Executive impairments in Obsessive Compulsive Disorder: A systematic review with emotional and non-emotional paradigms

María Tubío Fungueiriño1, Montse Fernández Prieto2, Sandra Carvalho3, Jorge Leite4, Ángel Carracedo5, and Óscar F. Gonçalves6
1 Universidade de Santiago de Compostela, 2 Instituto de Investigación Sanitaria de Santiago (IDIS), 3 University of Minho (Portugal), 4 Universidade Portucalense (Portugal), and 5 Fundación Pública Galega de Medicina Xenómica (FPGMX)

Abstract

Precedent: Impairments in executive functioning may be associated with compulsive symptoms in Obsessive Compulsive Disorder (OCD). The aim of this study was to conduct a systematic review of cognitive flexibility, inhibitory control and working memory in OCD patients, using emotional and non-emotional paradigms. Method: we reviewed research published in PubMed, Web of Science, PsychInfo, Scopus, Scielo, and ProQuest Psychology databases, from January 2008 to April 2019. The review followed a two-stage process. In the first stage, we selected only studies using neutral stimuli paradigms, while in the second we selected executive-emotional paradigms. Results: The first stage of the review provided 16 final results, while the second stage, with emotional stimuli, provided 3 results. Conclusions: There is some initial evidence for the existence of executive impairments in OCD, as expressed in the performance and/or processing of working memory inhibitory control and cognitive flexibility. There is also initial evidence that these latter two could be modulated by the presentation or mental representation of negative valence stimuli or images, as well as the presence of aversive contingencies. Keywords: Obsessive compulsive disorder, inhibitory control, working memory, cognitive flexibility, emotional.

Alteraciones ejecutivas en el Trastorno Obsesivo Compulsivo: una revisión sistemática con paradigmas emocionales y no emocionales. Antecedentes: las alteraciones en el funcionamiento ejecutivo podrían estar asociadas a los síntomas compulsivos del Trastorno Obsesivo Compulsivo (TOC). El objetivo de este estudio fue realizar una revisión sistemática en flexibilidad cognitiva, control inhibitorio y memoria de trabajo en pacientes con TOC, empleando paradigmas emocionales y no emocionales. Método: revisamos investigaciones publicadas en PubMed, Web of Science, Psychinfo, Scopus, Scielo y ProQuest Psychology databases, desde enero de 2008 hasta abril de 2019. La revisión siguió un proceso de dos etapas: la primera centrada en estudios con paradigmas neutros y la segunda con paradigmas ejecutivos emocionales. Resultados: la primera etapa de búsqueda arrojó un resultado de 16 estudios, mientras que la segunda, con paradigmas emocionales, arrojó tres resultados. Conclusiones: a pesar de la escasa cantidad de investigación, existen evidencias de alteraciones ejecutivas en TOC que se expresan en la ejecución o en el procesamiento de memoria de trabajo, control inhibitorio y flexibilidad cognitiva. También hay evidencias de que estos dos últimos componentes podrían estar modulados por la presentación o representación mental de estímulos negativos, así como por la presencia de contingencias aversivas.

Palabras clave: Trastorno Obsesivo Compulsivo, control inhibitorio, memoria de trabajo, Flexibilidad cognitiva, emocional.
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Executive function processes refer to high-level mental operations necessary to regulate cognitions, emotions and behaviors. Some of the core executive functions include inhibitory control (i.e., the ability to inhibit prepotent responses), working memory (i.e., the capacity to hold and update information relevant for the demands), and cognitive flexibility (i.e., the ability to change strategies in face of changing environmental demands) (Diamond, 2013; Snyder et al., 2015).

