Effects of bariatric surger and weight loss on resting-state functional connectivity

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1 Abstract

2 Introduction

Over the past decades, the global burden of obesity has increasingly been confronted as a matter of urgency by research. Besides metabolic dysfunctions, obesity has been consistently associated with reduced gray matter volume, less intact white matter structure and reduced cognitive function (Beyer et al. 2019; Zhang et al. 2018). Luckily, dietary interventions such as caloric restriction and related metabolic improvements, and weight loss have been suggested to improve neuronal plasticity and cognitive performance (Witte et al. 2009; Zhang et al. 2018; Veronese et al. 2017). In some cases behavioral intervention fail to yield the desired success regarding weight loss. There are non-behavioral alternatives at hand. Bariatric surgery is one promising option to combat morbid obesity, as it rapidly improves weight status, metabolic dysfunctions, and co-morbidities, such as diabetes [@]. Roux-en-Y gastric bypass (RYGB) is the most common procedure as it not only restricts the food intake by reducing stomach volume but also affects the absorption of macronutrients and the hormonal profile [@]. Other widely used procedures are vertical sleeve gastrectomy (VSG) and gastric banding (GB) which only restrict food consumption. Precise mechanisms as to how bariatric surgery leads to recovery are yet to be elucidated. As a first step, a comprehensive understanding of the concurrent physiological changes underlying weight loss and recovery is needed. This will inform inferences about potential mechanisms and either support interventions proven to be effective or ideally allow imitating them with less invasive alternatives.

Little is known about the potential beneficial effects of bariatric surgery on brain function in the obese population. Thus, one recently emerging research focus is how brain metabolism and functional connectivity changes in response to surgery, in particular with regard to hedonic motivations for food, which play a fundamental role in weight relapse. The reward network comprising the ventromedial prefrontal cortex (vmPFC), the striatum (STR) but also the anterior insula (antIns) has been linked to food valuation processes in decision-making in lean individuals (Bartra, McGuire, and Kable 2013; Hare, Malmaud, and Rangel 2011; Hutcherson et al. 2012; Schmidt et al. 2018; Wiemerslage et al. 2016). These regions also seem to be altered after bariatric surgery (Lips et al. 2014; Hogenkamp et al. 2016; **???**). Obese individuals exhibited increased connectivity between frontal and mesolimbic regions and weaker connectivity within regions of the mesolimbic system (encompassing limbic and striatal regions). But these differences seemed to normalize, as trends reversed when looking at the resting state connectivity after compared to before the surgery (Duan et al. 2020). Resting state activitiy increased in subcortical regions, such as the insula and striatum (Wiemerslage et al. 2016). Interestingly, patients report changes in food preferences and eating behavior after the surgery that may influence weight loss beyond malabsorption of nutrients and restricted food ingestion. Those psychophysiological and behavioral effects are presumably related to post-surgical changes in visceral sensory perceptions and endocrinological signaling. Corresponding information is processed by the fronto-mesolimbic system and affects appetite and reward signalling which may influence weight regulation (Mulla, Middelbeek, and Patti 2017; Nudel and Sanchez 2019).

Because multiple resting state networks are relevant to obesity and associated with abnormal neurocircuitry interactions (Ding et al. 2020), extensive research has been devoted to investigating the the relationship between the control network and the reward network. However, the dynamics within the default network may also be of importance because it is associated with processing of self-referent as well as introspective information, such as hunger sensation [@;@] and appetite (Tregellas et al. 2011). Weight regulation and energy expenditure, on the other hand, are highly dependent on a complex interplay of external and internal sensory processing, as well as molecular homeostasis regulation.

The default mdoe network is mainly composed of the posterior cingulate cortex (PCC)/precuneus, the medial prefrontal cortex (MPFC) and inferior and lateral parietal cortex (IPC, LPC; approx. BA 39) (Raichle 2015). The right ventral anterior cingulate cortex (VACC), superior frontal cortex (SFC), and inferior temporal cortex (ITC) show weaker but also reliable association with the PCC over the course of one year. Even broader conceptions count left VACC, middle temporal gyrus (MTG), and parahippocampal cortex, although associations with the PCC are not as stable (Chou et al. 2012). Functional connectivity of this network has been shown to be linked to BMI (Beyer et al. 2017) and altered after bariatric surgery (Olivo et al. 2017). Generally, studies show an increased activation in the default mode network, especially in the precuneus and posterior cingulate cortex (PCC) in obese individuals [Kullmann et al. (2011); @]. Comparing spontaneous activitiy before and after surgery shows a decrease in areas including superior frontal regions, and a decrease superior parietal lobule when in sated state (Wiemerslage et al. 2016). Concerning spontaneuous functional connectivity in these regions, patient having undergone bariatric surgery resemble normal-weight individuals rather than obese individual in having a weaker connectivity within the default mode network (Frank et al. 2013). A longitudinal study investigating confirmed that while there was stronger connectivity in the default model network in obese patients before the surgery, it seemed weakened over the course of one year. Because differences between lean controls and obese individuals that existed prebariatric surgery were no longer detectable after the surgery, the authors argue for a normalization in functional connectivity(Olivo et al. 2017). Consistent with these findings, other studies reported a reduction of functional connectivity of these and other regions of the default mode network, such as the VMPFC after the surgery (Li et al. 2018).

… It has been stated that among patients undergoing surgery, change in BMI was correlated with the changes in connectivity of the default mode network, namely between the PCC/precuneus and the DLPFC (Li et al. 2018). On the other hand, there are also indicators of reduced functional integrity, e.g. for the anterior cingulate cortex (ACC) at resting state compared to lean individuals (Kullmann et al. 2011). …

As described previously, several studies have investigated the effects of bariatric surgery on the intrinsic functional connectivity in patients. Yet, to our knowledge there is no quasi-experimental study, comparing a cohort of patients to a cohort with similar characteristics but unexposed to the intervention, i.e. bariatric surgery, over an extended time period as would be demanded to draw more substantiated inference (George et al. 2016). In this study, we aim to bridge this gap and investigate possible dynamics of within-reward network connectivity before and after bariatric surgery by comparison with a contemporaneously measured waiting-control group. Moreover, we will explore whether the changes in functional connectivity are associated with the amount of weight lost after bariatric surgery treatment in obesity to explore a potential gradient link. In addition, we will investigate potential changes in within-network functional connectivity after surgery in other resting-state networks such as default mode network (DMN). Participants are measured at baseline, at 6 months and at 24 months to capture both phases of rapid weight-loss and maintenance as expected from non-surgical interventions (Shai et al. 2008). Notably, we will consider that different courses in increase and decrease of functional connectivity that are not necessarily linear are possible over the course of one year, depending on the phase of weight management (Olivo et al. 2017).

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