EPP1054

The role of interleukin 10 in the development of the schizophrenia deficit syndrome in the light of the disconnection hypothesis

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Introduction: One of the subtypes of schizophrenia is the deficit syndrome (DS). Because of different risk factors, course, response to treatment weak prognosis, researches on this group of patients are important. Etiology of schizophrenia is often hypothesized as the inflammation process. Due to the imbalance of certain cytokines (interleukin-10 (IL-10) -antyinflamation cytokine, among others) changes in the function and structure of central nervous system may occur. That process could stand behind the outbreak of psychotic and deficit symptoms of the illness. Subinflammation can have an impact on the white matter structure. Disturbances in this area can cause impairment of cortical communication and hence, produce psychopathology. One of the structures that seem to have the basis of the deficit syndrome isinferior longitudinal fasciculus (ILF). ILF is a bundle of association fibers with interconnects temporal cortex with ocapital cortex.
Objectives: The aim of our study was to investigate a relationship between the integrity of ILF and interleukin – 10.
Methods: 39 schizophrenia subjects divided into two groups DS (16) and non-deficyt sydrome (NDS) (23) and 18 healthy controls (HC) participated in the study. A DTI analysis was performed on all study participants. The psychopathology of schizofrenia was assessed using the Positive and Negative Syndrome Scale (PANSS). The ILF analysis was then conducted using fractional anisotropy (FA) and mean diffusivity (MD) parameters. Blood samples were obtained to analyze serum level of IL-10 level.
Results: The differences in FA value in left ILF between DS and HC group were confirmed. The difference in values of IL-10 between groups were not confirmed. A negative correlation was found between FA values in left ILF and IL-10 ($p = 0.033$) among DS group.
Conclusions: The imparment of the structure of ILF may be involved in ethiopatogenesis of DS. Moreover, changes in IL-10 levels may be related to the microstructure of ILF bundle.

Disclosure of Interest: None Declared

EPP1055

Evenamide, as an add-on to antipsychotics, benefits patients with treatment resistant schizophrenia: 6-month interim results from the first 100 patients in an ongoing international randomized study

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Introduction: Treatment resistance schizophrenia (TRS) develops in ~ 30% of patients in about 5 years from starting treatment with 5-HT2/D2 APs, resulting in increased morbidity, suicidality, and mortality. Findings from neurochemistry, neurometabolism, functional imaging in TRS patients indicate abnormalities in glutamatergic neurotransmission (Moghaddam B et al 2012; 37 4-15) rather than excess of dopamine synthesis (Demjaha A et al 2014; 75 11-3; Mouchlianitis E et al 2016; 42 744-52), suggesting the need to add a drug that attenuates glutamate release. Evenamide, a selective inhibitor of voltage-gated Na^+ channels, is devoid of biological activity at >130 CNS targets, normalizes glutamate release without affecting basal levels, and demonstrated benefits in animal models of psychosis as monotherapy and as an add on to APs (including clozapine), reversing deficits produced by amphetamine, scopolamine, phencyclidine, or ketamine
Objectives: Studies 014/015 were designed to evaluate the safety and preliminary efficacy of evenamide given orally at 3 fixed doses (7.5, 15 and 30 mg bid) in patients with TRS not responding to a therapeutic dose of an AP. Assessment of efficacy was based on changes of PANSS and CGI-S/C, while tolerability was assessed based on all safety measures
Methods: Study 014 is a 6-week, randomized, rater-blinded, international study with completers continuing assigned doses for an additional 46 weeks in an extension study (Study 015). Patients were initially randomized to 7.5 or 15 mg bid; the Independent Safety Monitoring Board (ISMB) allowed randomization to 30 mg bid after reviewing safety data from the first 50 patients. At baseline, patients were moderately to severely ill (CGI-S of 4 to 6), with a PANSS total score of 70-90 and predominant positive symptoms (score of 4 or more on at least 2 core symptoms and a PANSS positive total score ≥ 20), along with functional deficits (GAF ≤ 50). Efficacy ratings were performed by a psychiatrist blinded to the evenamide dose. Data were analyzed as a single group using descriptive statistics to assess changes from baseline to endpoint (Week 30)
Results: Interim, group-blinded, 30-week results for safety and efficacy data (PANSS and CGI) for the first 100 patients (including 6 on 30 mg bid) will be presented. Patients randomized to 7.5, 15, and 30 mg bid had all safety and efficacy data pooled in a single group to maintain the blind in the study. All results will be submitted to the ISMB, relevant health authorities and the FDA
Conclusions: This trial is the first international TRS trial of an NCE AP used as an add-on to a single typical or atypical AP. Results of this study may change the treatment of future TRS patients

Disclosure of Interest: None Declared

EPP1056

Characterization of "Responder" in patients with Treatment-Resistant Schizophrenia (TRS) treated with a new antipsychotic added to their current antipsychotic monotherapy

