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CEREBELLUM INVOLVEMENT IN OBSESSIVE-COMPULSIVE DISORDER RELATED BRAIN NETWORK MODEL

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Abstract

Conventional obsessive-compulsive disorder related brain network model relies mainly on cortico-striato-thalamo-cortical areas. However, recent findings consistently point cerebellar structural and functional differences in obsessive-compulsive disorder patients compared to healthy controls. Here we briefly reviewed these studies and argued that cerebellum should be involved in obsessive-compulsive disorder related brain network model for a better understanding of the nature of this disorder.

Keywords: Obsessive-compulsive disorder, OCD, cerebellum.

Obsessive-compulsive disorder (OCD) is a chronic mental disorder typically characterized by the presence of recurrent, persistent and intrusive thoughts (obsessions) leading to intentional repetitive behaviors or mental acts (compulsions) to avoid anxiety. OCD was classified under the anxiety disorders spectrum in DSM-4-TR, but is grouped under a new spectrum that is called the obsessive-compulsive and related disorders in the new DSM-5 (APA, 2013). Theoretical models suggest that OCD is related with functional and structural abnormalities in cortico–striato–thalamo–cortical (CSTC) network in general (Eng et al., 2015) and orbitofronto-striatal circuits in particular (Menzies et al., 2008). However in several studies, posterior brain regions including cerebellum is consistently reported as areas manifesting structural and functional changes in OCD patients. Therefore a number of recent research and review papers suggest the involvement of cerebellum in OCD related brain network model (Menzies et al., 2008; Hou et al., 2012; Ping et al., 2013; Kim et al., 2015).

Cerebellum is well known as the center crucial for movement related functions such as movement coordination and motor learning. On the other hand, many recent studies revealed its role in cognitive functions and that the functional or anatomical abnormalities of cerebellum is associated with a variety of psychiatric disorders (see Phillips et al., 2015 for review). In the light of these evidences in neuroimaging study on OCD, increasing attention have now been paid to the cerebellum (Hou et al., 2012).

Ample evidence suggests the neuroanatomical and functional changes in OCD as compared to heathy controls (HCs). A majority of the structural studies used voxel based morphometry (VBM) as the main method of investigation and most of them consistently reported increased gray matter (GM) volume (Pujol et al., 2004; Kopřivová et al., 2009; Okada et al., 2015) with a few exceptions that found decreased GM volume (Kim et al., 2001). However, most of recent studies pointed cerebellum as one of the main areas that distinguished OCD patients from HCs (Kim et al., 2015). Studies of white matter (WM) changes in OCD revealed that compared to HCs, patients had significantly higher fractional anisotropy (FA) values.

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in various tracts in left cerebellar and brainstem white matter (Zarei et al., 2011). Despite all these studies some studies did not find cerebellar abnormalities in OCD (see Piras et al., 2015 for a review).

Regarding the functional projections of aforementioned structural abnormalities in cerebellum, some studies has investigated patients with OCD. In brief, fMRI studies reported decreased activation in the cerebellum during task switching (Woolley et al., 2008) and interference inhibition (Nabeyama et al., 2008; Woolley et al., 2008) which increased with the clinical improvement and task performance (Nabeyama et al., 2008). Regarding functional connectivity, patients with OCD presented decreased amplitude of low frequency fluctuations (ALFF) (Hou et al., 2012) and increased intra-regional synchronized activity (ReHo) in the bilateral cerebellum (Ping et al., 2013; Hou et al., 2014). However, some other studies found decreased cerebellar connectivity in OCD as compared to healthy controls (Zhang et al., 2011). Taken as a whole, it appears to be that there is no clear consensus about the direction of functional changes in OCD, though abnormal activity was present for most of the studies.

Cerebellar findings are also shown to be related with OCD disease severity. GM volume in cerebellum was found to be correlated with severity level and again the results are not unidirectional; both positive (Zarei et al., 2011) and negative correlations were found (van den Heuvel et al., 2009). Cerebellar abnormalities and their relation with treatment response was investigated in a few studies. In a single-photon emission-computed tomography (SPECT), researchers found that responders showed a decrease in regional cerebral blood flow (rCBF) in cerebellar vermis and an increase in cerebellum tonsil compared to HCs (Wen et al., 2013). The same study pointed that the reduction in the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) score was positively correlated with pre-treatment rCBF in cerebellum. Another study reported an inverse correlation between the ReHo of the cerebellum and the Y-BOCS compulsive scores (Ping et al., 2013).

Taken as a whole, in light of these recent studies, it may be plausible to include cerebellum to the traditional CSTC network in OCD. Thus, it may be necessary to revisit the CSTC model (Menzies et al., 2008; Hou et al., 2012; Ping et al., 2013; Kim et al., 2015). In fact, a few studies have already shown the relationship between cerebellum and CSTC network. (see Eng et al., 2015 for a review). Besides, some other studies have argued that cerebellum may contribute to the regulation of CSTC network (Tobe et al., 2010).

CSTC model worked quite well for understanding OCD related brain changes and their relation with the behavioral manifestations of OCD, but recent findings point alterations in other brain regions and suggested to extend CSTC model. One drawback of neuroimaging studies in general is the exclusion of cerebellar regions in data acquisition stages. Therefore, it is not entirely clear whether or not cerebellar abnormalities were consistent for previous neuroimaging work in OCD. Besides, there is the well-known registration error in cerebellum due to the restraints of VBM techniques. The exclusion of cerebellum from the models of psychiatric disorders may cause imperfect understanding of the nature of those disorders. A suggestion for future studies may be the segmentation of cerebellum separately and evaluating the association between symptoms, treatment response and prognosis of patients suffering from OCD. Lastly, further research is required to reveal whether the supervisory role of cerebellum over CSTC circuit is consistent together with their implications in OCD to place cerebellum in the right spot in OCD related brain network model.

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