Some studies found evidence of impairments in OCD patients in cognitive flexibility, inhibitory control and working memory (Abramovitch et al., 2013; Abramovitch & Cooperman, 2015). However there is no clear consensus about the extent of executive functions are impaired in OCD (Kashyap, Kumar, Kandavel, & Reddy, 2013; Gruner & Pittenger, 2017; Yun et al., 2017). Part of the evidence for characterizing OCD as an executive impairment disorder comes indirectly from studies showing that brain regions predominate the prefrontal cortex (for executive functions) or thalamic region (for working memory) are altered in these patients (Stuss & Knight, 2002; Shah, Pesiridou, Baltuch, Malone, & O’Reardon, 2008; Gonçalves et al., 2016).

Emotions could interfere with executive functions per se (mood) in neutral stimuli paradigms or by the influence that stimuli evokes in emotional executive tasks (Song et al., 2017). This is no different in people suffering from OCD, as evidence suggests that apart from executive deficits, patients exhibit significant emotional impairments (Daros, Zakzanis, & Rector, 2014). These emotional impairments may have contributed for the previous classification of OCD as an anxiety disorder. However some authors suggest that anxiety in OCD is probably the expression of an affective-motivational imbalance between the defensive (i.e., fear response) and appetitive mechanisms (i.e., ingestion, copulation, and care giving responses) which, in turn, may be responsible for a more extended emotional deregulation (Gonçalves et al., 2015, 2016, 2017).

The co-existence of executive and emotional impairments could be caused by an imbalance of activation between ventral and dorsal regions (Mataix-Cols & van den Heuvel, 2006; Theiss, McHugo, Zhao, Zald, & Olatunji, 2019), frontal-posterior dissociation (Gonçalves, Marques, Lori, Sampaio, & Branco, 2010) or even inter-hemispheric imbalance (Gonçalves et al., 2011). Building on these hypotheses, Mataix-Cols and van den Heuvel (2006) recommended the need to study the relationship between emotional and executive component in OCD.

The objective of the present study was to systematically review the research on three core executive processes in OCD based on Diamond’s model (Diamond, 2013) (cognitive flexibility, working memory and inhibitory control) as well as the eventual modulation of these executive processes by emotional mechanisms. In the first case, selected studies must have employed neutral stimuli paradigms (experimental paradigms with neutral stimuli) while in the second case, studies were required to include emotional paradigms. These emotional paradigms should be experimental tasks with emotional stimuli as images (e.g. from the IAPS [Lang, Bradley, & Cuthbert, 1997]), words (e.g. ANEW [Bradley & Lang, 1999]), sounds (e.g. IADS [Fernández-Abascal et al., 2008]).

Method

Instruments

In order to identify the relevant research published from January 2008 to April 2019, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was followed to carry out this systematic review. We searched information on PubMed, Web of Science, PsychInfo, Scopus, Scielo and ProQuest Psychology Database.

Procedure

Two filters were preset in all search databases: studies published from 2008/01/01 to 2018/04/30 and English and Spanish language of publication. On a first stage, we selected studies with non-emotional paradigms using the following search terms/combinations: (“obsessive compulsive disorder” OR “ocd”) AND (“executive function” OR “inhibitory control” OR “inhibit*” OR “working memory” OR “cognitive flexibility” OR “flexib* OR “switching”) AND (“go no go” OR “n back” OR “n-back” OR “task switching”). In order to explore how emotional stimuli could modulate executive functions in OCD, the following search/combinations terms were selected: (“obsessive compulsive disorder” OR “ocd”) AND (“executive function” OR “inhibitory control” OR “inhibit*” OR “working memory” OR “cognitive flexibility” OR “flexib* OR “switching”) AND (“emotional stimuli” OR “emotion*”).

