



Behavioral and electrophysiological correlates of cognitive control in ex-obese adults



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ABSTRACT

Impaired cognitive control functions have been documented in obesity. It remains unclear whether these functions normalize after weight reduction. We compared ex-obese individuals, who successfully underwent substantial weight loss after bariatric surgery, to normal-weight participants on measures of resistance to interference, cognitive flexibility and response inhibition, obtained from the completion of two Stroop tasks, a Switching task and a Go/NoGo task, respectively. To elucidate the underlying brain mechanisms, event-related potentials (ERPs) in the latter two tasks were examined. As compared to controls, patients were more susceptible to the predominant but task-irrelevant stimulus dimension (i.e., they showed a larger verbal Stroop effect), and were slower in responding on trials requiring a task-set change rather than a task-set repetition (i.e., they showed a larger switch cost). The ERP correlates revealed altered anticipatory control mechanisms (switch positivity) and an exaggerated conflict monitoring response (N2). The results suggest that cognitive control is critical even in ex-obese individuals and should be monitored to promote weight loss maintenance.

1. Introduction

Obesity has been often associated with adverse neurocognitive outcomes, primarily in the form of executive function alterations (for reviews, [Fitzpatrick, Gilbert, & Serpell, 2013](#); [Prickett, Brennan, & Stolwyk, 2015](#); [Smith, Hay, Campbell, & Trollor, 2011](#)). Among these functions, available evidence suggests that obese adults are impaired in cognitive control, not necessarily involving food-related items.

Cognitive control abilities refer to a set of processes, such as resistance to interference, cognitive flexibility and response inhibition, which regulate, coordinate and sequence lower level processes towards adaptive goal-directed behaviors ([Braver, 2012](#); [Shallice, 1994](#)). Resistance to interference entails processes aimed on the one hand to suppress stimulus dimensions irrelevant to the task goal but eliciting over-learned and automatic response, and, on the other hand, to selectively respond to weaker but goal-relevant stimulus dimensions. These processes have been traditionally assessed by the Stroop Color Word test, which requires to name the ink color of a word while ignoring its meaning. Obese adults have been found to exhibit higher

interference effect than normal-weight controls on this test because of their higher susceptibility to the predominant but task-irrelevant stimulus dimensions (i.e., the word reading; [Cohen, Yates, Duong, & Convit, 2011](#); [Fagundo et al., 2012](#)), irrespectively of medical and psychiatric comorbidities (such as hypertension, diabetes, cardiac disease, thyroid disease, bipolar disorders, and alcohol/drug abuse; [Gunstad et al., 2007](#)).

Cognitive flexibility involves processes that allow the rapid shift from one task to another, in accordance with the change of environmental cues and/or internally formed goals ([Braver, Paxton, Locke, & Barch, 2009](#)). It has been usually examined by means of task-switching tests, such as the Wisconsin Card Sorting Test and the Trail Making Test. Compared to normal-weight controls, obese individuals make more errors (especially perseverations) on the Wisconsin Card Sorting Test ([Cohen et al., 2011](#); [Fagundo et al., 2012](#)) and are slower in executing the Trail Making subtest, which requires to alternate between number and letter series ([Cohen et al., 2011](#); [Fergenbaum et al., 2009](#)).

Response inhibition refers to the ability of withholding an already prepared motor action in compliance with contextual cues. Typically, it has been investigated with the Stop Signal Task or Go/NoGo paradigms.

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Findings on these tasks are mixed (Calvo, Galioto, Gunstad, & Spitznagel, 2014; Nederkoorn, Smulders, Havermans, Roefs, & Jansen, 2006). By comparing functional magnetic resonance images of obese and lean women, Hendrick, Luo, Zhang, and Li (2012) observed differences in brain activations during stop as compared to go trials despite similar behavioral performance between groups.

From a neural point of view, all these control processes are mediated by multiple and distinct brain circuits, mainly involving prefrontal areas (e.g., Cole & Schneider, 2007; Vallesi, 2012). Neuroimaging findings confirmed that obesity is associated with structural and functional brain alterations of the prefrontal cortex (García-García et al., 2015; Lavagnino, Arnone, Cao, Soares, & Selvaraj, 2016; Marqués-Iturria et al., 2013; Pannacciulli et al., 2006; Walther, Birdsill, Glsky, & Ryan, 2010; Willeumier, Taylor, & Amen, 2011).

Evidence supporting that obesity is negatively associated with cognitive functioning comes from studies on patients after bariatric surgical intervention. Bariatric surgery has emerged as the most effective procedure to achieve rapid, significant and long-lasting weight reduction in individuals with moderate to extreme obesity (Maciejewski et al., 2016; O'Brien, MacDonald, Anderson, Brennan, & Brown, 2013; Padwal et al., 2011; Sjöström et al., 2004). Longitudinal studies have documented that weight loss induced by the surgery produces rapid and significant cognitive improvements (for reviews Handley, Williams, Caplin, Stephens, & Barry, 2016; Spitznagel et al., 2015; Veronese et al., 2017). Furthermore, improvements in executive functioning persist for at least 3 years after surgery (Alosco et al., 2014). Interestingly, Marques et al. (2014) found no differences in brain metabolism at rest between obese women 6 months after surgery and normal weight controls, whereas there were significant differences before surgery. These findings suggest that cognitive functioning tends to go towards normalization following weight loss. Nevertheless, research on the normalization of cognitive control functions in ex-obese individuals is limited and it remains unclear whether patients who lost significant weight perform similarly to normal-weight individuals. To the best of our knowledge, the neurofunctional mechanisms of cognitive control during the execution of a task involving not food-related materials in post-bariatric patients have not been investigated yet.

