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# Cannabis and cognitive function: relevant to psychosis

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# Cannabis and cognitive function: relevant to psychosis

## **Abstract**

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## Symposia

### Cannabis and Psychosis: From Neuroscience to Clinical Intervention (NISAD Symposium)

#### A Baker

Centre for Mental Health Studies, The University of Newcastle, New South Wales, Australia

#### Overview

Cannabis use has been associated with the onset, course and relapse of psychosis. Population studies and data from samples of young people at high risk for psychosis have indicated that cannabis use may be related to the onset of psychosis. Cannabis use has also been found to have a deleterious impact on psychotic symptom severity and has emerged as the strong predictor of psychotic relapse. To date, there has been little collaboration between neuroscience and clinical research groups examining the link between cannabis use and psychosis, despite the potential for these fields to inform the other. This symposium seeks to begin to redress this gap.

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01-01

#### Heterozygous neuregulin 1 mice are more sensitive to the behavioural effects of D9-tetrahydrocannabinol

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**Rationale:** Environmental stressors such as cannabis use may precipitate schizophrenia especially if the individual has a genetic vulnerability to the disease. Human and animal research indicates that neuregulin 1 (*Nrg1*) is a susceptibility gene for schizophrenia.

**Aim:** The aim of this study was to investigate whether dysfunction in the *Nrg1* gene modulates the behavioural effects of 9-tetrahydrocannabinol (THC), the major psychotropic component of cannabis.

**Methods:** Heterozygous *Nrg1* transmembrane-domain knockout mice (*Nrg1* HET) were treated with acute THC (0, 5 or 10 mg/kg i.p.) 30 min before being tested in the open field (OF), hole board, light-dark (LD), elevated plus maze (EPM), social interaction (SI) and prepulse inhibition (PPI) tests.

**Results:** *Nrg1* HET mice showed differences in baseline behaviour in regard to locomotor activity, exploration and anxiety. More importantly, they were more sensitive to the locomotor suppressant actions of THC compared with wild-type-like (WT) mice. In addition, *Nrg1* HET mice expressed a greater THC-induced enhancement in per cent PPI than WT mice. The effects of THC on anxiety-related behaviour were task dependent, with *Nrg1* HET mice being more susceptible than WT mice to the anxiogenic effects of THC in LD, but not in the EPM, SI and OF tests.

**Conclusions:** *Nrg1* HET mice were more sensitive to the acute effects of THC in an array of different behaviours including those that model symptoms of schizophrenia. It appears that variation in the schizophrenia-related neuregulin 1 gene alters the sensitivity to the behavioural effects of cannabinoids.

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01-02

#### Cannabis and cognitive function: relevant to psychosis

#### N Solowij

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Cognitive impairments are among the most debilitating symptoms of mental illness and most highly predictive of functional outcomes. Cannabis intoxication impairs cognitive processes and there is increasing evidence for longer lasting impairment with long-term or heavy cannabis use. Cognitive dysfunction associated with chronic cannabis use is similar in many respects to the cognitive endophenotypes that have recently been proposed as vulnerability markers of schizophrenia. The prevalence of cannabis use among people with psychotic disorders, the potential for cannabis to trigger psychotic symptoms and episodes, and the neurobiological interactions between the endogenous cannabinoid system and the pathology associated with psychosis indicate a need to further investigate the nature and mechanisms of cognitive impairments associated with cannabis use. The endogenous cannabinoid system plays a significant role in attention, learning and memory in particular, and in mediating

inhibitory and excitatory regulatory mechanisms in the brain. There is evidence that the endocannabinoid system is altered in schizophrenia and accumulating evidence of disturbances in the system associated with exposure to cannabis or cannabinoids. This presentation will summarize what is known about the long-term cognitive effects of cannabis, describing some of the most recent research and its relevance to psychotic disorders.

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01-03

### **fMRI in schizophrenia and cannabis users**

**M Cohen<sup>1,2,4</sup>, V Carr<sup>1,2,4</sup>, PB Ward<sup>3,4</sup>, T Ehlkes<sup>4</sup>, P Johnston<sup>2,4</sup>, R Thienel<sup>4</sup>, U Schall<sup>1,2,4</sup>**

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**Background:** The cerebral activation changes associated with the overlapping cognitive features of cannabis use and schizophrenia have not been systematically studied. The Tower of London Task (TOL) was used to assess functional brain activation in these two groups and in comorbid first-episode schizophrenia and cannabis users.

**Methods:** Event-related functional magnetic resonance imaging measured cerebral activation during the TOL task in 12 patients with first-episode schizophrenia, 17 recently abstinent long-term cannabis users, 7 recently abstinent cannabis using patients with schizophrenia and 17 healthy subjects. A two-stage random-effects analysis was used to model the BOLD response to assess cortical activation as a function of increasing task difficulty and to assess for the main effect of each diagnosis.

**Results:** We found prefrontal activation deficits in patients with schizophrenia that overlapped with cannabis users. A statistical trend in the comorbid subjects for reduced BOLD activation in the left superior parietal lobule and prefrontal cortices was observed. The diagnosis of schizophrenia largely accounted for the prefrontal deficit, while a history of heavy cannabis use associated with increased BOLD activation in the visual cortex.

**Conclusions:** There were common deficits in activation of the dorsolateral prefrontal cortex to the most difficult tasks. Ancillary brain regions were recruited, possibly to subserve the demands of complex TOL tasks. The combination of cannabis use and schizophrenia

may exert a synergistic effect on altering frontal lobe recruitment during high-demand cognitive tasks.

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01-04

### **Visual scanpath comparisons between those people with and without comorbid cannabis abuse: the implications for eye movement research in schizophrenia**

**C Loughland<sup>1,2</sup>, K McCabe<sup>1,2</sup>, S Quinn<sup>2</sup>, M Hunter<sup>1,2</sup>, T Lewin<sup>1,3</sup>**

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**Background:** Cannabis use is associated with substantial social cognition impairment, as are illnesses such as schizophrenia. Schizophrenia is also strongly associated with comorbid cannabis use. Studies examining face processing disturbances show that people with schizophrenia display impaired visual scanpath (VS) strategies when viewing face stimuli. No studies to date have examined the impact of cannabis use on VS performance, and whether VS disturbances in schizophrenia are further impaired by comorbid cannabis use. This study examines whether VS disturbances to face stimuli are observed in cannabis users.

**Methods:** The sample consisted of 20 subjects with regular cannabis use and 20 healthy controls. Subjects were screened for psychosis (SCID-N/P). IQ was assessed using the NART and neuropsychological functioning using the RBANS. Personality was assessed using the SPQ and the IPDE. VSs were recorded using a ViewPoint (6.0) eye tracker. Recognition accuracy was recorded concurrently.

**Results:** Preliminary analysis indicates that the two groups did not differ from each other on age, gender, secondary school completion, IQ or neuropsychological functioning. However, cannabis users had significantly higher scores than controls on the SPQ items of odd beliefs/magical thinking and odd speech, but did not differ from each other on VS or facial expression recognition accuracy.

**Conclusions:** These findings suggest that the social cognition disturbances observed in cannabis users may be associated with social cue and personality disturbances rather than disturbances in face perception and processing. The implications for VS research in schizophrenia will be discussed.