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LETTER TO THE EDITOR

Social communication in Tourette syndrome: a glimpse at the contribution of the insula and the prefrontal cortex

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Sir,

We read with great interest the paper 'Tourette syndrome: a disorder of the social decision-making network', recently published in *Brain* (Albin, 2018). In this article, Albin explored the possibility that Tourette syndrome is characterized by neural abnormalities localized to several important brain regions associated with social behaviour and social decision-making. The author focused on several brain structures such as the amygdala, the periaqueductal grey, the hypothalamus, and basal ganglia, outlining key details on the relevance of these neural structures to support the view of this syndrome as disorder of social communication.

Despite the growing body of evidence from psychometric studies (Eddy, 2018) showing abnormalities of social cognition in Tourette syndrome, the social behaviour dimension has been relatively under-explored. A core phenomenological feature of the Tourette spectrum is obscene (coprophenomena, e.g. coprolalia, coprographia and copropraxia) and non-obscene socially inappropriate behaviours (NOSIBs). Although social disinhibition appears to be a highly heritable symptom type within Tourette syndrome-related phenotypes (Hirschtritt *et al.*, 2016), its association with a dysfunctional connectivity within the social behaviour network (SBN) has not been investigated in case-control studies. Brain imaging studies investigating the functional neuroanatomy of social behavioural anomalies are surprisingly scant and limited to single case studies. In Stern *et al.* (2000) the insular activity was particularly pre-eminent in a Tourette syndrome patient affected by coprolalia, whereas Gates *et al.* (2004) described a Tourette syndrome patient in whom coprolalia was associated with activation of the left middle frontal gyrus.

As a complement to Albin's thought-provoking view and in keeping with the findings from these isolated case studies, we believe it is interesting to expand the discussion to two further neural regions that are key components of the SBN, namely the insula and the ventro-medial prefrontal cortex (vmPFC). A recent review of our group (Vicario *et al.*, 2017) suggested that dysfunction of these two cortical regions has a central role in the pathogenesis of defects in social decision-making behaviours, such as moral reasoning and decision-making, across different neurological and psychiatric disorders, including obsessive-compulsive disorder, the second most common behavioural comorbidity of Tourette syndrome. Importantly, the neural connectivity of both these regions is altered in Tourette syndrome (Jeffries *et al.*, 2002; Müller-Vahl *et al.*, 2009; Tinaz *et al.*, 2015; Cavanna *et al.*, 2017; Greene *et al.*, 2017).

Tinaz *et al.* (2015) used graph theory-based neural network analysis of resting state functional MRI data to demonstrate higher connectivity of the right dorsal anterior insula with urge- and tic-related cortico-striato-thalamic regions, as well as a positive correlation between functional connectivity between this portion of the insula and the supplementary motor area and severity of premonitory urges.

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This change of functional connectivity could affect social cognitive fitness besides influencing awareness and processing of bodily sensations. The insular cortex has been linked to affiliative behavioural patterns in an intracortical microstimulation study on non-human primates, with particular regard to social and communicative behaviour (Caruana *et al.*, 2011). Moreover, a variety of orofacial motor programmes, crucial for social communication including affiliative behaviour, has been localized to the anterior and centro-ventral insular sectors (Jezzini *et al.*, 2012). A body of human imaging studies exploring empathy for others' pain have shown activations in the anterior insula, also involved in the direct experience of pain. This evidence supports the computational role of the anterior insula in processing emotionally charged states in order to guide adaptive, goal-directed behaviours in dynamic social contexts (Bernhardt and Singer, 2012). Kim *et al.* (2016) reported greater insular activation in response to tasks involving the Theory of Mind (ToM) dimension, i.e. the ability to think about mental states such as beliefs and emotions, a social cognition dimension, which is known to be affected in Tourette syndrome (Eddy *et al.*, 2011). New imaging studies are therefore needed to understand which subdivisions of the insula are characterized by dysfunctional connectivity in Tourette syndrome, and how this relates to social cognition performance.

In a recent, large voxel-based morphometry study, Greene *et al.* (2017) reported reduced white matter volume bilaterally in the orbital and medial prefrontal cortex of Tourette syndrome patients. Different subregions of the orbital frontal cortex appear to be associated with different features of social cognition (Nestor *et al.*, 2013). Moreover, in healthy subjects the volume of the orbital prefrontal cortex was found to correlate with the size of social networks (Powell *et al.*, 2012).

Shamay-Tsoory *et al.* (2007) also documented an impairment of the 'affective' subtype of the ToM dimension in association with dysfunctional connectivity of the vmPFC. Like for the insular region, more research is necessary to understand the correlation between structural and functional connectivity changes and social cognition performance in patients with Tourette syndrome.

Overall, our considerations corroborate the hypothesis of a social communication deficit in Tourette syndrome, at the same time highlighting the importance to include the insula and the PFC as two key structures requiring exploration in future research on the social behaviour network of Tourette syndrome.

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