PL06 Obsessive Compulsive Disorder

Chair: Brian Dean, Australia

Speaker: Naomi Fineberg, UK

Title: Mapping Compulsivity: Cognitive Domains, Neural Circuitry And Treatment

Fineberg Naomi A [1,2,3], Apergis-Schoute Annemieke M[4], Vaghi Mathilde [4,5], Banca Paula [4,5], Chamberlain Samuel R[3,4,6], Cinosi Eduardo[2,7], Reid Jemma[1,2], Bullmore Edward T[3], Sahakian Barbara J[3,4], Robbins Trevor W[4,5].

[1]Hertfordshire Partnership University NHS Foundation Trust, Rosanne House, Parkway, Welwyn Garden City, Hertfordshire, AL8 6HG, UK. Tel 01707364055. Email; naomi.fineberg@btinternet.com [2]University of Hertfordshire, Dept. of Postgraduate Medicine, College Lane Hatfield, UK [3]Department of Psychiatry, School of Clinical Medicine, University of Cambridge, Addenbrooke's Hospital, Cambridge, UK. [4]Behavioural and Clinical Neurosciences Institute, University of Cambridge, Cambridge, UK [5]Department of Experimental Psychology, University of Cambridge, Cambridge, UK [6]Cambridge and Peterborough NHS Foundation Trust, Cambridge, UK [7]Department of Psychiatry, University Gabriele D'Annunzio, Chieti, Italy

Abstract

Obsessive compulsive related disorders (OCRDs) represent some of the most costly, functionally disabling and treatment-resistant brain disorders. Approximately 40% of cases fail to respond to all available treatments. Compulsions are repetitive, unwanted, stereotyped thoughts and behaviors designed to neutralize imaginary harmful outcomes. Patients with OCRD show difficulty flexibly shifting attentional focus away from inappropriate intrusive harm-related thoughts and behaviours, resulting in perseverative compulsions observed at the clinical level. The neurobehavioral relationship between cognitive inflexibility and fear and anxiety processing in OCRD is not well understood. Clarification of the neuropsychological basis for these abnormalities may identify new trans-diagnostic treatment targets and advance treatment development.

Growing evidence from human and animal research suggests that the neurocognitive mechanisms mediating behavioural inhibition (motor inhibition, reversal learning, set-shifting) and habit learning (shift from goal-directed to habitual responding) variably contribute toward vulnerability to compulsive activity in a broad range of disorders characterized by compulsivity. In OCD, distributed network perturbation appears focussed around the pre-frontal cortex, caudate, putamen and associated neuro-circuitry. According to recent fMRI analysis, OCD-related attentional set-shifting deficits was predicted by reduced resting state functional connectivity between the dorsal caudate and the ventrolateral prefrontal cortex. In contrast, the experimental provocation of symptoms was shown to involve reduced neural activation in brain regions implicated in goal-directed behavioural control (ventromedial prefrontal cortex (vmPFC), caudate nucleus) with concordant increased activation in regions implicated in habit learning (pre-supplementary motor area, putamen).

The vmPFC plays a multifaceted role in integrating affective evaluative processes while mediating flexible behavior and is implicated in fear learning and anxiety disorders. New findings from a neuroimaging study of Pavlovian fear reversal, in which OCD patients failed to flexibly update fear responses despite normal initial fear conditioning, suggest an absence of vmPFC safety signaling in OCD, which potentially undermines explicit contingency knowledge, and which may go some way to explain the link between abnormal threat and safety expectancies and cognitive inflexibility in OCD. Promising results from a small number of treatment-studies using neuro-modulation to target nodes within this frontal-striatal circuitry indicate new treatment-possibilities for refractory obsessive-compulsive disorders.