prevent the full effects of the positive shift in information processing being seen with antidepressant drug treatment.

This approach may also be a useful way of screening and understanding novel interventions for depression. Current screening relies on animal models of depression which have limited predictive validity for new agents and nearly all novel compounds for the treatment of depression fail when efficacy is assessed. The use of human models of emotional processing may therefore provide information which can be used to screen and select the most promising agents for further assessment in randomized clinical trials. We have recently shown effects of novel candidate treatments on emotional processing suggesting that this approach may be valid. In particular, both ketamine and a novel NMDA antagonist reduced negative processing in depressed patients in behavioural and fMRI models. Both of these agents have efficacy in the treatment of depression and highlight that change in emotional processing is not restricted to one particular neurochemical action but may be an important marker for the effective treatment of depression.

Together, these results suggest that psychological processes are important to consider in depression and its treatment and may be a useful approach for improving current treatments and developing novel interventions for this disabling disorder.

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Posters

P.3.001 Neural responses during response inhibition and anticipation of reward in healthy controls and in drug-dependent individuals

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Functional magnetic resonance imaging (fMRI) studies indicate that drug-dependent individuals tend to show dysfunction in frontal regions related to cognitive control while performing tasks probing response inhibition [1] and dysfunctions in reward-related regions (particularly the ventral striatum) while performing tasks probing anticipation of rewards [2]. However the nature of the dysfunction varies between studies. Reasons for these discrepancies include individual differences in comorbid symptoms (e.g. depression, OCD) and patterns of drug use (e.g. years of use, months abstinent), which could act as confounding variables.

The present fMRI study therefore aimed to investigate the extent to which these variables may influence neural activations during response inhibition (using the Go–NoGo task) and during anticipation of reward (using the monetary incentive delay task) in individuals dependent on cocaine (n = 17), alcohol (n = 43), and opiates (n = 27), as well as healthy controls (n = 68). Multiple regression was used to correlate activations during response inhibition and anticipation of reward with clinical variables of interest: depressive and obsessive–compulsive symptoms, years of drug use, and months abstinent.

During response inhibition, healthy controls showed activations in regions previously associated with cognitive control. Individuals dependent on cocaine and alcohol did not show significantly different activations in these regions. However, opiate-dependent individuals showed significant hypoactivation in right cuneus and right calcarine gyrus. There were no correlations between opiate- and alcohol-dependent individuals' depressive and obsessive–compulsive symptoms and neural activity during the task. In cocaine-dependent individuals, depressive symptoms were positively correlated with activity in right superior medial and middle frontal gyri and right angular gyrus. Obsessive–compulsive symptoms were positively correlated with activations in left middle frontal gyrus (MFG). Years of cocaine use were positively correlated with activity in intra-parietal sulcus, and negatively correlated with activity in right anterior cingulate cortex (ACC). Months abstinent from cocaine correlated with response in right ACC, right insula, and right MFG. Years of opiate use were positively correlated with activity in the left cerebellum, while months abstinent from opiates positively correlated with activity in the left insula.

During anticipation of reward, healthy controls showed activations in several reward-related regions. Cocaine-dependent and alcohol-dependent individuals showed hyperactivations in the insula and frontal regions, and hypoactivity in temporal and somatosensory regions. In opiate-dependent individuals, hyperactivations were observed in frontal and striatal regions and hypoactivations in thalamus, and temporal regions. In cocaine- and opiate-dependent individuals we observed positive correlations between depressive and obsessive–compulsive symptoms

and activity in frontal and striatal regions. There were also significant correlations between brain responses during anticipation of reward and years of use and months abstinent in all three dependent groups.

Our findings suggest that comorbid psychiatric symptoms and drug use history significantly influence brain mechanisms of impulse control and reward processing. These influences may account for some of the discrepancies in the previous literature. Our findings also have implications for mechanisms of treatment and recovery. For example, the findings related to months abstinent from substances provide some confidence that long term abstinence from substances can lead to recovery of function at the neuronal level.

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P.3.002 White matter alterations and symptom dimensions models in obsessive–compulsive disorder: a diffusion tensor imaging study

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Background: Obsessive–Compulsive Disorder (OCD), considered as a unitary entity by current psychiatric taxonomies, is highly heterogeneous in its manifestations. This heterogeneity partly explains, beyond methodological discrepancies, the inconsistency of results in current brain imaging research in the disorder, particularly in Diffusion Tensor Imaging studies. OCD is probably best described by a multidimensional model involving several symptom dimensions, whose precise number and phenotypes are debated.

Purpose: We aimed at investigating white matter (WM) alterations associated with OCD, controlling for the impact of variables known to affect WM structure, and specifically for the effect of both current and lifetime pharmacological treatment on the observed differences. Then, we tested two different symptom dimensions models [1,2] within OCD patients, analysing their WM correlates, for both prevailing current symptom dimension and symptom dimension at onset.

Methods: We compared 58 patients and 58 age- and gender-matched healthy controls, with Tract-Based Spatial Statistics on Diffusion Tensor images, using TFCE correction ($p = 0.05$). With respect to the symptom dimensions, separate analyses were then carried on the sole OCD sample. The diffusion measures Fractional Anisotropy (FA), Axial Diffusivity (AD), Radial Diffusivity (RD) and Mean Diffusivity (MD) were used as parameters of WM organisation.

Results: We observed a widespread reduction of FA and increase of RD in almost all brain tracts between OCD patients and healthy controls. The differences, however, appeared to be carried by the effect of previous and current medications. In particular, lifetime treatment was associated with a decrease in FA in the tracts surrounding the thalami, site of major alteration in OCD according to both neuroanatomic models and research findings on the disorder.

In the analysis of symptom dimensions, only a finer-grained five-factors model [2] allowed for the identification of specific neural correlates. Patients having current Symmetry/Perfectionism dimension show a reduction in RD and MD in a large cluster involving the body of corpus callosum and several left WM regions, including: left uncinate fasciculus, left inferior longitudinal fasciculus and/or inferior fronto-occipital fasciculus, and left superior longitudinal fasciculus. Furthermore, patients having Doubt/Checking dimension at onset show a widespread reduction of AD, encompassing corpus callosum, and bilaterally the thalamic radiations, internal capsule, cingulum, corona radiata and inferior longitudinal fasciculus. Finally, patients having Rituals/Superstition dimension at onset show an increase in FA in the genu of corpus callosum, bilateral posterior limb of the internal capsule, bilateral anterior thalamic radiations and left external capsule.

Conclusion: Present results confirm the effect of medications on OCD white matter, and seem to suggest a disorder-specific, and therefore site-specific, effect of medications on brain systems. Furthermore, our findings provide support to a multidimensional model of OCD, and indicate that the distinction of clinically homogenous dimensions may be of utmost importance for the identification of reliable neural correlates. Finally, we evidence, to our knowledge for the first time, that onset symptom dimensions are associated with enduring alterations of WM structure, suggesting the relevance of the type-of-onset for future investigations on OCD neuroanatomy and aetiopathology.