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### Title

P.2.143 Does cannabis use affect endogenous cannabinoids in schizophrenia?

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other hand, in areas of life that are influenced by social conditions such as partnership or the professional situation.

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#### P.2.142 Neurocognitive measures of prefrontal cortical dysfunction in schizophrenia: Prefrontal fast oscillations and WCST in patients with schizophrenia

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**Objective:** Bursts of gamma oscillations (30 Hz and more) are associated with various behavioral alerts or sensory coding in animal models. This electroencephalographic activity, generated mostly by the entorhinal cortex, also reflects the burden of neurocognitive tasks in human beings. Hypothetically, schizophrenic psychopathology could be related to the distorted or limited capacity decision channels, so the gamma range activity may be considered as a prime target of neurocognitive studies in schizophrenia. The aim of this study was to identify functional links between the dominant prefrontal fast frequency component and the WCST performance.

**Methods:** 28 schizophrenic patients (ICD-10 criteria for paranoid type, PANSS $\geq$ 60) and 28 healthy subjects without neurological or psychiatric disorders, match-paired in age, gender and handedness were assessed with the Wisconsin Card Sorting Test (WCST). The EEG was recorded continuously and 20-millisecond samples analyzed. Because the WCST reflects predominantly the integrity of prefrontal and cingulate functioning in such domains like attention and executive functioning its results were compared in prefrontal areas (Fp1, Fp2, Fp7, and Fp8). The gamma band (30–50 Hz) or the fastest obtainable signals were examined and computed by means of the FFT method (the Fast Fourier Transform). All patients were newly admitted and treated with both typical and atypical antipsychotics. The mean daily chlorpromazine equivalent medication level was 442 mg.

**Results:** Patients with schizophrenia performed worse on the WCST with respect both to correct responses ( $p < 0.002$ ) and preservative errors ( $p < 0.02$ ). Surprisingly, the patients' WCST total completed categories index was indistinguishable from healthy controls' one ( $p < 0.07$ ). On the other hand nearly all prefrontal frequencies were significantly different between groups: Fp1  $p < 0.000$ , Fp2  $p < 0.000$ , Fp7  $p < 0.08$  (n.s.), Fp8  $p < 0.000$ . Moreover, there were only weak or mild correlations between prefrontal frequencies and the WCST performance in the patients' group, comparing to statistically moderate interrelationships in the controls' group.

**Conclusion:** The established links and differences between the WCST performance and the prefrontal oscillation scores suggest the existence of both functional and pathological backgrounds. Pathologically distributed fast oscillations may explain more general attentional deficits observed in schizophrenic population.

#### P.2.143 Does cannabis use affect endogenous cannabinoids in schizophrenia?

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**Purpose of the study:** The endogenous cannabinoid system represents a neurotransmitter system based on lipid neurotransmitters of which anandamide (AEA) and 2-arachidonoylglycerol are the best characterized. These endogenous cannabinoids bind to G-protein coupled cannabinoid receptors. Cannabis use is frequent among schizophrenic patients and is suspected to precipitate psychotic symptoms in vulnerable subjects. However, the underlying neurobiological principles of these clinical findings remain conjectural so far. The aim of this study was to investigate levels of AEA in cerebrospinal fluid (CSF) and serum in schizophrenic patients with different patterns of cannabis use compared to healthy controls.

**Methods:** AEA and two non-cannabinoid analogs of anandamide, palmitoylethanolamide (PEA) and oleylethanolamide (OEA), were purified from CSF or serum and quantified by isotope dilution high performance liquid chromatography/mass spectrometry (HPLC/MS) in 47 antipsychotic-naïve first-episode paranoid psychotic patients and 84 healthy volunteers. Cannabis use was differentiated into low frequency cannabis use (LFCU) with less than 5 times of cannabis use in life and moderate cannabis use (HFCU) with more than 20 times lifetime. In addition, HFCU psychotic patients were differentiated in those with recent cannabis use (positive urine drug screening) and no recent cannabis use.

**Summary of results and statistical assessments:** AEA concentrations in cerebrospinal fluid (CSF) are not significantly different between healthy volunteers with low frequency cannabis use (V-LFCU) and with moderate cannabis use (V-HFCU). In contrast, AEA CSF in V-LFCU and V-HFCU is significantly lower than in first-episode antipsychotic-naïve psychotic patients with low cannabis use (S-LFCU), but not in those with higher frequency use without (S-HFCU) or with acute cannabis use (S-HFACU). AEA in CSF in S-HFCU patients is significantly lower than in S-LFCU patients. Patients with frequent and acute cannabis use (S-HFACU) show higher so not significantly different levels of AEA in CSF compared to S-HFCU patients. Non-parametric statistical analysis using a Kruskal-Wallis test with pairwise post hoc Mann-Whitney Tests between groups ( $\alpha$ -level = 0.005 adjusted by Bonferroni correction for 10 tests) was applied.

**Conclusion:** Our data reflect different levels of anandamide in CSF of schizophrenic patients depending on the frequency of cannabis use preceding the first manifestation of a paranoid psychosis. This raises first evidence, that the endogenous cannabinoid system does not only play an adaptive role in schizophrenia but is also affected by previous cannabis use in first-episode patients.