-compulsive disorder. *Biological Psychiatry*, 69, 867–874.

- Fineberg, N. A., Potenza, M. N., Chamberlain, S. R., Berlin, H. A., Menzies, L., Bechara, A., Sahakian, B. J., Robbins, T. W., Bullmore, E. T. & Hollander, E. (2010). Probing compulsive and impulsive behaviours, from animal models to Endophenotypes: A narrative review. *Neuropsychopharmacology*, 35, 591–604.
- Foa, E. B., Huppert, J. D., Leiberg, S., Langner, R. & Kichic, R. (2002). The obsessive-compulsive inventory: Development and validation of a short version. *Psychological Assessment*, 14(4), 485–496.
- Fuchs, M., Kastner, J., Wagner, M., Hawes, S. & Ebersole, J. S. (2002). A standardized boundary element method volume conductor model. *Clinical Neurophysiology*, 113, 702–712.
- Hesse, S., Müller, U., Lincke, T., Barthel, H., Villman, T., Angermeyer, M. C., Sabri, O. & Stengler-Wenzke, K. (2005). Serotonin and dopamine transporter imaging in patients with obsessive-compulsive disorder. *Psychiatry Research: Neuroimaging*, 140, 63–72.
- Holden, C. (2001). “Behavioral” addictions: Do they exist? *Science*, 294, 980–982.
- Jasper, H. H. (1958). The ten-twenty electrode system of the international federation. *Electroencephalography and Clinical Neurophysiology*, 10, 371–375.
- Jones, C. L., Minati, L., Harrison, N. A., Ward, J. & Critchley, H. D. (2011). Under pressure: Response urgency modulates striatal and insula activity during decision-making under risk. *Plos One*, 6, 1–11.
- Jones, S. R. & Fernyhough, C. (2007). Neural correlates of inner speech and auditory verbal hallucinations: A critical review and theoretical integration. *Clinical Psychology Review*, 27, 140–154.
- Karadag, F., Oguzhanoglu, N. K., Kurt, T., Oguzhanoglu, A., Atesci, F. & Ozdel, O. (2003). Quantitative EEG analysis in obsessive-compulsive disorder. *International Journal of Neuroscience*, 113, 833–847.
- Knecht, S., Deppe, M., Dräger, B., Bobe, L., Lohmann, H., Ringelstein, E.-B. & Henningsen, H. (2000). Language lateralization in healthy right-handers. *Brain*, 123, 74–81.
- Lancaster, J. L., Woldorff, M. G., Parsons, L. M., Liotti, M., Freitas, C. S., Rainey, L., Kochunov, P. V., Nickerson, D., Mikiten, S. A. & Fox, P. T. (2000). Automated Talairach Atlas labels for functional brain mapping. *Human Brain Mapping*, 10, 120–131.
- Liu, X., Hairston, J., Schrier, M. & Fan, J. (2011). Common and distinct networks underlying reward valence and processing stages: A meta-analysis of functional neuroimaging studies. *Neuroscience and Biobehavioural Reviews*, 35, 1219–1236.
- Marcks, B. A. & Woods, D. W. (2007). Role of thought-related beliefs and coping strategies in the escalation of intrusive thoughts: An analogue to obsessive-compulsive disorder. *Behaviour Research and Therapy*, 45, 2640–2651.
- Marks, I. (1990). Behavioural (non-chemical) addictions. *British Journal of Addiction*, 85, 1389–1394.
- Martin-Soelch, C., Missimer, J., Leenders, K. L. & Schultz, W. (2003). Neural activity related to the processing of increasing monetary reward in smokers and nonsmokers. *European Journal of Neuroscience*, 18, 680–688.
- Mataix-Cols, D. & van den Heuvel, O. A. (2006). Common and distinct neural correlates of obsessive-compulsive and related disorders. *Psychiatric Clinics of North America*, 29, 391–410.
- Mazziotta, J., Toga, A., Evans, A., Fox, P., Lancaster, J., Zilles, K., Woods, R., Paus, T., Simpson, G., Pike, B., Holmes, C., Collins, L., Thompson, P., MacDonald, D., Iacoboni, M., Schormann, T., Amunts, K., Palomero-Gallagher, N., Geyer, S., Parsons, L., Narr, K., Kabani, N., Le Goualher, G., Boomsma, D., Cannon, T., Kawashima, R. & Mazoyer, B. (2001). A probabilistic atlas and reference system for the human brain: International Consortium for Brain Mapping (ICBM). *Philosophical Transactions of the Royal Society London B Biological Sciences*, 356(1412), 1293–1322.
- Morin, A. (2009). Self-awareness deficits following loss of inner speech: Dr. Jill Bolte Taylor’s case study. *Consciousness and Cognition*, 18, 524–529.
- Morin, A. & Michaud, J. (2007). Self-awareness and the left inferior frontal gyrus: Inner speech use during self-related processing. *Brain Research Bulletin*, 74, 387–396.