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Introduction: Numerous authors have proposed "responder" criteria for patients with schizophrenia treated with antipsychotic monotherapy (Leucht, S et al 2009; 438 7-14; Suzuki T et al, 2012; 197 1-6; Kane J et al 1988; 45 789-96). These suggest reductions greater than 30% on the PANSS total score, improvements of 1 category or more on the CGI-S, or CGI-C ratings of very much, much or minimally improved, as well as various permutations and combinations of the above. No study has met the responder definition of Kane et al in the last 30 years in monotherapy studies in TRS patients. However, a widely accepted definition of response in patients with TRS treated with a putative antipsychotic added to their background antipsychotic monotherapy, is not currently available, and more work is needed on this highly relevant topic (Suzuki, T et al 2011; 133 1-3).
Objectives: Combining PANSS (30-item anchored scale), CGI-C and CGI-S (both 7-point Likert scales), three of the most accepted scales to evaluate patients with schizophrenia worldwide, we propose two different definitions of response in TRS population
Methods: Study 014 was designed to evaluate the safety and preliminary evidence of efficacy of evenamide, a NCE added to an antipsychotic monotherapy, given orally at 3 fixed doses (7.5, 15 and 30 mg bid) in patients with TRS not adequately responding to a therapeutic dose of an AP. Assessment of efficacy was based on changes of the PANSS and CGI-S/C. We reviewed the efficacy data of the first 100 patients at various timepoints up to 30 weeks.
Results: We assessed multiple definitions involving all the three measures (PANSS, CGI-S, and CGI-C) to determine one that would define a "responder" by categories that may be clinically meaningful. Review of the data indicated two definitions of responders based on the different combinations of the individual measures. "Full responder" was defined as PANSS total score improvement $\geq$ 20%; CGI-C at least much improved (i.e. 1,2); CGI-S at least one point improvement and reaching at least mildly ill (i.e. a score of at least 3 or less). "Partial responder" was defined as PANSS total score improvement $\geq$ 15%; CGI-C rated as any improvement (i.e. 1,2,3); CGI-S at least one point improvement. These two categories are alternatively true and patients not fulfilling the criteria for the above categories are considered as "non-responders". Further descriptive analysis will be presented.
Conclusions: These definitions may change the selection of compounds used as add-on therapy for TRS patients as well as the study designs to evaluate them.

Disclosure of Interest: None Declared

EPP1057

Biomarkers as Proxies for Cognitive Reserve: the role of high density lipoprotein cholesterol in first episode of psychosis

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Introduction: The proxies used to compose cognitive reserve (CR) in first episode of psychosis (FEP) have varied in the literature. The development of FEP is linked to the peripheral pathways of the central nervous system (Leboyer *et al.* Psychopharmacology 2016; 233(9) 1651-60) Furthermore, schizophrenia has been linked to the metabolic system, indicating that alterations in the levels of biological parameters, in particular high-density lipoproteins (HDL) (Gjerde *et al.* Eur Arch Psychiatry Clin Neurosci 2020; 270 (1) 49-58) cause worse global functioning and cognitive impairment (Adamowicz *et al.* J Clin Med 2020; 9(2) 537). Despite this knowledge, no research has considered the introduction of biomarkers as proxies for CR.
Objectives: The present study aimed to create a quantifiable and objective CR index that adjusts for the multifactorial nature of FEP.
Methods: We included 668 patients who had FEP and 217 healthy controls who were assessed for sociodemographic information and levels of biological parameters: waist circumference, hypertension and levels of HDL, triglycerides and glucose. The main analyses were multiple regression analysis, principal component analysis (PCA) and exploratory factor analysis (EFA).
Results: Regression analyses showed that HDL was the top performing biological parameter in a model containing years of education and unemployment ($F=11.80$; $p<0.001$) while also outperforming other parameters in a correlation analysis with a composite of the same variables ($r= 0.21$; $p<0.001$). In EFA analyses combining all possible components, we found that the most optimal proxies for the composition of biological CR were years of education and HDL. The results using PCA indicated that biological CR would have a greater explanatory power for the phenomenon than classical CR, increasing 7.27% of the explanation for FEP patients and 16.08% for healthy controls.
Conclusions: This article proposes an objective and quantifiable method to measure CR, taking into account endogenous and exogenous factors. This index, introducing biomarkers as proxies could provide a more accurate CR score for FEP patients.

Disclosure of Interest: None Declared

EPP1058

Positive and Negative Syndrome Scale (PANSS) predictors of hospitalization during home treatment on 1045 patients with schizophrenia in acute crisis

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Introduction: Several factors related to the risk of requiring psychiatric hospitalization have been described in patients diagnosed with schizophrenia treated with methods other than home treatment. With regard to the symptoms, high global illness severity and positive symptoms of schizophrenia have been most frequently