To address this issue, we recruited a group of patients who successfully reached a significant weight loss after bariatric surgery and a group of age- and education-matched normal-weight controls. All participants were invited to complete four computerized tasks assessing resistance to interference, cognitive flexibility, and response inhibition, namely two Stroop tasks (verbal and spatial), a cued task-switching (Switching task) and a Go/NoGo task (the Sustained Attention to Response Test, SART). The electrophysiological signal was simultaneously recorded during the execution of the two latter tasks. The analysis of event-related potentials (ERPs) allowed us to detect fast brain responses mediating cognitive processing and, importantly, to elucidate the mechanisms underlying control processes. Unlike previous ERP studies (Hume, Howells, Rauch, Kroff, & Lambert, 2015; Nijs, Franken, & Muris, 2010; Nijs, Muris, Euser, & Franken, 2010), we focused on electrophysiological correlates of cognitive control processes exclusively evoked by non food-related stimuli, with the aim to investigate general cognitive control functions, above and beyond attentional biases towards food-related materials. If the substantial weight loss in ex-obese patients reflected and/or induced normal cognitive control processes, no significant differences should emerge between the two groups. Alternatively, we expected to find differences in behavioral and/or electrophysiological responses to stimuli demanding higher cognitive control, as detailed below.

In the case of the Stroop tasks, we predicted a larger interference effect ('Stroop effect'), which means a worsening in performance (i.e., a decrease in accuracy and/or a slowing in RTs) on incongruent compared to congruent trials in the patient group.

In the Switching task, we predicted a higher 'switch cost', which means a worsening in performance on switch compared to repeat trials,

in terms of accuracy and/or RTs. Altered ERP responses to cue and target stimuli were also expected. In cued task-switching paradigms, the most robust ERP component is represented by a positive potential elicited by the onset of the cue (i.e., the signal that instructs the task to be implemented on the upcoming target), larger for switch relative to repeat trials, named 'switch-positivity' (for a review see Karayanidis & Jamadar, 2014). This potential has a parietal distribution on the scalp and emerges starting from about 150 ms after the cue onset, for a duration that varies depending on task parameters (Nicholson, Karayanidis, Poboka, Heathcote, & Michie, 2005). It reflects proactive control processes that prepare in advance the cognitive system to shift task-set on the upcoming target and includes mechanisms of goal shifting and rule activation (i.e., the loading of the relevant task goal and rules and the inhibition of the irrelevant ones; Karayanidis et al., 2010). Another robust ERP component is represented by a positive potential time-locked to the onset of the target, smaller for switch relative to repeat trials (Barceló, Periañez, & Nyhus, 2007; Karayanidis, Whitson, Heathcote, & Michie, 2011; Kieffaber & Hetrick, 2005; Nicholson, Karayanidis, Davies, & Michie, 2006). This relative negativity for switch trials has been sometimes referred to as 'switch-negativity' (Karayanidis et al., 2003; Karayanidis, Coltheart, Michie, & Murphy, 2003). When preceded by a long cue-to-target interval, it emerges as early as 150 ms and reaches maximal amplitude around 400 ms after the target onset. This component has a parietal scalp distribution and reflects the recruitment of reactive control processes, which intervene to resolve the stimulus-driven interference (Kiesel et al., 2010). With this in mind, we made the following predictions: if ex-obese patients fail in proactive control, the amplitude of their cue-related switch-positivity would be less pronounced than that of the control group; on the other hand, if they fail in reactive control, they should show a less pronounced target-related switch-negativity.

In the SART, we expected to find more commission errors on the NoGo trials and altered ERP correlates as indexes of impaired inhibitory processes in patients. Specifically, the N2 and NoGo-P3 components, elicited by the NoGo trials, were examined (O'Connell et al., 2009; Zordan, Sarlo, & Stablum, 2008). The N2 is a negative potential occurring at about 200 ms after the onset of NoGo stimuli over fronto-central sites, whereas the NoGo-P3 is a positive potential occurring approximately at 300 ms after the onset of NoGo stimuli in a more anterior scalp position relative to the parietal Go-P3 (Eimer, 1993; Falkenstein, Hoormann, & Hohnsbein, 1999). Although the specific functional role of these ERP components is debated (Falkenstein, 2006; Smith, Johnstone, & Barry, 2007; Smith, Johnstone, & Barry, 2008), there is consensus that the N2 mainly reflects conflict monitoring rather than response inhibition per se, while the NoGo-P3 mainly reflects the suppression of a planned response (Donkers & Van Boxtel, 2004; Enriquez-Geppert, Konrad, Pantev, & Huster, 2010; Nieuwenhuis, Yeung, van den Wildenberg, & Ridderinkhof, 2003; Randall & Smith, 2011). Conflict especially occurs when a response must be refrained in contexts in which NoGo trials are rare and there is a prepotent tendency to make a go response, as is the case for the SART. We expected that patients exhibit altered N2 and/or in NoGo-P3 amplitude if they have problems in conflict monitoring and/or response inhibition, respectively.

2. Method

2.1. Participants

Socio-demographic characteristics of the enrolled sample are summarized in Table 1. A total of 21 patients (aged from 21 to 61 years) and 22 normal-weight controls (aged from 20 to 60 years) took part in the study. Participants were included if they had a BMI < 35 kg/m², if they reported normal or corrected-to-normal visual acuity, normal color vision, normal hearing, no neurological disorders (e.g., epilepsy, dementia), no major psychiatric disorders (e.g., bipolar, schizophrenia),

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