- Naqvi, N. H. & Bechara, A. (2008). The hidden island of addiction: The insula. *Trends in Neurosciences*, 32, 56–67.
- Naqvi, N. H., Rudrauf, D., Damasio, H. & Bechara, A. (2007). Damage to the insula disrupts addiction to cigarette smoking. *Science*, 315, 531–534.
- Nichols, T. E. & Holmes, A. P. (2002). Nonparametric permutation tests for functional neuroimaging: a primer with examples. *Human Brain Mapping*, 15, 1–25.
- Nielen, M. M., den Boer, J. A. & Smid, H. G. (2009). Patients with obsessive-compulsive disorder are impaired in associative learning based on external feedback. *Psychological Medicine*, 39, 1519–1526.
- Opitz, P. C., Rauch, L. C., Terry, D. P. & Urry, H. L. (2012). Prefrontal mediation of age differences in cognitive reappraisal. *Neurobiology of Aging*, 33, 645–655.
- Parvas, M. A., Alia-Klein, N., Woicik, P. A., Volkow, N. D. & Goldstein, R. Z. (2011). Neuroimaging for drug addiction and related behaviours. *Review of Neuroscience*, 22, 609–624.
- Pascual-Marqui, R. D. (1999). Review of methods for solving the EEG inverse problem. *International Journal of Bioelectromagnetism*, 1, 75–86.
- Pascual-Marqui, R. D. (2002). Standardized low-resolution brain electromagnetic tomography (sLORETA): Technical details. *Methods Find Exp Clin Pharmacol*, 24(Suppl. D), 5–12.
- Paulus, M. P. (2007). Neural basis of reward and craving – A homeostatic point of view. *Dialogues in Clinical Neuroscience*, 9, 379–387.
- Paulus, M. P., Rogalsky, C., Simmons, A., Feinstein, J. S. & Stein, M. B. (2003). Increased activation in the right insula during risk-related decision making is related to harm avoidance and neuroticism. *NeuroImage*, 19, 1439–1448.
- Paulus, M. P. & Stein, M. B. (2006). An insular view of anxiety. *Biological Psychiatry*, 60, 383–387.
- Perros, P., Young, E., Ritson, J., Price, G. & Mann, P. (1992). Power spectral EEG analysis and EEG variability in obsessive-compulsive disorder. *Brain Topography*, 4, 187–192.
- Rachman, S., Shafran, R., Mitchell, D., Trant, J. & Teachman, B. (1996). How to remain neutral: An experimental analysis of neutralization. *Behaviour Research and Therapy*, 33, 779–784.
- Rasmussen, S. A. & Eisen, J. L. (1994). The epidemiology and differential diagnosis of obsessive-compulsive disorder. *Journal of Clinical Psychiatry*, 55(Suppl), 5–10.
- Rassin, E. (2001). The contribution of thought-action fusion and thought suppression in the development of obsession-like intrusions in normal participants. *Behaviour Research and Therapy*, 39, 1023–1032.
- Reid, M. S., Flammino, F., Howard, B., Nilsen, D. & Pritchep, L. S. (2008). Cocaine cue versus cocaine dosing in humans: Evidence for distinct neurophysiological response profiles. *Pharmacology, Biochemistry and Behavior*, 91, 155–164.
- Riecker, A., Ackermann, H., Wildgruber, D., Dogil, G. & Grodd, W. (2000). Opposite hemispheric lateralization effects during speaking and singing at motor cortex, insula and cerebellum. *NeuroReport*, 11, 1997–2000.
- Rosso, I. M., Makris, N., Britton, J. C., Price, L. M., Gold, A. L., Zai, D., Bruyere, J., Deckersbach, T., Killgore, W. D. S. & Rauch, S. L. (2010). Anxiety sensitivity correlates with two in-

- lices of right anterior insula structure in specific animal phobia. *Depression and Anxiety*, 27, 1104–1110.
- Rotge, J.-Y., Dominique, G., Dilharreguy, B., Cuny, E., Tognol, J., Bioulac, B., Allard, M., Burbaud, P. & Aouzerate, B. (2008). Provocation of obsessive–compulsive symptoms: a quantitative voxel-based meta-analysis of functional neuroimaging studies. *Journal of Psychiatry Neurosciences*, 33, 405–412.
- Roth, R. M., Saykin, A. J., Flashman, L. A., Pixley, H. S., West, J. D. & Mamourian, A. C. (2007). Event-related fMRI of response inhibition in obsessive–compulsive disorder. *Biological Psychiatry*, 62, 901–909.
- Salkovskis, P. M. (1985). Obsessional-compulsive problems: A cognitive-behavioural analysis. *Behaviour Research and Therapy*, 23, 571–583.
- Salkovskis, P. M. (1996). Cognitive-behavioural approaches to the understanding of obsessional problems. In R. Rapee (Ed.), *Current controversies in the anxiety disorders*. New York: Guilford Press.
- Saxena, S. & Rauch, S. L. (2000). Functional neuroimaging and the neuroanatomy of obsessive–compulsive behavior. *Psychiatric Clinics of North America*, 23, 563–586.