Data analysis

Studies were selected based on the following eligibility criteria: (a) adult human samples (aged between 18 and 65 years old); (b) participants in the experimental group diagnosed with OCD following the criteria established by the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association in its fourth version (DSM-IV and DSM-IV-TR) or in its fifth version (DSM-5); (c) studies aiming to assess working memory, cognitive flexibility and/or inhibitory control; (d) published in English or Spanish; (e) only paper or short communication format (excluding book chapters, reviews, meta-analysis and congresses abstracts); (f) published in scientific journals, (g) original research, (h) using Go/No-Go, Task Switching or N-back paradigms, (i) using a control group; (j) using neutral stimuli (for the first stage review); (k) using emotional stimuli (for the second stage review).
Results

On the first stage (studies with neutral stimuli) the initial search resulted in 142 studies. After eliminating duplicate articles, 82 studies were selected for title and abstract inspection. After applying eligibility criteria, 32 studies were selected for complete reading. Thirteen papers were additionally removed due to criteria shown in the flow diagram (following PRISMA guidelines [Moher et al., 2015] see Figure 1). A total of 16 studies were included for final analysis. These studies were distributed according to the executive function under analysis: studies using task-switching paradigms (Table 1); studies with Go/No-Go paradigms (Table 2); studies with N-back paradigms (Table 3).

On the second stage (studies with emotional stimuli) the initial search resulted in 428 studies. Following the elimination of duplicate articles, 412 studies were selected for title and abstract inspection. After applying eligibility criteria, 16 studies were selected for complete reading. The other 377 papers were additionally removed due to criteria shown in the flow diagram (Figure 2). After reading the remaining 16 articles only 3 were found to meet the eligibility criteria (Table 4).

Discussion

There is increased evidence that OCD patients show significant executive impairments. The objective of the present article was...
to systematically review the research on three core executive functions in OCD patients: working memory, inhibitory control and cognitive flexibility. Additionally, given the co-existence of cognitive and emotional symptoms in OCD, we also reviewed studies looking at the emotional modulation of executive functioning in OCD.

We will first discuss the results of the research on executive functioning with neutral stimuli paradigms followed by a discussion of the few studies looking at executive functioning in emotional laden paradigms.

### Executive impairments with neutral stimuli paradigms

**Cognitive flexibility.** The four studies that met the eligibility criteria (Gu et al., 2008; Han et al., 2011; Meiran, Diamond, Toder, & Nemets, 2011; Remijnse et al., 2013) suggested that OCD patients showed an impaired performance in task-switching paradigms. These impairments were evident in increased switching costs, i.e., decreased performance when changing across task conditions. These costs were reflected in lower accuracy rate (Gu et al., 2008; Han et al., 2011; Stern et al., 2017) but they were

**Table 2**

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample (N) / Mean age (years)</th>
<th>p value</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Page et al., 2009</td>
<td>10 male OCD / 39.1</td>
<td>p&lt;0.01</td>
<td>Unaltered behavioral performance, but hypo-activation in fronto-striatal and parietal-temporal brain regions during inhibitory and high load attention tasks, respectively</td>
</tr>
<tr>
<td>Abramowitch et al., 2012</td>
<td>30 male OCD / 32 / 30 male ADHD / 29.5 / 30 male HC / 30.1</td>
<td>p=0.0001</td>
<td>OCD and ADHD groups performed poorly in terms of inhibitory control but not on impulsivity</td>
</tr>
<tr>
<td>Keskin-Ergen et al., 2014</td>
<td>26 EO OCD (12 men) / 24.5 33 LO OCD (11 men) / 25 54 HC (23 men) / 26.2</td>
<td>p=0.05</td>
<td>LO group tends to respond slowly in comparison to HC. No differences in performance between LO and EO</td>
</tr>
<tr>
<td></td>
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<td>LO group presented decreased N2 amplitude comparison with HC and a shorter latency in comparison with EO and HC groups</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>EO and LO groups showed a decreased P3 amplitude, but only topography is altered in LO group (more anterior)</td>
</tr>
<tr>
<td>Tolin et al., 2014</td>
<td>24 HD (8 men) / 47.7 24 OCD (18 men) / 33.5 24 HC (4 men) / 51.3</td>
<td>p=0.05</td>
<td>No differences in terms of behavioral performance between groups. OCD patients show hyper-activation in orbitofrontal gyrus</td>
</tr>
<tr>
<td>Thomas et al., 2015</td>
<td>20 OCD (9 men) / 39 20 PD (3 men) / 38 20 HC (7 men) / 33</td>
<td>p=0.05</td>
<td>Increased RT in both OCD and PD when compared to HC. Alterations in topography location of ERP components (P2, N2 and P3) when compared to HC</td>
</tr>
<tr>
<td>Hough et al., 2016</td>
<td>15 HD (4 men) / 54.1 17 OCD (9 men) / 36.1 25 HC (13 men) / 44.8</td>
<td>p=0.05</td>
<td>There were a decrease in RT between OCD and both HD and HC. OCD showed greater activity in DLPFC, insula, visual cortex and cerebellum than HD</td>
</tr>
<tr>
<td>Rasmussen et al., 2016</td>
<td>26 s-OCD / 26 c-OCD / 21 HC / -</td>
<td>p=0.05</td>
<td>There were no differences between groups</td>
</tr>
<tr>
<td>Saremi et al., 2017</td>
<td>35 OCD (26% men) / 32.4 35 HC (26% men) / 32.6</td>
<td>p=0.01</td>
<td>OCD group showed lower accuracy and larger RT</td>
</tr>
</tbody>
</table>


