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Commentary

The elusive functional bases of appetite control in the brain

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On paper: Rémi Neveu, Dorine Neveu, Edouard Carrier, Aurelia Gay, Alain Nicolas, Giorgio Coricelli. *Goal directed and self-control systems in bulimia nervosa: an fMRI study*

The pursuit to understand human control over appetite has its roots in ancient Buddhism, Greek philosophy, Western medicine, and more recently neuroscience. Over the last two decades, sophisticated functional neuroimaging in the clinical neurosciences has progressed, but so too has the complexity of *appetite control* as a concept, particularly in the field of eating disorders. This lack of clarity is reflected in the prominence of brain imaging studies with titles referencing self-regulation, cognitive inhibition, cognitive restraint and top-down control – to name but a few terms that broadly encompass appetite control. In further demonstration of this intangibility, a recent systematic review of thirty-two neuroimaging studies of bulimia nervosa (BN) and binge eating disorder (BED) concluded that the heterogeneity of scanner paradigms, neuroimaging modalities, illness stage, and strength of the reported findings prevented solid definitions as to the neural substrates of deficits in appetite control, although dysfunction in fronto-striatal circuitry appeared key [1]. Alongside the relatively rare incidence of eating disorders (between 1 and 5%), the continuing rise in the general population of obesity and other appetite control disorders (e.g. drug craving, binge drinking, risky sexual behaviour), combined with the burden that these disorders place on healthcare systems, encourages the pursuance of understanding the nuances of brain systems that define appetite control.

The functional magnetic resonance imaging (fMRI) study by Neveu and colleagues attempts to gauge the nuances of appetite control in BN. Putting their study in context, Neveu and colleagues correctly emphasise that most brain imaging studies of eating disorders to date have focused on severe – often fatal – appetite control in anorexia nervosa (AN), with BN and BED trailing behind in research publications. In contrast, a rich body of neuroimaging evidence classifies AN by heightened activation of prefrontal cortex executive control networks, reduced activation of somatosensory regions - such as the parietal and insular cortices (linked to body image disturbances) - and hyposensitivity within the dopaminergic mesolimbic saliency network, including aberrant striatal activation [2]. Moreover, direct comparisons of brain activation in AN and BN provide further insights into the underlying neurobiology at the extremes of appetite control, as shown by a previous fMRI study where women with AN and BN passively viewed appetizing food images [3]. In BN compared to AN, deactivation of parietal cortex and dorsal posterior cingulate cortex (somatosensory areas), and greater activation of the striatum (reward/motivation processing), superior temporal gyrus, right insula (associated with anxiety) and supplementary motor area (linked to uncontrolled decision-making behaviour) was observed. These regional activation differences are in line with recent, more sophisticated analyses of neural processes in BN using multi-variate analyses based on machine learning [4]. Cyr and colleagues demonstrated that women with BN show diminished recruitment of prefrontal cortex circuitry and deficient regulation of the striatum by the prefrontal regions that may classify both chronic and sub-threshold BN with lower disorder severity.

The Neveu et al. paper progresses the state-of-the-art research of appetite control with their nuanced fMRI paradigm, which sought to personalize the measurement of neural activation and connectivity to uncontrolled food-image preference choices in women with BN. The authors did this by using prior individual ratings of the tastiness and healthiness of food images as a basis for measuring the neural substrates of subsequent controlled (healthy) or uncontrolled (unhealthy + tasty) decisions concerning which food images healthy versus BN women preferred to eat [5]. The authors revealed that while both groups made more uncontrolled choices to eat the food in the images simply because it appeared tasty, the women with BN exercised uncontrolled decisions by choosing unhealthier (and tasty) food, whereas the healthy women made healthier choices overall. The uncontrolled decisions of the BN women were reflected in increased ventrolateral prefrontal cortex (vlPFC) activation, which was in turn functionally connected to increased activation of the dorsolateral prefrontal cortex (dlPFC). These results are ground-breaking, because the authors show for the first time how potentially losing control of one's healthy appetite goals is linked to a specific neural pattern.

The vlPFC is an integration hub combining sensory information arising from the internal milieu (related to reward and saliency processing in dopaminergic regions, including the striatum, hippocampus, amygdala) and external information arising from salient objects (e.g. tasty food) [6]. The vlPFC receives projections from the orbitofrontal cortex (OFC), which aids in the evaluation of the motivational and emotional context of the perceived object. As such, if an object is deemed highly salient and congruent with one's motivational goals (e.g. the desire to consume some highly palatable food), the vlPFC will typically show increased activation in response to that object. Relatedly, the dlPFC is a major hub supporting executive functions such as working memory that keep in mind for delayed periods cognitive strategies for future goals. Therefore, activation of the dlPFC appears to be significantly

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related to staving-off immediate distractions, which in behavioural terms may manifest as appetite control. That said, reduced activation in the dlPFC and its related prefrontal cortex executive control network may reflect more efficient neural processing. Conversely, hyperactivation of the dlPFC may demonstrate the need to exercise greater cognitive restraint and increased mental effort to maintain control [7].

With nuanced neural substrates of appetite control getting closer to being defined by the latest neuroimaging studies, further research is needed to understand the processes involved in strengthening appetite control. By doing so, rates of resistant-to-treatment sometimes fatal eating disorders, and more prevalent health conditions such as obesity and substance use disorders, may be significantly reduced. Real-time fMRI is one candidate approach to improving appetite control processes, using neurobiological feedback during a brain scan, so that a person can learn to link a heightened sense of appetite control to second-by-second changes in brain activation - in the fronto-striatal circuitry for example [8]. Furthermore, there is a growing interest in altering inherent neuroplasticity in prefrontal cortex networks via cognitive training using progressively difficult working memory tasks as an adjunct to treatment [9]. The rationale is that by strengthening the fronto-striatal circuitry, more efficient neural processing will be achieved that can support cognitive strategies for achieving abstract goals as opposed to succumbing to immediate rewards (e.g. being able to choose healthy over unhealthy food). However, despite rapid neuroscientific advances in the field of appetite control, it is still not fully elucidated how long-term changes in the brain correspond to improvements in restrictive or excessive eating behavior. As such, until further studies like the Neveu et al. study are conducted that can detect nuances in neural activation between extremes of appetite control, ways to improve eating and related disorders will remain elusive.

Disclosure

The author declares no conflict of interest.

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