

magnetic resonance imaging (fMRI) studies of neural correlates of anxiety sensitivity in PD suggested positive correlations between anxiety sensitivity and several brain regions involved in the pathophysiology of PD. Poletti et al. reported that neural activity regarding emotional processing in cortico-limbic network such as medial prefrontal cortex, anterior cingulate cortex and insula is associated to anxiety sensitivity in PD [2]. Different fMRI study showed that anxiety sensitivity is associated positively with level of midbrain activation during fear conditioning, which has been proposed to represent a core pathway for the development of PD. Although several functional imaging studies of anxiety sensitivity in PD suggested the alteration of neural activity previously, no study investigated WM alterations of patients with PD in relation to the anxiety sensitivity. The objective of this study is to investigate the WM correlates of anxiety sensitivity in PD.

Methods: One hundred twelve right-handed patients with PD and 48 Healthy Control (HC) subjects were enrolled in this study. The Anxiety Sensitivity Inventory-Revised (ASI-R), the Panic Disorder Severity Scale (PDSS), the Albany Panic and Phobia Questionnaire (APPQ), the Beck Anxiety Inventory (BAI), and the Beck Depression Inventory (BDI) were administered. Tract-based spatial statistics were used for diffusion tensor MRI analysis.

Results: We conducted correlation analysis between the ASI-R scores and the FA values of the WM regions for each patients with PD and HC subjects group. In patients with PD group, FA values of the splenium of corpus callosum, the tapetum, the fornix / stria terminalis, the retrolenticular part of internal capsule, the posterior thalamic radiation, the posterior corona radiata, the sagittal striatum (including inferior longitudinal fasciculus and inferior fronto-occipital fasciculus) and the superior longitudinal fasciculus showed significant positive correlations with ASI-R total scores ($p=0.008$; Family Wise Error (FWE)-corrected) [3]. Only fear of publicly observable anxiety reaction ($p=0.005$; FWE-corrected) and fear of cognitive dyscontrol subscale scores ($p=0.003$; FWE-corrected) also showed significant positive correlations with FA values of these WM regions. When we used an analysis of covariance (ANCOVA) design, using gender, age at scan, and intracranial volume as covariates, the results remained the same. Conducting correlation analysis among HC subjects showed no significant results.

Conclusion: The current study suggests that the WM correlates of anxiety sensitivity in PD may be associated with parieto-temporo-limbic WM regions. Among the patients with PD, the ASI-R total scores were significantly correlated with the fractional anisotropy values of the splenium of corpus callosum, the tapetum, the fornix / stria terminalis, the retrolenticular part of internal capsule, the posterior thalamic radiation, the posterior corona radiata, the superior longitudinal fasciculus and the sagittal stratum ($p=0.008$; Family Wise Error (FWE)-corrected). These WM regions were also significantly correlated with APPQ scores ($p=0.003$; FWE-corrected) and BDI scores ($p=0.001$; FWE-corrected) in the panic patients. Conducting correlation analysis among HC subjects showed no significant results.

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P.1.i.003 The role of the serotonin 2A receptor in the fabric and modulation of personal meaning in lysergic acid diethylamide (LSD)-induced states

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Abnormalities in the attribution of personal relevance to stimuli are critical features of many psychiatric disorders such as schizophrenia, addiction, and mood disorders [1]. However, the neuronal substrates enabling meaningful and personally relevant experiences are largely unknown. Lysergic acid diethylamide (LSD) is a prototypical hallucinogen which has high affinity at serotonin (5-HT)-2A/C, -1A/B, -6, and -7, and dopamine D2/D1 receptors (R). Animal studies suggest that LSD produces its psychedelic effects primarily via agonist action at 5-HT2AR although D2R may also be implicated. A core feature of LSD-induced psychedelic states is an increased sense of meaning of objects [2]. Ketanserin is a selective 5-HT2AR antagonist which may in combination with LSD and functional magnetic resonance imaging (fMRI) offer the opportunity to determine the role of the 5-HT2AR system in personal meaning processing.

In a double-blind, randomized, counterbalanced, cross-over study we therefore assessed the neural and behavioral response to personally meaningful, neutral, and personally meaningless music using fMRI and behavioral meaningfulness ratings. Twenty-two healthy participants received either (1) placebo + placebo (Pla condition), (2) placebo + LSD (100 µg po, LSD condition), or (3) ketanserin (40 mg po) + LSD (100 µg po, Ket+LSD condition) at three different occasions. Subjective drug effects were assessed using the Altered States of Consciousness Rating Scale (5D-ASC). Behavioral data were analyzed by repeated-measures analyses of variance with treatment (Pla, LSD, Ket+LSD) and scale (5D-ASC scales) or music category (meaningful, neutral, meaningless) as within-subject factors followed by Bonferroni-corrected simple main effects analyses or paired comparisons in case of significant interactions or main effects. fMRI data were analyzed using a general linear model (GLM) as implemented in SPM12.

Meaningfulness ratings were increased for meaningless and neutral music under LSD compared to both Pla and Ket+LSD (all $p < 0.05$). Furthermore, listening to meaningless music compared to neutral and personally meaningful music was associated with increased BOLD signal in medial and lateral frontal brain areas in the LSD condition compared to both Pla and Ket+LSD conditions. (brain areas: dorsal anterior cingulate cortex, supplementary motor area, dorsomedial prefrontal cortex, ventrolateral prefrontal cortex, all $p < 0.05$, FWE corrected). Furthermore, subjective drug effects were significantly increased after LSD administration compared to placebo on all 5D-ASC scales (all $p < 0.05$) except for anxiety and spiritual experience (all $p > 0.30$). These LSD-induced effects were fully blocked by ketanserin (all $p < 0.05$).

