

FORMING VERY FIRST IMPRESSIONS: EFFECTS OF STIMULUS DURATION AND SPATIAL FREQUENCY IN SCHIZOPHRENIA

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Background: People form first impressions of others all the time, which affects how they view situations and interact with others. Some impressions are mediated by affective stimuli, such as facial expressions. Other impressions arise from judgment of neutral faces. For instance, individuals can assess the degree to which others are potentially threatening, without being in immediate danger, which is important for survival value. Healthy controls have previously been shown to form threat impressions in faces with neutral expression in 39 ms. These impressions appear to be mediated by low spatial frequency (LSF) content in the facial images, and some studies have reported a preferential impairment of LSF processing in individuals with schizophrenia. The current study investigated how quickly individuals with schizophrenia can form consistent impressions of threat compared with controls, independent of emotional cues. **Methods:** Patients (n = 40) and healthy controls (n = 38) were presented with intact, low, or high spatial frequency filtered neutral faces and asked to rate the level at which they perceived each face to belong to a threatening person on a scale of 1 to 5. Participants saw faces for 39, 156, 390, and 1703 ms. In order to assess the temporal lower limit of impression formation, intraclass correlations were calculated for ratings made at each duration for each group, respectively, using 1703 ms duration as the comparison duration. **Results:** Consistent with previous results, controls demonstrated a significant relation between ratings of intact faces presented for 39 ms and those presented for 1703 ms (ICC = .342, 95% CI: .121 to .531, p = .002). This suggests that controls were able to extract necessary facial information at 39 ms to form a threat impression similar to the impression formed at 1703 ms. Results for patients indicated that 39 ms was insufficient time to make consistent threat impressions. However, patients did demonstrate a significant relation with threat judgments between ratings made at 390 ms and 1703 ms (ICC = .580, 95% CI: .404 to .715, p < .001). LSFs contributed to judgments of threat in healthy controls in the 39 ms condition, whereas patients needed longer stimulus durations to utilize LSFs. **Conclusion:** Results indicate that individuals with schizophrenia may need a longer time to make a “first impression” of threat, which may be related to longer time needed for LSF information to be utilized. These findings have implications for social interactions in this population.

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COGNITIVE FUNCTIONING ASSOCIATED WITH STIMULANT USE IN PATIENTS WITH NON-AFFECTIVE PSYCHOSIS, THEIR UNAFFECTED SIBLINGS AND HEALTHY CONTROLS

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Background: While cannabis use and its relationship with cognitive functioning has been studied extensively in patients with schizophrenia, little is known about the effect of stimulant use (amphetamines, cocaine, ecstasy) on cognitive functioning in these patients. The current study examined (1) whether recency and frequency of stimulant use is associated with cognitive functioning, and (2) whether these associations differ between patients with psychotic disorder, their unaffected siblings, and controls. **Methods:** This cross-sectional study included 1,077 patients with non-affective psychosis, 1,032 unaffected siblings, and 582 healthy controls. Participants completed a comprehensive cognitive test battery. Stimulant use was assessed by urinalysis and by the Composite International Diagnostic Interview (CIDI). Using random-effect regression models the main effects of Stimulant Use (current, lifetime frequent, lifetime infrequent, never use) and the interaction with Diagnostic Status (patient, sibling, control) on cognitive functioning were assessed, while correcting for possible confounders. **Results:** Patients were more often lifetime users of stimulants compared to non-affected siblings and controls (25.6% vs. 9.5% vs. 5.8%). The interaction term between Stimulant Use and Diagnostic Status was not significant for any of the cognitive outcome variables, indicating similar effects of stimulant use in all three groups. Current stimulant users showed more errors in verbal learning in comparison to never users (Cohen's d -0.60; p < .005). Lifetime frequent (i.e. daily to weekly) stimulant use was significantly associated with worse immediate and delayed verbal recall, working memory, and acquired knowledge (Cohen's d -0.22 to -0.29; p < .005). Lifetime infrequent (less than weekly) stimulant use was not associated with significant cognitive alterations in comparison to never use. **Conclusion:** Findings suggest that the association between stimulant use and cognitive functioning is similar in patients with psychosis, unaffected siblings and controls. The presence of cognitive deficits associated with lifetime stimulant use is dependent on the frequency of use, with no observed deficits in infrequent users and modest negative effects in frequent users.

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INDIVIDUALS WITH SCHIZOPHRENIA FAIL TO SHOW NORMATIVE INVERTED-U ACTIVATION IN RESPONSE TO FINE-GRAINED WORKING MEMORY LOAD MANIPULATION

