

## In this Issue

### The neuropsychology of disgust

Beginning with the landmark case of Phineas Gage (Harlow, 1868), studies of neurological patients with ventromedial prefrontal cortex (vmPFC) damage have time and again demonstrated a critical role for this brain area in various aspects of emotion, social cognition and decision-making. The importance of vmPFC for social and affective function is further underscored by a host of clinical neuroimaging studies, which have demonstrated abnormal patterns of vmPFC activity in psychiatric disorders such as major depression, post-traumatic stress disorder, obsessive-compulsive disorder, schizophrenia, psychopathy and autism. Specifying the essential functions of vmPFC may therefore be a key step in elucidating the neuropathophysiological mechanisms underlying diverse forms of socio-affective dysfunction in mental illness. In this regard, lesion studies are an indispensable methodological approach; the loss of vmPFC function through focal lesions (e.g. as a result of tumor, stroke or aneurysm) affords a unique opportunity to assess in humans the causal contribution of vmPFC to particular psychological faculties. In this issue, Ciaramelli *et al.* (2012b) present the latest advance in this line of lesion patient research.

The investigators focus on the negative emotion ‘disgust’, which can apply to physical objects, such as rotten food or bodily excrement, as well as immoral or socially unacceptable behavior, such as lying or cheating. To determine whether vmPFC is especially critical for the social/moral connotation of disgust, the study team developed a task involving a series of disgust-inducing hypothetical scenarios, with the key experimental manipulation being the subcategory of disgust featured in each scenario. ‘Core’ disgust scenarios involved contamination or physical impurity (e.g. deciding whether to eat a slice of pizza from an ant-infested kitchen), whereas ‘interpersonal’ disgust scenarios involved contact with an unsavory or deviant other (e.g. deciding whether to share a park bench with a vagrant) and ‘moral’ disgust scenarios involved exposure to a moral transgression (e.g. deciding whether to divulge a friend’s infidelity to his wife). The investigators found a remarkably specific effect of vmPFC damage; the vmPFC lesion patients exhibited normal sensitivity to ‘core’ and ‘moral’ disgust-inducing actions but endorsed an abnormally high proportion of the ‘interpersonal’ disgust actions. These results therefore associate vmPFC damage with a relatively specific insensitivity to the social status of others, rather than a general flattening of negative affect or overall decision-making impairment. These intriguing findings illuminate several interrelated issues in contemporary social, cognitive and affective neuroscience.

One is the iterative fractionation and refinement of broad constructs, such as ‘disgust’ and ‘morality’, into subcomponents with distinct underlying neural substrates. In recent years, a number of studies have converged to suggest that the feeling of ‘moral’ disgust is derived from, or at least psychologically and physiologically related to, the

feeling of ‘physical’ or ‘core’ disgust. For example, one study showed that the muscle activity that characterizes the facial expression of physical disgust (raising the upper lip and wrinkling the nose) is elicited not only by drinking unpleasant-tasting liquids and viewing pictures of contamination, but also when experiencing unfair treatment, which represents a more abstract moral transgression (Chapman *et al.*, 2009). Another set of studies have shown that experimental manipulations of the feeling of ‘core’ disgust can influence the severity of subsequent moral judgment (Wheatley and Haidt, 2005; Schnall *et al.*, 2008a,b). Despite these putative psychological links between ‘core’ and ‘moral’ disgust, one functional magnetic resonance imaging (fMRI) study has demonstrated partially dissociable patterns of neural activity, with notably greater mPFC activity for ‘moral’ versus ‘core’ disgust stimuli (Schaich Borg *et al.*, 2008). This subspecification strategy has also been effectively applied to domains of moral judgment outside of disgust. For example, a pioneering fMRI study of moral judgment distinguished between ‘personal’ and ‘impersonal’ harms, and identified a number of brain areas, including mPFC, that respond differently to scenarios depicting one or the other type of harm (Greene *et al.*, 2001). Moreover, abnormalities in judgments of personal (but not impersonal) harms have been associated with damage to vmPFC (Ciaramelli *et al.*, 2007; Koenigs *et al.*, 2007) as well as administration of specific psychoactive drugs, such as citalopram (Crockett *et al.*, 2010) and lorazepam (Perkins *et al.*, 2012). Similarly, differentiating between intentional and accidental harms has revealed distinct patterns of neural activity (Young *et al.*, 2007), as well as selective abnormalities in moral judgment following vmPFC damage (Young *et al.*, 2010a; Ciaramelli *et al.*, 2012a) and transcranial magnetic stimulation applied to the temporoparietal junction (Young *et al.*, 2010b). Ciaramelli *et al.*’s approach thus extends a fertile strategy of linking subclasses of socio-moral judgment to distinct neuroanatomical substrates.

