

remission rates among study completers in both treatment groups, suggest better outcomes associated with long-acting treatments, resulting in sustained symptomatic and functional remission.

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The Five-Factor Model Personality Traits in Schizophrenia: Meta-Analysis

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Abstract

Personality is an important factor in the pathogenesis of schizophrenia because it affects patients' symptoms, cognition and social functioning. Several studies have reported specific personality traits in patients with schizophrenia compared with healthy subjects. However, the results were inconsistent among studies, as the sample size in each study was not sufficient. The NEO Five-Factor Inventory (NEO-FFI) measures five personality traits: Neuroticism (N), Extraversion (E), Openness (O), Agreeableness (A) and Conscientiousness (C). Here, we performed a meta-analysis of these personality traits assessed by the NEO-FFI in 427 patients with schizophrenia and 455 healthy subjects from the published literature and investigated possible associations between schizophrenia and these traits. There was no publication bias for any traits ($P > 0.10$). Because we found evidence of significant heterogeneity in all traits among the studies ($P < 0.10$), we applied a random-effect model to perform the meta-analysis. Patients with schizophrenia showed a higher score for N and lower scores for E, O, A and C compared with healthy subjects ($P < 0.05$). The effect sizes of these personality traits ranged from moderate to large. These differences were not affected by possible confounding factors, such as age and gender ($P > 0.05$). These findings suggest that patients with schizophrenia have a unique personality profile compared with healthy subjects.

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Longitudinal change in neurocognition and its relation to symptomatic and functional changes over 2 years in individuals at clinical high-risk for psychosis

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Abstract

Background: Negative symptoms and functional disability represent the core of schizophrenia and both are associated with cognitive impairments. We explored the course of cognitive change and its relation to symptomatic and functional changes

in individuals at clinical high-risk (CHR) for psychosis to identify cognitive indicators of long-term course. Such attempts may offer insight into the pathological changes associated with the development of illness in the prodromal state.

Methods: Forty-seven CHR individuals completed neurocognitive, clinical, and functional assessments at baseline and 2-year follow-up; twenty-eight healthy controls were assessed for neurocognitive and functional measures at baseline and 2-year follow-up. The delta values of CHR individuals in neurocognitive, clinical, and functional domains were determined from differences between baseline and follow-up scores to estimate the degree of change.

Results: Although overall longitudinal cognitive performance of CHR individuals improved, the magnitude of improvement was not statistically different from that of normal controls at the group level. However, the individual data yielded two groups of CHR subjects showing opposite trajectories of cognitive change in semantic fluency (i.e., improvement or decline), which was significantly associated with changes in negative symptoms and functional measures. Moreover, the relationship between negative symptoms and functioning were more strengthened over time than baseline.

Conclusions: Our findings show that semantic fluency seems to be a neurocognitive indicator reflecting clinical courses in CHR individuals. The longitudinal relationship of negative symptoms and functioning with semantic fluency may represent ongoing pathological processes in neural systems involving aberrant fronto-temporal interaction in the early phase of schizophrenia.

Keywords: Clinical high-risk, schizophrenia, neurocognition, negative symptom, functional outcome, longitudinal.

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The effect of bilateral saccadic eye movements on the performance of recognition memory task in patients with schizophrenia

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Abstract

Background: Episodic memory impairments in patients with schizophrenia have been well demonstrated. Previous studies have shown that horizontal saccadic eye movements improve the retrieval of episodic memories in healthy individuals. The present study was conducted in order to investigate whether the memory-enhancing effects of bilateral saccadic eye movements could occur in schizophrenic patients.

Methods: Twenty-one right-handed patients with schizophrenia participated in this study. Participants learned facial stimuli, which consisted of neutral and angry faces. Subsequently, they performed a recognition memory task using the facial stimuli after bilateral saccadic eye movements and eye fixation. Recognition accuracy, response bias and mean response time to hits were compared. Two-way repeated measure analysis of variance was performed for statistical analysis.

Results: Mean response time after bilateral saccadic eye movements was significantly shorter than that after eye fixation

($F = 5.812$, $P < 0.05$). In addition, response bias was significantly reduced after bilateral saccadic eye movements relative to that after eye fixation ($F = 10.366$, $P < 0.01$). Statistically significant interaction effects were not observed between eye movement conditions and face emotion types.

Conclusion: The present study showed that bilateral saccadic eye movements enhanced the performance of recognition memory task in patients with schizophrenia. This finding suggests that bilateral saccadic eye movements may be used for cognitive rehabilitation in patients with schizophrenia.