LSD increased the attribution of personal relevance to previously meaningless stimuli. This effect appears to be attributable to 5-HT2AR stimulation, since these alterations are normalized after pretreatment with ketanserin. Furthermore, surprisingly virtually all LSD-induced psychological effects were blocked by 5-HT2AR antagonism, despite LSD's additional action on dopamine receptors. The current results emphasize the pivotal role of the 5-HT2AR in the generation of personal meaning in medial and

lateral frontal brain structures implicated in self-referential processes [3]. These findings may be relevant for increasing our understanding of the biochemical underpinnings of personal meaning processing and may reveal prospective targets in the treatment of psychiatric illnesses characterized by alterations in meaning attribution.

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P.1.i.004 Transcranial direct current stimulation improves symptoms, mood, and self-regulatory control in bulimia nervosa: a proof-of-principle clinical trial

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Background: Bulimia nervosa (BN) is a disabling condition, characterised by recurrent episodes of binge-eating and inappropriate compensatory behaviours, which affects up to 7% of young women [1]. Available treatments are only partially effective [2], thus there is a need to develop novel therapeutic strategies. Evidence suggests that disturbed eating in BN is underpinned by alterations in self-regulatory control, and by aberrations in frontostriatal circuitry encompassing the dorsolateral prefrontal cortex (DLPFC) [3]. Selective manipulation of this region with transcranial direct current stimulation (tDCS) may therefore alleviate symptoms of the disorder. tDCS has induced therapeutic effects in food cravers, obese individuals, and patients with various psychiatric disorders [4]; however, its clinical utility in BN has not been explored.

Objective: This double-blind sham-controlled proof-of-principle clinical trial investigated the effects of bilateral tDCS over the DLPFC in adults with BN.

Methods: Thirty-nine participants (two males) received three 20-minute sessions of tDCS in a randomised/counterbalanced order: anode right/cathode left (AR/CL), anode left/cathode right (AL/CR), and sham. A battery of psychological/neurocognitive measures was completed before and after each stimulation session. For variables with normally distributed data, the effects of tDCS were evaluated using two-way repeated measures ANOVAs and planned contrasts. Where data were not normally distributed, Wilcoxon signed-rank tests were used to compare pre- and post-tDCS scores for each condition separately.

Results: A repeated measures ANOVA revealed a significant stimulation $\times$ timepoint interaction for eating disorder cognitions (measured with the Mizes Eating Disorder Cognitions Questionnaire-Revised) [$F(1.63, 62.02) = 3.83$, $p = 0.035$]: AR/CL tDCS reduced eating disorder cognitions when compared to AL/CR [$F(1, 38) = 4.42$, $p = 0.042$, $r = 0.32$] and sham [$F(1, 38) = 5.17$, $p = 0.029$, $r = 0.35$] stimulation. Wilcoxon signed-rank tests showed that both active conditions suppressed the self-reported urge to binge-eat [AR/CL: $Z = -2.42$, $p = 0.016$, $r = -0.27$,

AL/CR: $Z = -2.52$, $p = 0.012$, $r = -0.28$] and increased self-regulatory control during a temporal discounting task [AR/CL: $Z = -2.91$, $p = 0.004$, $r = -0.33$, AL/CR: $Z = -3.04$, $p = 0.002$, $r = -0.34$], whereas sham tDCS had no effect on these variables [urge to binge-eat: $Z = -1.26$, $p = 0.207$, $r = -0.14$, self-regulatory control: $Z = -1.74$, $p = 0.083$, $r = -0.20$]. A repeated measures ANOVA showed a trend towards a significant stimulation $\times$ timepoint interaction for mood (assessed with the Profile of Mood States) [$F(2, 70) = 2.92$, $p = 0.060$]: compared to sham stimulation, mood improved after AR/CL [$F(1, 35) = 5.15$, $p = 0.030$, $r = 0.36$] but not AL/CR [$F(1, 35) = 2.32$, $p = 0.137$, $r = 0.25$] tDCS.

Conclusions: These data provide preliminary evidence that bilateral tDCS applied to the DLPFC has the potential to induce transient therapeutic effects in individuals with BN. They also elucidate possible mechanisms of action and inform the design of future trials, particularly in relation to electrode montage selection. Multi-session trials are needed to determine whether tDCS has potential for development as a treatment for BN.

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P.1.i.005 Changes in default mode network connectivity during spontaneous migraine attack: a resting state fMRI case report

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Migraine patients during interictal phase repeatedly showed alterations in the default mode network (DMN) resting state functional connectivity consisting of increased connectivity between the DMN and insula and decreased connectivity of DMN with other networks [1,2]. Most of these variations are not migraine specific and show similarities with altered brain network functions in other pain disorders. Thus investigating the functional connectivity changes of DMN during migraine attacks may further shed light on migraine specific functional deficits. So far only one study investigated the effect of migraine attack on functional connectivity during pharmacologically induced attacks but no data of spontaneous migraine attacks are available [3]. In the present study we analysed resting state fMRI data of a 24 years old female patient with migraine without aura who participated in two resting state functional scans (31 days apart) and suffered a migraine attack at the second occasion. She was pain-free in the preceding 72 hours both times. At the second occasion 1 hour before the scan she developed a mild bilateral headache, which gradually worsened during the examination. The ictal images were recorded when the pain although was only moderate (3 on a