S14.02

Cannabidiol as an antipsychotic agent

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Background: The human endocannabinoid system interacts with various neurotransmitter systems and the endocannabinoid anandamide was found significantly elevated in CSF and inversely correlated to psychopathology (Giuffrida et al. 2004) providing a link to the neurobiology of schizophrenia. While delta-9-tetrahydrocannabinol, the psychoactive compound of Cannabis sativa, shows psychedelic properties, the major herbal cannabinoid compound cannabidiol was suggested recently a re-uptake inhibitor of anandamide. In addition potential antipsychotic properties have been hypothesized.

Methods: We performed an explorative, 4-week, double-blind, controlled clinical trial on the effects of purified cannabidiol in acute schizophrenia compared to the antipsychotic amisulpride. The antipsychotic properties of both drugs were the primary target of the study. Furthermore, side-effects and anxiolytic capabilities of both treatments were investigated.

Results: 42 patients fulfilling DSM-IV criteria of acute paranoid schizophrenia or schizophreniform psychosis participated in the study. Both treatments were associated with a significant decrease of psychotic symptoms after 2 and 4 weeks as assessed by BPRS and PANSS. However, there was no statistical difference between both treatment groups. In contrast, cannabidiol induced significantly less side effects (EPS, increase in prolactin, weight gain) when compared to amisulpride.

Conclusions: Cannabidiol proved substantial antipsychotic properties in acute schizophrenia. This is in line with our suggestion of an adaptive role of the endocannabinoid system in paranoid schizophrenia, and raises further evidence that this adaptive mechanism may represent a valuable target for antipsychotic treatment strategies.

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S14.03

Anxiolytic effects of cannabidiol

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Background and Aims: Cannabidiol (CBD) constitutes up to 40% of cannabis sativa plant and has quite different psychological effects to the plant's best-known constituent, delta-9-tetrahydrocannabinol (delta-9-THC). This study examines the current knowledge of the effects of CBD on anxiety.

Method: Articles were identified through a search of MEDLINE using the key word cannabidiol and anxiety. No search limits were included. Additional references were located through review of the bibliographies of the articles identified.

Results: In animal studies CBD has shown similar effects to anxiolytic drugs in conditioned emotional paradigms, the Vogel conflict test, and the elevated plus maze test. In humans, oral administration of CBD in healthy volunteers decreases and antagonizes the anxiogenic effect of high doses of delta-9-THC. CBD may thus posses inherent anxiolytic properties unrelated to THC-type activity. This is consistent with its anxiolytic effect on anxiety elicited by simulated public speaking test. In addition, SPECT and fMRI neuroimaging studies have confirmed that CBD has anti-anxiety properties and that these effects are mediated by an action on limbic and paralimbic brain areas.

Conclusions: These results support the hypothesis that CBD may be a future therapeutic option for anxiety. However, future studies of CBD in clinical anxiety such as panic and social anxiety disorder and comparative studies of its anxiolytic effects with those produced by benzodiazepines and other anti-anxiety compounds are clearly indicated.

S14.04

CBD and the neural correlates of anxiety

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Aims: The study sought to examine the neurophysiological effects of cannabidiol (CBD) on the emotional processing using functional Magnetic Resonance Imaging (fMRI).

Method: Fifteen healthy male participants (age range 18-35) with a lifetime exposure to cannabis of 15 times or less were recruited in a double blind event-related fMRI design. Prior to each scanning session, participants were given an oral dose of either 600mg CBD or a placebo. The blood levels of drugs were monitored via an intravenous line, while systolic and diastolic blood pressure and heart rate (beats per minute) were recorded manually. During the scan, subjects were presented with 10 different facial identities, each identity expressing 50% or 100% intensities of fear or a neutral expression. Neuropsychological performance and symptoms ratings were recorded at baseline, immediately before scanning (1 hr), immediately after scanning (2 hr), and one hour post scanning (3 hr).

Results: CBD had no significant effect on the gender discrimination task. Reaction times were significantly faster when processing 100% fearful faces than compared to 50% fearful and neutral faces. CBD had a significant effect on brain activation in response to faces with emotional expressions, decreasing activation in the right posterior cingulate gyrus and in the right cerebellum, when compared to placebo. Furthermore, a significant interaction effect was observed. In the right cingulate gyrus CBD attenuated activation during the processing of intense fearful faces but had no effect of neural response to neutral or mild fearful faces.

Conclusion: CBD significantly modulates the neurophysiological response associated with anxiety.

S14.05

Cannabis and psychosis

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Cannabis use is approximately twice as high among people with schizophrenia as among the general population. Evidence for cannabis use predisposing to psychoses later in life came many years ago from a study of Swedish conscripts. A dose-response relationship was observed

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