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Soluble Fas ligand (sFasL) as a predictor of reduction of general psychopathology in schizophrenia after antipsychotic treatment

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Introduction Dysregulation of the apoptotic process is associated with the etiopathogenesis of schizophrenia, which is observed at the brain and peripheral blood levels. A significant negative correlation between the duration of the disease and serum sFasL concentration was demonstrated by other authors. It was shown that an increased rate of apoptosis is more pronounced in neuroleptic-free patients with the first-episode of schizophrenia than in patients with chronic disease.
Aim Search for a predictor of good response to antipsychotic treatment based on the analysis of the sFasL plasma level and its relationship with clinical symptoms.
Methods Fifty-three patients with chronic schizophrenia and 46 healthy individuals were enrolled in the study. The concentration of sFasL was measured by ELISA. Clinical assessments (PANSS, SANS, SAPS) and blood analyses were conducted three times: during the active phase of disease (at admission), after 4 weeks of pharmacotherapy, and after reaching remission.
Results In the schizophrenia group, non-altered levels of sFasL ($P = 0.1$; U Mann-Whitney test), compared to the control, were detected at admission. The initial level of sFasL correlated negatively ($r = -0.33$; $P = 0.04$; Spearman's rank) with blood leukocyte count. Despite clinical improvement, no significant changes in the level of sFasL were observed. However, the sFasL level correlated negatively with the PANSS general psychopathology reduction after 4 weeks of pharmacotherapy ($r = -0.7$; $P = 0.04$) and after remission ($r = -0.39$; $P = 0.026$).
Conclusions The results indicate a possible role of sFasL in apoptosis of blood leukocytes and suggest that the reduction of sFasL level can predict level of PANSS general psychopathology after antipsychotic treatment in schizophrenia.
Disclosure of interest The authors have not supplied their declaration of competing interest.

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Basic symptoms as subjective cognitive deficit in schizophrenia: Cognitive, clinical and functional associations

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Introduction Basic symptoms are subjective complaints that present at the early states in psychotic disorders and persist in the long-term. They can be studied using hetero applied clinical instruments or self-administered questionnaires. Basic symptoms can be useful as screening tools in at risk populations.
Aims To determine if basic symptoms (subjective cognitive deficits) are associated with the objectively measured cognitive deficit after controlling for functioning and symptomatology.
Methods One observational, transversal, psychopathological and neuropsychological study was performed on a schizophrenia outpatients sample ($n = 78$). Correlations were measured by using Spearman's Rho coefficient. Basic symptoms were registered by using the Frankfurt Complaints Questionnaire (FCQ-3); cognitive status was assessed by Repeatable Battery for the Assessment of Neuropsychological Status (RBANS); clinical status was assessed by PANSS and Clinical Global Impression (CGI); functional status was measured with Global Assessment of Functioning (GAF).
Results All the dimensions were related to subjective complaints: cognitive functioning ($r = -.38$; $P < .001$); positive symptoms ($r = .54$; $P < .001$); negative symptoms ($r = .26$; $P < .02$); general symptoms ($r = .41$; $P < .001$); CGI ($r = .57$; $P < .001$); GAF ($r = -.45$; $P < .001$). The association between subjective and objective cognitive deficit remains significative after controlling for the clinical and functional variables, except when controlling for CGI.
Conclusions The evaluation of basic symptoms with FCQ-3 is related with an objective cognitive deficit and could be useful as a screening tool.
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Adjunctive memantine in clozapine-treated refractory schizophrenia: A one-year extension study

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Introduction In a recent 26-week placebo-controlled, crossover trial ($n = 52$) we found significant positive effects on verbal and visual memory, and negative symptoms in clozapine-treated patients with refractory schizophrenia.
Objectives In this 1-year extension study, we report the long-term effects and tolerability of memantine add-on therapy to clozapine.
Aims To evaluate the persistence of improvements in cognitive functioning and symptoms of memantine add-on therapy to clozapine in schizophrenia.
Methods Completers of the first trial who experienced a beneficial effect of memantine after 12 weeks continued memantine for one year. Primary endpoints were change from baseline to 26 weeks treatment and 26 weeks to 52 weeks treatment on memory and executive function using the Cambridge Neuropsychological Test Automated Battery (CANTAB), Positive and Negative Syndrome Scale (PANSS), and Clinical Global Impression Severity Scale (CGI-S). Secondary endpoints were change on the Health of the Nation

