

## Symposia

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

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#### 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

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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