FC81

Electrophysiological mechanisms underlying ERP amplitude reduction in patients with schizophrenia: A time-frequency analysis

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Background It is hypothesized that the event-related potentials are generated by different electrophysiological mechanisms, i.e., event-related power increase and enhanced degree of phase-locking over trial. The study aimed to characterize the relative contribution of these mechanisms to the ERP in patients with schizophrenia (SCZ).
Materials and methods One hundred and fifteen chronic stabilized SCZ and 62 healthy controls (HC) recruited to the study of the Italian Network for Research on Psychoses were included. Scalp potentials were recorded during a standard auditory oddball task. Stimulus-locked segments were extracted for all standard trials and correctly hit target trials. Trials contaminated by other artifacts were rejected. For each subject and stimulus type the event-related spectral perturbation (ERSP) and the inter-trial-coherence (ITC) were computed to assess event-related power increase and inter-trial phase-locking. The two groups were compared using Student's *t*-test followed by Bonferroni correction for multiple comparisons.
Results SCZ presented a reduced amplitude of both N100 and P3b. For both standard and target stimuli, at Cz and Pz, ERSP was reduced in SCZ in the delta-theta band (from 0 up to 400 ms). The ITC index, at the same channels, was reduced in SCZ in the delta band for standard stimuli (from 0 to 300 ms), and in both delta and theta bands for target stimuli (from 300 to 400 ms).
Conclusions Our results indicate that alterations of both mechanisms are involved in N100 and P3b amplitude reduction observed in SCZ. Inter-trial phase-locking abnormalities for N100 were limited to the delta band, while for P3b involved delta and theta frequencies.
Disclosure of interest The authors have not supplied their declaration of competing interest.

http://dx.doi.org/10.1016/j.eurpsy.2016.01.085

FC82

Methylenetetrahydrofolate reductase (*MTHFR*) gene polymorphisms and antipsychotic-induced metabolic disturbances in first-episode schizophrenia patients

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Introduction There is a scarcity of prospective studies addressing the influence of the *methylenetetrahydrofolate reductase* (*MTHFR*) gene polymorphisms on antipsychotic-induced metabolic changes in first-episode schizophrenia (FES) patients.
Objectives We aimed at investigating metabolic side effects of second-generation antipsychotics (SGAs) with respect to the *MTHFR* gene polymorphisms in FES patients.
Methods Polymorphisms in the *MTHFR* gene (C677T and A1298C) were investigated with respect to changes in body mass index (BMI) and waist circumference (WC) together with serum levels of glucose, lipids, homocysteine, vitamin B12 and folate after 12 weeks of treatment with SGAs in 135 FES patients.
Results The 677TT genotype was associated with significantly higher BMI, WC and serum levels of triglycerides, as well as significantly lower folate levels at baseline. Additionally, the 677T allele was associated with significantly lower folate levels at baseline. The 677CC homozygotes had significantly higher increase in BMI and serum levels of triglycerides. The 677TT genotype predicted significantly higher increase in homocysteine levels and significantly higher decrease in folate levels. These associations were also significant in the allelic analysis. Only the patients with the 677T allele had significantly lower folate levels and significantly higher homocysteine levels at the follow-up. The 677T allele was also related to significantly lower increase in WC. The 1298CC homozygotes had significantly higher weight gain in the course of treatment with SGAs.
Conclusions The *MTHFR* gene polymorphisms might predict antipsychotic-induced weight gain in FES patients. In addition, the *MTHFR* C677T polymorphism might be also predictive with respect to other metabolic adversities of SGAs.
Disclosure of interest The authors have not supplied their declaration of competing interest.

http://dx.doi.org/10.1016/j.eurpsy.2016.01.086

FC83

Clinical symptomatology and theory of mind in schizophrenia: Which relationship?

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Introduction Theory of mind (ToM) has repeatedly been shown to be compromised in many patients with schizophrenia (SCZ). It now seems to be quite well-established that patients with profound negative or disorganized symptoms perform poorly on ToM tasks. By contrast, findings in patients with predominant positive symptoms are much more ambiguous.
Objectives To investigate the relationship between ToM deficits and different symptoms dimensions in SCZ.
Methods Fifty-eight outpatients with stable SCZ completed the intention-inferencing task (IIT), in which the ability to infer a character's intentions from 28 short comic strip stories is assessed. Symptomatology evaluation comprised the Positive and Negative Syndrome Scale (PANSS), the Calgary Depression Scale for Schizophrenia (CDSS) and the Clinical Global Impressions Scale Improvement and severity (CGI).
Results The number of correct answers in the IIT negatively correlated with both the positive ($P = 0.015$) and negative ($P < 0.0001$) scales of the PANSS. ToM deficits were correlated with the conceptual disorganization, hallucinations and the suspiciousness/persecution items.
The patients who had more false answers in the IIT also had significantly higher scores at the positive ($P = 0.005$), negative ($P < 0.0001$) and general ($P < 0.0001$) scales of the PANSS. Worse IIT performance correlated with a higher severity index in the CGI. No correlations were found between IIT scores and CDSS scores.

https://doi.org/10.1016/j.eurpsy.2016.01.087 Published online by Cambridge University Press

Conclusions Our results confirm the relationship between ToM deficits and negative symtomps and suggest that ToM may also be correlated to specific positive symptoms.
Disclosure of interest The authors have not supplied their declaration of competing interest.