### Executive impairments with emotional stimuli paradigms

**Table 3**

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample (N) / Mean age (years)</th>
<th>p value</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nakao et al., 2009</td>
<td>40 OCD (16 men) / 33.3 25 HC (10 men) / 30.9</td>
<td>p=0.05</td>
<td>OCD and HC had identical performance in the N-back task. During the task, cleanliness/washing patients showed increased activation in right thalamus and left postcentral gyrus</td>
</tr>
<tr>
<td>Kashyap et al., 2012</td>
<td>150 OCD (94 men) / 27.6 177 HC (117 men) / -</td>
<td>p=0.021</td>
<td>Poor insight in OCD is associated with increased WM impairment</td>
</tr>
<tr>
<td>Koeh et al., 2012</td>
<td>21 OCD (5 men) / 29.4 21 HC (5 men) / 27.5</td>
<td>p=0.03</td>
<td>OCD group had slower RT in low-demanding tasks (1-back and 2-back). In terms of brain activity, there were no differences between OCD and HC in low cognitive-demand conditions, but in highly demanding trials OCD showed hypo-activation in dACC</td>
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<tr>
<td></td>
<td></td>
<td>p=0.05</td>
<td>Patients showed impaired performance, especially in trials with high memory load (3-back). OCD showed hypo-activation in SMA and IPL during WM</td>
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also evident in higher RT, suggesting a speed-accuracy tradeoff (Remijnse et al., 2013).

Consistent with behavioral data, neuroimaging studies showed abnormal activations in the frontal-striatal pathways, characterized by hyper-activated ventral regions and hypo-activated dorsal regions (Gu et al., 2008). Additionally, Han et al. (2011) found that task-switching performance and brain alterations tended to normalize after successful treatment.

Studies using clinical comparison groups (i.e., depression) reported similar task-switching costs along with identical frontal-striatal activations (Meiran et al., 2011; Remijnse et al., 2013), thus suggesting that task-switching impairments are not specific for OCD.

Inhibitory control. Inhibitory control has been the most studied executive function in OCD. In the present review, eight studies used the Go/No-Go task to probe inhibitory control in OCD, however with inconsistent findings. Regarding behavioral performance, while some studies did not find significant differences between OCD and HC (Page et al., 2009; Tolin, Witt, & Stevens, 2014; Rasmussen, Siev, Abramovitch, & Wilhelm, 2016), other studies showed significant impairments in terms of accuracy and/or RT (Response Time) (Abramovitch, Hermesh, & Schweiger, 2012; Keskin-Ergen et al., 2014; Thomas, Gonsalvez, & Johnstone, 2015; Hough et al., 2016; Saremi et al., 2017). Even when no differences in terms of performance were evident, research showed significant differences in terms of brain activation for the OCD patients during Go/No-Go tasks. For example, Page et al. (2009) reported abnormal frontal-subcortical activations in people with OCD during the performance of a Go/No-Go task, while Tolin et al. (2014) showed altered activations of the left frontal orbital/insular cortex. These
findings suggested the need for a compensatory brain response in OCD patients in order to maintain adequate performance during an inhibitory control task.