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Background: Patients with schizophrenia exhibit serious and clinically relevant deficits in working memory (WM). However, investigations of WM in patients with schizophrenia using functional Magnetic Resonance Imaging (fMRI) have largely failed to reveal a consistent abnormality in brain activation. One hypothesis is that patients exhibit a disordered relationship between the extent of activation in dorsolateral prefrontal cortex (DLPFC) and WM load. To test this hypothesis, we employed the self-ordered working memory task (SOT), which provides a finer-grained variation in WM load than existing tasks. **Methods:** Thirteen patients with schizophrenia and eighteen control participants matched on age, gender, and parental socio-economic status performed the SOT during fMRI. In each trial of the SOT participants are presented with eight line drawings of 3D objects in an array. On each step of the trial the object positions are rearranged, and participants must select any object that they have not previously selected, thereby producing a gradual increase in WM load. **Results:** Patients and controls exhibited above chance accuracy and monotonic declines in performance from steps two through eight, with patients also performing significantly worse than controls at these steps. Healthy controls exhibited an inverted-U response to increasing WM load in several brain regions, including bilateral DLPFC and posterior parietal cortex (PPC). Patients with schizophrenia exhibited no main effect of WM load in any brain region, even at a liberal statistical threshold. **Conclusion:** These data demonstrate an inverted-U relationship between WM load and critical brain regions involved in WM in healthy individuals. However, there was no evidence to suggest a similar relationship between WM load and brain activation in patients with schizophrenia. While the functional significance of this relationship remains somewhat speculative, the fact that healthy individuals maintained high levels of performance at later steps suggests they may have exhibited a flexible shift in strategy as their WM capacity was exceeded. Critically, patients with schizophrenia failed to show this shift at high WM loads. This study is arguably the most comprehensive investigation of the impact of variation in WM load on brain activation in patients with schizophrenia and matched controls carried out to date, and reveals several new directions for research into the functional impairment underlying WM deficits in patients with schizophrenia.

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REWARD-RELATED NEURAL RESPONSES AS PREDICTORS OF PSYCHOTIC SYMPTOMS IN CHRONIC SCHIZOPHRENIA PATIENTS

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Background: We have previously found evidence of abnormal reward-related neural activity, in patients with schizophrenia (SZ), in many brain regions, including targets of dopamine projections, such as medial and ventral prefrontal cortex (PFC). Given the purported roles of dopamine in both psychosis and the modulation of expected value (EV) representations in ventromedial (VM) PFC, we sought to examine whether neural signals related to EV would be predicted by psychosis severity. **Methods:** In a 3-T MRI scanner, we administered 17 patients and 17 matched controls a Monetary Incentive Delay (MID) task, in which cues predicted gains and losses of various magnitudes. This task has frequently been used to examine neural activity associated with the anticipation of rewards and punishments. Participants needed to respond to a target within a variable time window in order to receive the maximum monetary gain, or avoid the maximum loss. Because the time window was calibrated to enable

in-time responses on 2/3 of trials, subjects won less than the anticipated amount (on gain trials), or lost more than the anticipated amount (on loss trials), on only a minority of trials. We computed Pearson coefficients between measures of psychotic symptom severity (from the Brief Psychiatric Rating Scale, BPRS) and an MRI measure of reward- (vs. punishment-) anticipation in a VMPFC ROI, drawn from previous analyses of the same data. **Results:** When we examined cue-evoked activity in our MID task, specifically in VMPFC, we observed no group differences in the contrast in neural responses to anticipated gains and anticipated losses. Within the group of SZs, however, we found that the magnitude of this contrast was predicted both by patients' ratings of Unusual Thought Content ($r = -0.598$, $p = 0.011$), from the BPRS, and by their average ratings from four items comprising a "reality distortion" cluster ($r = -0.649$, $p = 0.005$; see McMahon et al., 2002). In short, SZs with more severe psychotic symptoms showed less positive (normal) responses to cues predictive of rewards, in VMPFC, relative to cues predictive of punishments. **Conclusion:** These results add to a body of evidence indicating that abnormal brain responses to salient events in brain reward networks are tied to psychotic symptoms. They suggest, in particular, that disruptions in VMPFC representations of the incentive value of stimuli may factor in the emergence of psychosis.

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COMPARING THE EXECUTIVE FUNCTION IN SCHIZOPHRENIA AND BIPOLAR DISORDER: A META-ANALYSIS WITH HAYLING SENTENCE COMPLETION TEST

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Background: Patients with bipolar disorder and patients with schizophrenia are both associated with impaired executive functions. However, it is far less clear whether the observed executive dysfunction is related to the particular disorders or the pattern of symptoms. To this aim, a meta-analysis on an executive function test capturing semantic inhibition, the Hayling Sentence Completion Test (HSCT), was conducted to examine the potential differential executive dysfunctions in semantic inhibition in bipolar disorder and schizophrenia. **Methods:** A total of 13 studies were included in the current analysis. The Comprehensive Meta-Analysis software package was used to compute pooled effect sizes and homogeneity. **Results:** In patients with bipolar disorder, the meta-analysis procedure produced significant mean effect sizes of 0.719 for Total Latency of Task A, 0.930 for Total Latency of Task B and 0.332 for Total Error of Task B. In patients with schizophrenia, the meta-analysis yielded significant mean effect sizes of 0.749 for Total Latency of Task A, 0.981 for Total Error of Task B, 0.588 for Type A Error of Task B and 0.641 for Type B Error of Task B. Between-group comparisons were also made for the Total Latency time scores of Task A and for Total Error of Task B, no significant difference was found between patients with schizophrenia and bipolar disorder. **Conclusion:** These results were consistent with previous studies and suggested that patients with either schizophrenia or bipolar disorder were less likely to be intact in the HSCT test. Moreover, the findings also indicated that patients with schizophrenia might have a wider range of semantic inhibition impairments in HSCT than patients with bipolar disorder.

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