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BACOPA MONNIERI (BRAHMI) CAN RECOVER AND PREVENT COGNITIVE DEFICIT IN SUB-CHRONIC PHENCYCLIDINE RAT MODEL OF SCHIZOPHRENIA BY ELEVATING VESICULAR GLUTAMATE TRANSPORTER TYPE 3 IN THE BRAIN

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Abstract

Background: Glutamatergic hypofunction is implicated in schizophrenia. Reduced presynaptic glutamatergic markers, remarkably vesicular glutamate transporter type 1 (VGLUT1) and 2 (VGLUT2) indicates glutamatergic deficit leading to cognitive impairment in schizophrenia. However, few studies in VGLUT3 have been reported. Brahmi (*Bacopa monnieri*), a traditional herbal medicine, might be a new treatment and prevention for cognitive deficit in schizophrenia by changing cerebral VGLUT3 density.

Objective: To study cognitive enhancement- and neuroprotective effects of Brahmi on novel object recognition task and cerebral VGLUT3 immunodensity in sub-chronic phencyclidine (PCP) rat model of schizophrenia.

Material and Method: Cognitive enhancement effect study; rats were assigned to three groups; Group-1: Control, Group-2: PCP-administration, Group-3: PCP + Brahmi. Neuroprotective effect study; rats were assigned to three groups; Group-1: Control, Group-2: PCP-administration, Group-3: Brahmi + PCP. Discrimination ratio (DR) representing cognitive ability was obtained from novel object recognition task. VGLUT3 immunodensity was measured in prefrontal cortex, striatum and cornu ammonis fields 1-3 (CA1-3) of hippocampus using immunohistochemistry.

Results: DR was significantly reduced in PCP group compared with control. This occurred alongside VGLUT3 reduction in prefrontal cortex, striatum and CA1-3. PCP + Brahmi showed a higher DR score compared with PCP alone and this occurred alongside a significantly increased VGLUT3 immunodensity in prefrontal cortex and striatum. Brahmi + PCP group also showed a higher DR score compared with PCP alone and this occurred alongside a significantly increased VGLUT3 immunodensity in prefrontal cortex, striatum and CA1-3.

Conclusion: Reduced cerebral VGLUT3 produced cognitive deficit in rats receiving PCP. Interestingly, receiving Brahmi after PCP administration can restore this cognitive deficit by increasing VGLUT3 in prefrontal cortex and striatum. Receiving Brahmi before PCP administration can also prevent cognitive impairment by elevating VGLUT3 in prefrontal cortex, striatum and CA1-3. Therefore, Brahmi could be a new frontier of restoration and prevention of cognitive deficit in schizophrenia.

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GPR52 agonists show pro-cognitive properties

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Abstract

GPR52 is an orphan G protein-coupled receptor which is mainly expressed in the brain and shows a unique co-expression profile. In the striatum it is expressed almost exclusively in neurons also expressing D2-like dopamine receptors, whereas in the cortex it mainly co-expresses with the D1-like dopamine receptor. Because GPR52 is Gs-coupled, this has led to the prediction that agonists of GPR52 may have both antipsychotic and pro-cognitive properties by their action in the striatum and the prefrontal cortex, respectively. This makes GPR52 a particularly interesting target for the treatment of schizophrenia. While tool compounds have, indeed, been shown to reverse pharmacologically induced striatal hyperdopaminergic states, direct evidence for their efficacy in cognition was lacking. Here, we show data from *in vitro*, *ex vivo* and *in vivo* studies strongly supporting the hypothesized pro-cognitive efficacy.

Tool compounds were synthesized following Takeda patents WO2010/018874, WO2011/093352 and WO2012/020738 and their *in vitro* efficacy was confirmed in stably transfected HEK cells. The compounds led to a robust increase of intracellular cAMP concentrations, with an EC50 of 30nM for the tool compound chosen for further characterization. To test the hypothesis that this increase in cAMP affects synaptic transmission in the prefrontal cortex, layer V responses to layer II stimulation were measured in prefrontal cortical rat brain slices. Bath application of the tool compound led to a robust and sustained increase in excitatory post-synaptic potentials, suggesting the possibility of pro-cognitive efficacy. To test this, working memory performance was measured in mice in the T-maze spontaneous alternation task. The deficit induced by the NMDA receptor antagonist MK-801 was dose-dependently reversed by the administration of the GPR52 tool compound agonist.

Together, these data show that GPR52 agonists also have potential for treatment of cognitive symptoms in psychiatric disorders characterized by cortical dopaminergic or glutamatergic hypofunction, such as schizophrenia.

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Evaluation of plasma and cerebrospinal fluid G72 protein levels and their correlations with psychiatric symptoms in schizophrenia and major depression

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Abstract

It has widely been accepted that D-serine plays a pivotal role in the regulation of glutamate neurotransmission as an endogenous co-agonist for the N-methyl-D-aspartate-type glutamate receptor (NMDAR). Consequently, the putative NMDAR dysregulation in the pathophysiology of schizophrenia and mood disorders could be due to disturbed D-serine signaling. Some studies described the changed D-serine levels in serum, plasma and cerebrospinal fluid (CSF) of patients with schizophrenia and major depressive disorder (MDD). Furthermore, G72 gene that