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Background: Aspects of cognitive function and schizotypy have been proposed as potential endophenotypes for schizophrenia. It is unknown if the expression of these endophenotypes at the population level is modulated by the genetic variability of candidate susceptibility genes for schizophrenia.

Methods: We examined the potential impact of 19 single nucleotide polymorphisms (SNPs) within five susceptibility genes for schizophrenia (COMT, DTNP1, NRG1, DAOA/G32 and DAAO genes) on cognition and self-rated schizotypy, in a representative population of 2,243 young male military conscripts. Single SNP and haplotype associations were evaluated.

Results: Val carriers of the COMT val 158 met polymorphism, were associated with higher scores on the negative schizotypy factor, and a greater variability of response in attention capacity. DTNP1 SNPs rs2619522 and rs760761 exhibited several single marker associations, the minor alleles being associated with lower attention capacity but also a decrease in positive and paranoid schizotypy scores. DTNP1 haplotype load had borderline associations with non verbal IQ, paranoid schizotypy and sustained attention. For individual NRG1 polymorphisms, isolated but weak signals of association were noted with sustained attention and working memory, but not schizotypy. The risk allele of functional SNP8NRG243177 was associated with reduced spatial working memory capacity. An isolated effect of DAAO haplotype variability was noted on negative and disorganization schizotypy. No convincing association of DAOA/G32 variability was detected.

Conclusion: DTNP1 and val 158 met COMT, and less so NRG1 and DAAO variants, may exert gene-specific modulating effects on schizophrenia endophenotypes at the population level.

S13.05

Neurocognitive deficits in clinical high risk subjects: Relationship to symptoms and disease progression

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Background and Aims: Psychosis is preceded by cognitive and physiological alterations. This may be useful in the risk assessment in subjects with putatively prodromal symptoms, and could contribute to better understand the temporal unfolding of the disease.

Methods: The early recognition and intervention program of the German Research Network on schizophrenia defines early and late prodromal stages according to psychopathological criteria. For concurrent and prospective validation of these risk stages, subjects undergo neurocognitive, electrophysiological and oculomotor assessments of putative vulnerability markers. About 125 early prodromal subjects (defined by the presence of basic symptoms, Klosterkoetter et al. 2001), and 90 late prodromal subjects (defined by attenuated positive symptoms or by brief occurrences of psychotic symptoms) have been assessed at inclusion.

Results: As compared to psychiatrically healthy matched controls, late prodromals have significantly inferior verbal memory, verbal fluency, visual motor skills, and working memory. Impairments are qualitatively similar, but less pronounced in subjects in an early prodromal stage, with deficits of immediate verbal memory, verbal fluency and visuomotor performance being significant. Both groups show reduced auditory startle prepulse inhibition. Impairments are not correlated with depression and general distress scores, and are also largely independent of prodromal and attenuated positive symptoms. In early prodromals, global cognitive performance is related to the occurrence of psychotic symptoms during follow-up. Auditory P 300 is reduced in both prodromal groups, and predicts transitions to psychosis.

Conclusions: Neurocognitive and neurophysiological assessments validate and improve psychopathological risk assessment, and allow to disentangle stable vulnerability markers from indicators of imminent risk.

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S14. SYMPOSIUM: NEUROCOGNITIVE AND CLINICAL EFFECTS OF CANNABINOIDS (Organised by the AEP Section on Neuroimaging)

S14.01

Effects of cannabis on memory and response inhibition

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Background: Cannabis has well established effects on cognitive processing but the neural basis of these is unclear. We used functional neuroimaging to investigate this, focusing on tasks that engaged verbal memory and response inhibition.

Methods: Subjects were 15 healthy males who had used cannabis < 25 times in their lifetime. Each subject was studied on 3 occasions, and was given either THC, CBD or placebo 1 hour prior to scanning, in a double-blind design. The order of drug administration was randomised and there was 1 month between each scanning session. During each session, images were acquired on a 1.5T GE camera while subjects performed a verbal paired associates memory task and a Go/No Go task. The modulatory effects of THC and CBD relative to placebo were examined by comparing activation during each task.

Results: During the encoding phase of the memory task THC attenuated activation in the left temporal cortex compared to placebo. During the go-no go task, THC attenuated activation in the right inferior frontal cortex. Neither of these effects were attributable to differences in behavioural performance, sedation, or intoxication. The severity of psychotic symptoms provoked by THC was a function of its effect on right inferior frontal activation during response inhibition.

Conclusions: The effects of cannabis on verbal memory and motor control may be mediated through the influence of THC on left temporal and right inferior frontal activity, respectively. The induction of psychotic symptoms by cannabis may reflect an effect of THC on right inferior frontal activity.

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