

## Altered Cortico-Striatal Functional Connectivity in Obsessive-Compulsive Disorder

B. J. Harrison<sup>1,2</sup>, C. Soriano-Mas<sup>2</sup>, J. Pujol<sup>2</sup>, H. Ortiz<sup>2</sup>, M. Lopez-Sola<sup>2</sup>, R. Hernandez-Ribas<sup>2</sup>, J. Deus<sup>2</sup>, P. Alonso<sup>3</sup>, M. Yucel<sup>1</sup>, C. Pantelis<sup>1</sup>, J. Menchon<sup>3</sup>, and N. Cardoner<sup>3</sup>

<sup>1</sup>Melbourne Neuropsychiatry Centre, Department of Psychiatry, The University of Melbourne, Melbourne, Victoria, Australia, <sup>2</sup>Institut d'Alta Tecnologia-PRBB, CRC Corporació Sanitària, Barcelona, Spain, <sup>3</sup>Department of Psychiatry, Bellvitge University Hospital, Barcelona, Spain

**Background:** Neurobiological models of obsessive-compulsive disorder (OCD) emphasize disturbances in the function and connectivity of brain cortico-striatal networks or 'loops'. Although neuroimaging studies of patients support this network model of OCD, very few have applied measurements that are sensitive to brain connectivity features.

**Aim:** Using resting-state functional magnetic resonance imaging (fMRI), we tested the hypothesis that OCD is associated with disturbances in the functional connectivity of primarily ventral cortico-striatal regions, measured from coherent spontaneous fluctuations of the blood oxygen level-dependent (BOLD) signal.

**Design & Setting:** Case-control cross-sectional design. Hospital referral OCD unit and MRI facility.

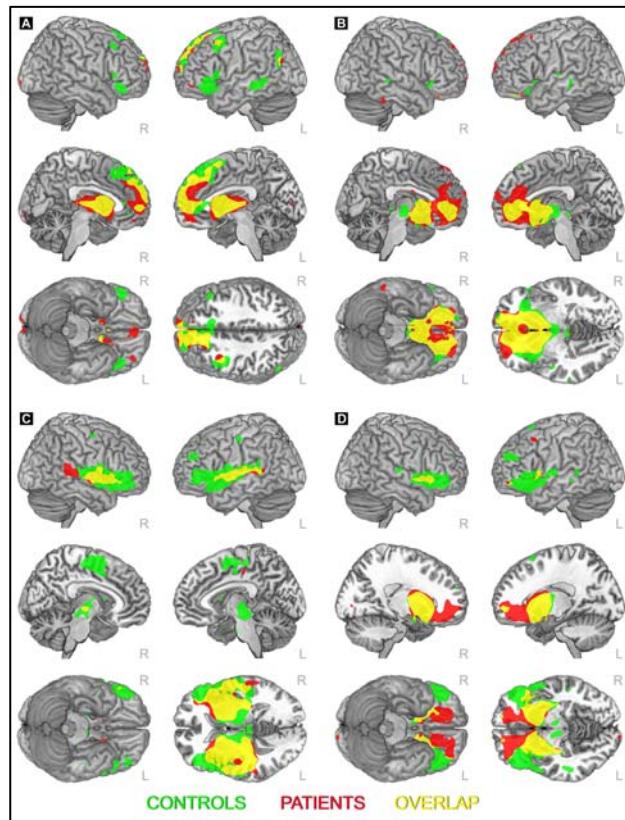
**Participants:** Twenty-one OCD patients (10 males and 11 females) and twenty-one healthy control subjects matched for age, gender and estimated intelligence.

**Main Outcome Measure(s):** Voxel-wise statistical parametric maps testing the strength of functional connectivity of four striatal 'seed' regions of interest with remaining brain areas. Seed placements were (A) dorsal caudate [ $x(\pm)=13, y=15, z=9$ ]; (B) ventral caudate (inferior), corresponding to the nucleus accumbens [ $x(\pm)=9, y=9, z=-8$ ]; (C) dorsal caudal putamen [ $x(\pm)=28, y=1, z=3$ ]; and (iv) ventral rostral putamen [ $x(\pm)=20, y=12, z=-3$ ].

**Results:** For both groups, there was a clear distinction in the pattern of cortical connectivity of dorsal and ventral striatal regions, in keeping with the notion of segregated motor, associative and limbic cortico-striatal networks.

Depicted right: Significant within-group cortico-striatal functional connectivity maps ( $P_{FDR} < 0.05$ ) for (A)=dorsal caudate; (B)=ventral caudate/accumbens; (C)=dorsal putamen; (D)=ventral putamen. Green overlay=controls; red=OCD patients; yellow=spatial overlap of connectivity maps between the groups.

Between groups, OCD patients had significantly increased functional connectivity along a ventral cortico-striatal axis, implicating the orbitofrontal cortex and surrounding areas. The specific strength of connectivity between the ventral caudate/nucleus accumbens and the anterior orbitofrontal cortex predicted patients' overall symptom severity ( $r^2 = .57, P < .001$ ). Additionally, OCD patients showed evidence for reduced functional connectivity of the dorsal striatum and lateral prefrontal cortex, as well as ventral striatum with the region of the midbrain ventral tegmental area.



**Conclusions.** This study provides direct support for the hypothesis that OCD is associated with functional alterations of brain cortico-striatal networks. In particular, our findings suggest abnormal and heightened functional connectivity of ventrolimbic cortico-striatal regions in OCD patients.