- Schreckenberger, M., Lange-Asschenfeldt, C., Lochmann, M., Mann, K., Siessmeier, T., Buchholz, H.-G., Bartenstein, P. & Gründer, G. (2004). The thalamus as the generator and modulator of EEG alpha rhythm: A combined PET/EEG study with lorazepam challenge in humans. *NeuroImage*, 22, 637–644.
- Shafraan, R., Thordardson, D. & Rachman, S. (1996). Thought-action fusion in obsessive–compulsive disorder. *Journal of Anxiety Disorders*, 10, 379–391.
- Shufman, E., Perl, E., Cohen, M., Dickman, M., Gandaku, D., Adler, D., Veler, A., Bar-Hamburger, R. & Ginath, Y. (1996). Electro-encephalography spectral analysis of heroin addicts compared with abstainers and normal controls. *Israeli Journal of Psychiatry and Related Sciences*, 33, 196–206.
- Torres, A. R., Prince, M. J., Bebbington, P. E., Bhugra, D., Brugha, T. S., Farrell, M. et al. (2006). Obsessive–compulsive disorder: Prevalence, comorbidity, impact, and help seeking in the British National Psychiatric Survey of 2000. *American Journal of Psychiatry*, 163, 1978–1985.
- Van den Heuvel, O. A., van der Werf, Y. D., Verhoef, K. M. W., de Wit, S., Berendse, H. W., Wolters, E. Ch., Veltman, D. J. & Groenewegen, H. J. (2010). Fronto-striatal abnormalities underlying behaviours in the obsessive–compulsive spectrum. *Journal of the Neurological Sciences*, 289, 55–59.
- Van den Hout, M., Kindt, M., Weiland, T. & Peters, M. (2002). Instructed neutralization, spontaneous neutralization and prevented neutralization after an obsession-like thought. *Journal of Behaviour Therapy and Experimental Psychiatry*, 33, 177–189.
- Van den Hout, M., van Pol, M. & Peters, M. (2001). On becoming neutral: Effects of experimental neutralizing reconsidered. *Behaviour Research and Therapy*, 39, 1439–1448.
- Van der Wee, N. J., Stevens, H., Hardeman, J. A., Mandl, R. C., Denys, D. A., van Megen, H. J. et al. (2004). Enhanced dopamine transporter density in psychotropic-naïve patients with obsessive–compulsive disorder shown by [123I](Sareen et al., 2007b)-CIT SPECT. *American Journal of Psychiatry*, 161, 2201–2206.
- Van Hell, H. H., Vink, M., Ossewaarde, L., Jager, G., Kahn, R. S. & Ramsey, N. F. (2010). Chronic effects of cannabis use on the human reward system: An fMRI study. *European Neuropsychopharmacology*, 20, 153–163.
- Velikova, S., Locatelli, M., Insacco, C., Smeraldi, E., Comi, G. & Leocani, L. (2010). Dysfunctional brain circuitry in obsessive–compulsive disorder: Source and coherence analysis of EEG rhythms. *Neuroimage*, 49, 977–983.
- Verdejo-García, A. & Bechara, A. (2009). A somatic marker theory of addiction. *Neuropharmacology*, 56, 48–62.
- Volkow, N. D., Chang, L., Wang, G. J., Fowler, J. S., Ding, Y. S., Sedler, M., Logan, J., Franceschi, D., Gatley, J., Hitzemann, R., Gifford, A., Wong, C. & Pappas, N. (2001). Low level of brain dopamine D2 receptors in methamphetamine abusers: Association with metabolism in the orbitofrontal cortex. *American Journal of Psychiatry*, 158, 2015–2021.
- Volkow, N. D. & Fowler, J. S. (2000). Addiction a disease of compulsion and drive: involvement of the orbitofrontal cortex. *Cerebral Cortex*, 10, 318–325.
- Volkow, N. D., Fowler, J. S., Wang, G. J., Hitzemann, R., Logan, J., Schlyer, D. J., Dewey, S. L. & Wolf, A. P. (1993). Decreased dopamine D2 receptor availability is associated with reduced frontal metabolism in cocaine abusers. *Synapse*, 14, 169–177.
- Wager, T. D., Davidson, M. L., Hughes, B. L., Lindquist, M. A. & Ochsner, K. N. (2008). Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron*, 59, 1037–1050.
- Weiler, J. A., Suchan, B. & Daum, I. (2010). When the future becomes the past: Differences in brain activation patterns for episodic memory and episodic future thinking. *Behavioural Brain Research*, 212, 196–203.
- Wolters, E. Ch., Veltman, D. J. & Groenewegen, H. J. (2010). Fronto-striatal abnormalities underlying behaviours in the compulsive-impulsive spectrum. *Journal of the Neurological Sciences*, 289, 55–59.
- Zucker, B. G., Craske, M. G., Barrios, V. & Holguin, M. (2002). Thought-action fusion: Can it be corrected? *Behaviour Research and Therapy*, 40, 653–664.