A related issue highlighted by this study is the potential for developing novel neuropsychological assessment instruments to probe specific aspects of social-affective function. In the realm of clinical neuropsychology, evaluation of social-affective function typically consists of simple self-report symptom inventories (e.g. Beck Depression Inventory, State-Trait Anxiety Inventory). In this respect, assessment of social-affective function lags far behind its ‘cognitive’ counterpart, where extensive batteries of performance-based tests have long been established. For example, in the domain of memory, there are dozens of standardized performance-based tests that probe the integrity of specific competencies (verbal vs. non-verbal, short-term vs. long-term, recall vs. recognition and so on). Similar batteries of performance-based tests have been developed to probe aspects of language, perception and executive function. Why are there not analogous performance-based clinical measures of social and affective function? After all, mood and anxiety disorders are the number one leading cause of disability in developed countries (WHO, 2008). Moreover, the National Institute of Mental Health proposes that a key step in the development of more effective treatments for psychiatric disorders is to

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identify specific domains of social, cognitive and affective dysfunction that cut across traditional diagnostic categories, and to link these domains of psychological function to their underlying neural circuitry (Insel *et al.*, 2010; <http://www.nimh.nih.gov/research-funding/rdoc/index.shtml>). A critical component of this strategy is improving the measurement of specific social and emotional competencies. The present study by Ciaramelli *et al.*, which suggests an association between a relatively specific socio-affective impairment (sensitivity to the social status of others) and a relatively focal brain area (vmPFC), appears to be a step in this direction.

Of course, vmPFC is known to play a far more diverse role in social and affective function than simply 'sensitivity to the social status of others.' This study thus begs the overarching question: what exactly does vmPFC do? Most current systems-level research on vmPFC focuses on one of three neural circuits. One circuit, involving the vmPFC and amygdala, is thought to underlie the regulation of negative emotion (Phelps *et al.*, 2004; Milad *et al.*, 2006; Rauch *et al.*, 2006). A second circuit, involving the vmPFC and ventral striatum, is thought to underlie aspects of reinforcement learning and subjective reward value (McClure *et al.*, 2004; O'Doherty, 2004, 2011). A third circuit, involving the vmPFC, dorsomedial PFC, posterior cingulate cortex/precuneus and inferior lateral parietal cortex (the so-called 'default mode network') is thought to underlie aspects of self-referential processing and rumination (Buckner *et al.*, 2008; Qin and Northoff, 2011; Whitfield-Gabrieli *et al.*, 2011). Is it the case that vmPFC consists of multiple, functionally and anatomically distinct subregions that correspond to each of these circuits? For example, might a subgenual sector have a particularly important role in modulating amygdala activity, whereas a pregenual sector may have a greater role in modulating the self-processing network? Or, alternatively, might vmPFC subserve some higher order meta-function, which integrates the activity of several different circuits representing various elements of social and affective processing, and translates these into an adaptive behavioral response?

Traditionally, human lesion studies have not been well suited to address the possibility of functionally and anatomically distinct subunits within the vmPFC. The reason for this is the gross etiology of naturally occurring lesions in this area of brain, coupled with the relative rarity of such patients. vmPFC lesion studies typically involve  $n=10$  or fewer vmPFC lesion patients, making it difficult to parse the contribution of putative vmPFC subunits to the observed impairments. This study attempts to address this issue through a correlation analysis, showing opposite relationships between interpersonal disgust acceptance rates and lesion volumes in Brodmann Areas 10 and 11, respectively. Although this correlation analysis represents a thoughtful (if only preliminary) approach to potential functional heterogeneity within vmPFC, a more comprehensive understanding will likely depend on increasing patient sample sizes.

In sum, through an inventive combination of moral psychology and behavioral neurology approaches, Ciaramelli *et al.* have demonstrated a critical role for vmPFC in processing interpersonal disgust. This study exemplifies the capability of human lesion studies to yield novel insight into the neuropsychological mechanisms underlying social and affective processing.

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