Inhibitory control in OCD patients has also been studied at the psychophysiological level. Keskin-Ergen et al. (2014) showed that OCD’s age of onset affects inhibitory control in different ways. At the behavioral level, patients with Late Onset (LO) OCD exhibited higher RTs, without differing from healthy controls in terms of accuracy. During the performance of a Go/No-Go task, LO OCD patients presented a decreased amplitude and latency in the N2 event-related potential (ERP) component, suggesting an alteration in the response monitoring process. Additionally, P3 ERP component was also altered in both Early and Late Onset OCD patients, although with different scalp distributions depending on the onset subtype. Similar results (increased RT and no effects in terms of accuracy) were reported by Thomas et al. (2014), but this time with altered N1, N2 and P2.

Similarly to what was found regarding cognitive flexibility, inhibitory control impairments may also be non-specific for OCD. For instance, similar behavioral impairments during the performance of Go/No-Go tasks were also shown in people suffering from ADHD (Abramovitch et al., 2012), and panic disorder (Thomas et al., 2014).

Working memory. For the working memory, research with the N-back task consistently shows decreased accuracy and/or increased RT in OCD patients (Nakao et al., 2009; Kashyap, Kumar, Kandavel, & Reddy, 2012; Koch et al., 2012; Heinzel et al., 2018). While some of the studies found these impairments already evident during low memory load tasks (Koch et al., 2012), others found increased impairment with increased memory load (Heinzel et al., 2018). However, different memory loads may be associated with different patterns of brain activation in OCD. For example, Heinzel et al. (2018), showed that, as the memory load increased, activity of the supplementary motor areas (SMA) and inferior parietal lobe decreased. Koch et al. (2011) found similar deactivations of the Anterior Cingulate Cortex (ACC) for high memory load conditions, contrasting with increased activation in the healthy controls. Different brain activations patterns explain the absence of alterations in OCD patients during low memory load tasks, because the existence of compensatory mechanisms (de Vries et al., 2014).

Finally, given the absence of studies with other clinical controls, we cannot conclude about the specificity of working memory impairments in OCD. However, it is important to note that different OCD subtypes may be associated with specific brain activations and performance patterns during the N-back task. For example, Koch et al. (2011) reported that decreased insight in OCD patients was associated with decreased N-back task performance. Nakao et al. (2009) showed that right orbitofrontal cortex activity was positively correlated with OCD severity during N-back task performance. Moreover, OCD patients that exhibited obsessions/checking rituals showed more working memory impairments than patients with cleanliness/washing rituals, and this was associated with decreases in activity in the left postcentral gyrus and the right thalamus.

Lastly, time passed since onset may also be an affecting OCD performance factor in N-back tasks. Nakao et al. (2009) showed that only the long-term group (20.3±6.1 years from OCD onset) had working memory impairments, while the short-term patients (5.5±3.1 years) did not exhibit these deficits. However, short-term OCD patients exhibited increased activation over the right dorso-lateral prefrontal cortex when compared to the long term and non-clinical controls, thus suggesting that abnormalities in terms of brain function occur during early stages of OCD.

Executive impairments with emotional paradigms

As presented above, research on executive impairments using emotional laden paradigms is scarce. Only three studies met our eligibility criteria. Two of them used the Go/No-Go task and one a task switching paradigm.

Using an emotional Go/No-Go paradigm with disgust-related and fear-related stimuli, Berlin et al. (2015) did not find differences in terms of behavioral performance between OCD and healthy controls. However, OCD patients showed increased activation in right anterior insula activations, along with other frontal, temporal and parietal regions, when compared to healthy controls when presented the emotional stimuli.