http://dx.doi.org/10.1016/j.eurpsy.2016.01.087

FC84

Effectiveness of long-acting injectables and clozapine in a real-world setting during the early-stages of psychotic illness

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Introduction Intervention in the early-stages of psychosis may be able to shape the clinical course; critical period (CP) is best represented by the first 5 years from first admission (FA).
Objectives To investigate the effectiveness of pharmacological intervention within and beyond the CP.
Aims (1) To compare hospitalization rates of patients stabilized on treatment with LAIs and CLZ. (2) To determine whether treatment with LAIs and CLZ within CP can influence hospitalization rates.
Methods Data were retrospectively collected from patients diagnosed with non-affective psychoses with FA between 2000 and 2014; 200 patients were then divided into three groups, according to stabilized treatment regimen during the final year of observation: treatment as usual (TAU), CLZ, LAIs. hospitalization duration (HSPD) and frequency (HSP) were calculated for each group.
Results Despite a major severity before assignment to either CLZ or LAIs treatment, HSPD and HSP in both groups shifted below those observed for the TAU arm. Patients who began treatment with LAIs within the CP showed a highly significant decrease of both HSPD and HSP (respectively 17.4 ± 18 vs. 2.6 ± 8.2; $Z = -2.856$; $P < 0.005$ and 1.1 ± 0.8 vs. 0.2 ± 0.5; $Z = -3.115$; $P < 0.005$). No significant changes in hospitalization rates were observed for subjects who began treatment with LAIs after the CP.
Conclusions Our study confirms that treatment with either CLZ or LAIs significantly impacts the course of psychotic disorders. The data seem to suggest that LAIs and CLZ should be considered more effective than conventional oral antipsychotics in the early-stages of psychotic illness. The difference among treatments tends to wane beyond the CP, especially for LAIs.
Disclosure of interest The authors have not supplied their declaration of competing interest.

http://dx.doi.org/10.1016/j.eurpsy.2016.01.088

FC85

Metabolic syndrome in patients with schizophrenia receiving long-term treatment with lurasidone, quetiapine XR, or risperidone

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Introduction Lurasidone has demonstrated low propensity for metabolic disturbance in adult patients with schizophrenia in short-term studies.
Objectives To evaluate metabolic syndrome occurrence during long-term lurasidone treatment in patients with schizophrenia.
Aims To compare metabolic syndrome rates with lurasidone versus other antipsychotic agents.
Methods Metabolic syndrome rates (as defined by the US National Cholesterol Education Program-Adult Treatment Panel III) were evaluated in adult patients with schizophrenia treated with lurasidone in 2 long-term, active-controlled studies (quetiapine XR or risperidone). In the quetiapine XR-controlled study, patients completing a 6-week, double-blind, placebo-controlled, fixed-dose trial of lurasidone (74 mg/d or 148 mg/d) or quetiapine XR (600 mg/d) continued on double-blind, flexibly dosed lurasidone (37–148 mg/d) or quetiapine XR (200–800 mg/d) for up to 12 months. In the risperidone-controlled study, patients received double-blind, flexibly dosed lurasidone (37–111 mg/d) or risperidone (2–6 mg/d) for up to 12 months.
Results Among patients without metabolic syndrome at baseline in the quetiapine XR-controlled study, 2.4% (2/84) of lurasidone-treated patients and 7.4% (2/27) of quetiapine XR-treated patients developed metabolic syndrome at month 12 (P = NS). Of patients without metabolic syndrome at baseline in the risperidone-controlled study, 10.3% (12/117) and 23.2% (16/69) of lurasidone- and risperidone-treated patients, respectively, developed metabolic syndrome at month 12 ($P = 0.02$).
Conclusions Long-term treatment with lurasidone was associated with lower rates of metabolic syndrome in patients with schizophrenia compared to treatment with quetiapine XR or risperidone.
Support Sunovion Pharmaceuticals Inc.
ClinicalTrials.gov identifiers NCT00789698, NCT00641745.
Disclosure of interest The authors have not supplied their declaration of competing interest.

http://dx.doi.org/10.1016/j.eurpsy.2016.01.089

FC86

Neurochemical and behavioral sensitization to d-amphetamine in healthy subjects measured with [^{11}C]-(+)-PHNO-PET

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Introduction It has been shown that patients with schizophrenia are super-sensitive towards dopamine-releasing agents such as amphetamine. Here, we studied the effects of amphetamine sensitization on amphetamine-induced dopamine release in healthy subjects.
Objectives To measure d-amphetamine-induced dopamine release as measured with the $D_{2,3}$ agonist radioligand [^{11}C]-(+)-PHNO-PET via change in non-displacable binding potential (BP_{ND}) and behavioral measures of d-amphetamine effects with drug effects questionnaire (DEQ) and subjective states questionnaire (SSQ).
Aims To study d-amphetamine-induced sensitization in healthy subjects on a behavioral and neurochemical level with [^{11}C]-(+)-PHNO-PET in order to gain more knowledge on sensitization-induced changes in the dopaminergic system.
Methods Twelve stimulant-naïve healthy male subjects underwent three 90-min [^{11}C]-(+)-PHNO-PET-scans and four oral administrations of d-amphetamine. After a naïve baseline scan,