

Effective connectivity of brain regions in depression

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We have recently published a paper showing which brain regions have altered functional connectivity in autism (Cheng et al., 2015). Functional connectivity is measured by the correlation between voxels in the brain, and when patient and control groups are compared, can provide useful information about how the different connectivity between areas is related to the disorder. This can help in understanding the disorder, and potentially in treating it. The functional connectivity has been measured by function magnetic resonance neuroimaging in the resting state.

We have now extended this approach to depression (Cheng et al., 2016). We are reporting the first brain-wide voxel-level resting state functional-connectivity neuroimaging analysis of depression with 421 patients with major depressive disorder and 488 controls.

As shown in Fig. 1, one major circuit with altered functional connectivity involved the medial orbitofrontal cortex BA 13, which is implicated in reward, and which had reduced functional connectivity in depression with memory systems in the parahippocampal gyrus and medial temporal lobe. The lateral orbitofrontal cortex BA 47/12, involved in non-reward and punishing events, did not have this reduced functional connectivity with memory systems, so that there is an imbalance in depression towards decreased reward-related memory system functionality.

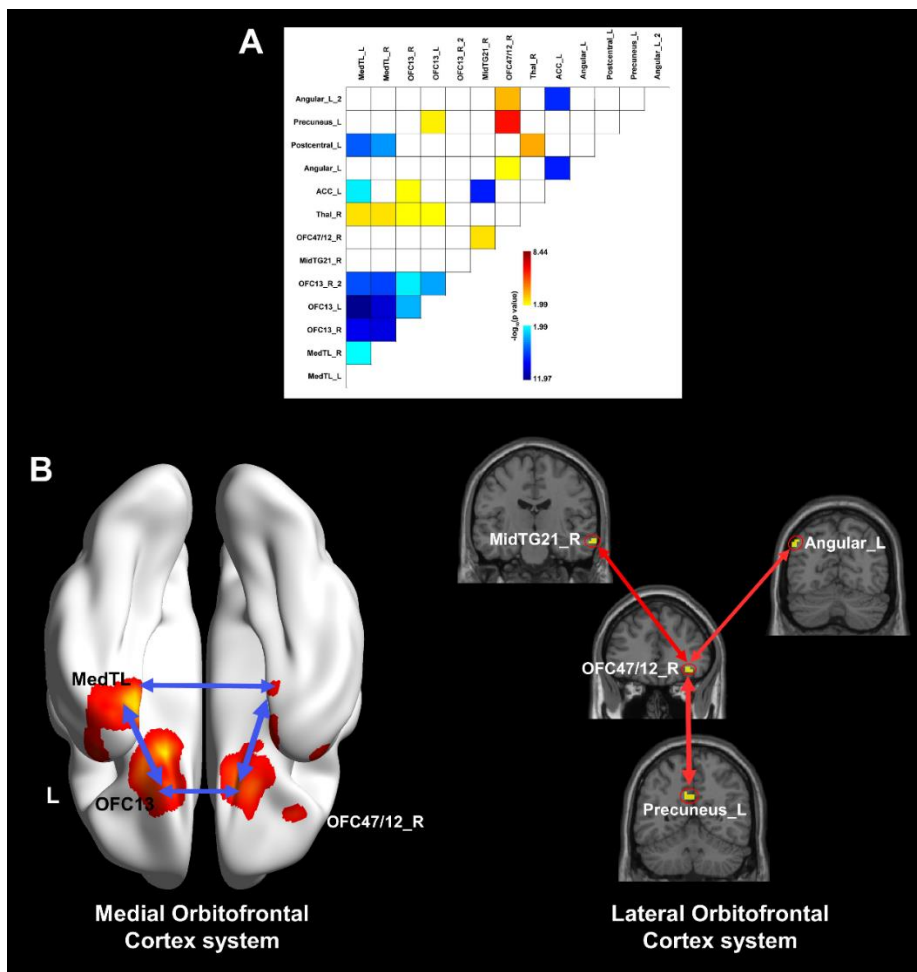
Second, BA 47/12 had increased functional connectivity with the precuneus, the angular gyrus, and the temporal visual cortex BA 21. This enhanced functional connectivity of the non-reward/punishment system (BA 47/12) with the precuneus (involved in the sense of self and agency), and the angular gyrus (involved in language) is thus related to the explicit affectively negative sense of the self, and of self-esteem, in depression. The reduced functional connectivity of the medial orbitofrontal, implicated in reward, with memory systems provides a new way of understanding how memory systems may be biased away from pleasant events in depression. The increased functional connectivity of the lateral orbitofrontal cortex, implicated in non-reward and punishment, with areas of the brain implicated in representing the self, language, and inputs from face and related perceptual systems provides a new way of understanding how unpleasant events and thoughts, and lowered self-esteem, may be exacerbated in depression. Relating the changes in cortical connectivity to our understanding of the functions of different parts of the orbitofrontal cortex in emotion helps to provide new insight into the brain changes related to depression.

New research for the project.

In the new research, we will use the same dataset, but will extend the analysis to the effective connectivity in depression. The effective connectivity goes beyond correlations, by measuring how much one brain region influences another. This is a measure that reflects causal interactions between brain regions. We have a new method available in a collaboration with M.Gilson and G.Deco for measuring the effectivity connectivity in depression (Gilson et al., 2016), and the project is to apply this method to the dataset which we already have to see whether the results with the algorithm produce important new results. The

project will be performed using Matlab code applied to the datasets. There is plenty of opportunity for original research, as further development of the algorithm is possible. The brain is a complex system, and measuring the interactions between its different regions in patients, and how these differ from controls, is highly appropriate for complexity science.

Figure 1. A. Cluster functional connectivity matrix. The color bar shows the $-\log_{10}$ of the p value for the difference of the functional connectivity. The matrix itself contains rows and columns for all cases in which there were 10 or more significant voxels within a cluster. B. The medial and lateral orbitofrontal cortex networks that show different functional connectivity in patients with depression. A decrease in functional connectivity is shown in blue, and an increase in red. MedTL –medial temporal lobe from the parahippocampal gyrus to the temporal pole; MidTG21_R – middle temporal gyrus area 21 right; OFC13 – medial orbitofrontal cortex area 13; OFC47/12_R – lateral orbitofrontal cortex area 47/12 right. The lateral orbitofrontal cortex cluster in OFC47/12 is visible on the ventral view of the brain anterior and lateral to the OFC13 clusters.



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