Morein-Zamir et al. (2013) used a motivational Go/No-Go paradigm to test if inhibitory control in OCD was different in the presence of reward and punishment contingencies. Overall, the authors found an increased error rate for OCD in the punishment condition but without the expected slowing following punishment.

Finally, Stern et al. (2017) tested if imaging positive and negative personal events would affect performance in a switching tasks in two conditions: internal focus (i.e., imagined positive and negative personal event scenarios) or external focus (i.e., color-word Stroop task). The authors found increased switching costs in the negative internal focus condition in OCD patients along with decreased activation in several brain regions (i.e., occipital cortex, thalamus, putamen).

Differences in results in terms of brain activation or behavioral performance in the three core executive functions are not unusual. Results are inconsistent, due to various causes. OCD is a highly heterogeneous disorder (Abramovitch et al., 2013; Bragdon et al., 2018; Fineberg et al., 2018), with several classifications of symptomatic dimensions.

Other cause of inconclusive results could be the highly comorbidty of OCD with other disorders, especially with Emotional Disorders as Depression or Dysthymic Disorder or Anxiety Disorders as Social Phobia or Panic Disorder (Remijnse et al., 2013 -some participants with pure OCD disorder and some others with comorbidities-; Heinz et al., 2018 -all pure OCD participants- and Page et al., 2009 -most of participants with comorbidities-). Even though this was enough to understand why results are not conclusive, there are other main cause than can explain it, as the use of medicated or non-medicated sample (Meiran et al., 2011 -medicated sample- and Gu et al., 2008, and Han et al., 2011 -medicated and non-medicated sample-).

Finally, there are also methodological causes that can be controlled, as not to carry the adequate statistical analysis related to the aim and to the sample (Abramovitch et al., 2013).

In the case of Berlin et al., (2015), healthy and OCD participants showed different patterns of brain activity during the presentation of emotional stimuli, but failed to provide an explanation about behavioral performance and brain activation during neutral stimulation in both healthy and OCD participants in their inhibitory task, and also in the characterization of executive functioning under emotionally positive stimuli.
The lack of a standardized criteria to perform investigation in OCD is an important limitation of the research carried out in this disorder. This could be interesting for future studies aiming to yield a wide view of impairments that could underlie executive functioning in OCD or even in other disorders.

There is growing acknowledgement that OCD is characterized by executive impairments and that these executive impairments are particularly evident in the context of emotional activation. Even though there is evidence for the existence of executive impairments in OCD, as expressed in the performance and/or processing of inhibitory control, task-switching and working memory tasks. Particularly during inhibitory control and task-switching paradigms, there is initial evidence that executive processes are modulated by the presentation of mental representation of negative valence stimuli/images, as well as the presence of aversive contingencies (i.e., punishment).

Even though more research is needed, the following tentative conclusions can be drawn from the present review:

(1) OCD patients showed impaired performance in task-switching and N-back tasks, but results are still inconsistent regarding performance in Go/No-go paradigms. Even in situations where performance remains unaffected (i.e., Go/No-Go), there is evidence in terms of alterations in OCD brain processing, suggesting the need for a compensatory brain response in OCD patients in order to maintain adequate executive performance.

(2) Studies with clinical comparison controls, suggested that executive impairments are not specific for OCD and that different OCD groups (i.e., subtypes; severity; age of onset) may be associated with different degrees of executive impairments.

(3) Finally, OCD performance in inhibitory and task-switching paradigms seem to be affected in paradigms inducting negative emotionality (e.g., negative valence stimuli, aversive contingencies).

Future studies should examine executive functioning with emotional and non-emotional paradigms in larger sample sizes, as well as incorporating what is already known about the brain networks that are altered in OCD. Since executive functioning impairment is not restricted to OCD, future studies should control depressive symptoms, as well as other variables, such as severity of OCD, chronicity (i.e., number of years since OCD was diagnosed), and heterogeneity of OCD symptoms.

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