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Outcome Scales (HoNOS) and Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS).
Results Of 32 completers who experienced a beneficial effect of memantine 23 patients continued memantine for one year. Memory improvement was sustained, verbal recognition memory improved even further between $t = 26$ weeks and $t = 52$ weeks. Continued treatment with memantine add-on to clozapine was associated with significantly improved PANSS positive, negative and overall score, CGI-S and HoNOS scores.
Conclusions In the extension phase the positive effect of memantine add-on therapy on verbal memory sustained and positive, negative and overall symptoms of schizophrenia, clinical global status and psychosocial functioning significantly improved. Memantine was well tolerated without serious adverse effects.
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Decreased interhemispheric resting state functional connection in schizophrenic patients with auditory hallucinations

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Introduction Auditory hallucination (AH) has been always concerned as a main core symptom of schizophrenia. However, the mechanisms of AH are still unclear.
Objectives The aim of this study is to further explore the complicated neuroimaging mechanism of AHs from a new insight by using voxel-mirrored homotopic connectivity (VMHC).
Methods Forty-two patients with AH (APG), 26 without AHs (NPG) and 82 normal controls (NC) participated in resting state fMRI scan. Correlation analyses were used to assess the relationships between VMHC and Hoffman scores. Additionally, ROI analysis was used to further know about the functional connectivity between the brain areas with changed interhemispheric FC and the whole brain.
Results APG showed reduced VMHC in the parahippocapus, fusiform gyrus, rolandic operculum, insula, heschl's gyrus and superior temporal gyrus (STG). Hoffman score of APG group had negative correlation with VMHC in these regions. Besides, ROI analysis supported decreased interhemispheric FC in schizophrenia with AH and verified functional connectivity abnormalities in schizophrenia.
Conclusions These findings suggest impairment of interhemispheric coordination and whole brain FC in schizophrenia with AH, which may be implicated to the neuroimaging mechanism of auditory hallucination. Furthermore, this research highly support dysconnectivity hypothesis that schizophrenia related to abnormalities in neuronal connectivity.
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Efficacy and safety of brexpiprazole in schizophrenia: Meta-analysis of three double-blind, randomized, placebo-controlled phase 3 studies

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Introduction Brexpiprazole is a serotonin-dopamine activity modulator that is a partial agonist at 5-HT1A and dopamine D2 receptors at similar potency, and an antagonist at 5-HT2A and noradrenaline alpha1B/2C receptors.
Objectives To evaluate the efficacy, safety, and tolerability of brexpiprazole in patients with acute schizophrenia in a meta-analysis of three phase 3 studies with brexpiprazole.
Aim The primary endpoint was change from baseline to week 6 in PANSS total score.
Methods Data from the 3 clinical studies in patients with acute schizophrenia were combined and analyzed using individual patient data meta-analysis. In two similarly designed studies (NCT01396421; NCT01393613), patients with acute schizophrenia were randomized to fixed-doses of brexpiprazole 2 mg/day, 4 mg/day or placebo (a low-dose treatment group was included in each study [0.25 mg and 1.0 mg]; not included in the meta-analysis). In the third study (NCT01810380), patients were randomized to flexible dosing of brexpiprazole (2 to 4 mg/day), placebo, or an active reference (quetiapine extended release). Changes from baseline for brexpiprazole vs. placebo were analyzed using an MMRM approach.
Results Brexpiprazole 2–4 mg ($n = 868$) was superior to placebo ($n = 517$) in change from baseline in PANSS total score (−20.1 vs. −14.3; estimated treatment difference to placebo: −5.8 [95% CI: −8.0; −3.6]; $P < 0.001$). The proportions of patients reporting TEAEs were similar between the brexpiprazole and placebo treatment groups (57.9% vs. 57.5%). No unexpected safety concerns were observed.
Conclusion This meta-analysis supports evidence from three individual trials that brexpiprazole is efficacious and safe in treating patients with acute schizophrenia.
Disclosure of interest The authors have not supplied their declaration of competing interest.

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Sleep disorders and stress

FC97

Sleep disturbances and substance use disorders: An international study of primary care and mental health specialty care patients

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Introduction There is no comprehensive evidence on the influence of sleep disturbances (SD) on substance use disorders (SUD) or treatment use patterns of individuals with comorbid disturbances.
Objective/aim To better understand comorbidities and treatment use patterns of individuals with SD and SUD.