The endocannabinoid system, its role in early psychosis and the influence of cannabis use hereon

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**TC2C**  
**USE OF CANNABIS IN A EAST-LONDON FIRST EPISODE PSYCHOSIS SAMPLE: DATA FROM THE GAP – GENETICS AND PSYCHOSIS – STUDY**

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**Background:** Exposure to cannabis is associated with a risk of developing psychosis. Individual susceptibility depends on age of onset of cannabis abuse and on genotype (Arseneault et al., 2004; Caspi et al., 2005). In the general population cannabis use is associated with lower educational achievement (MacLeod et al., 2004). There are no study addressing this association in individuals with psychosis. In this study we investigate whether early age at first cannabis use is associated with longer and regular use and whether cannabis use predicts level of educational achievement in a first-episode psychotic population.

**Method:** We collected demographic, clinical and cannabis use (age at first use, frequency, length of use) information in a sample of 200 first-episode psychosis patients. All the subjects were recruited as part of the Genetic And Psychosis (GAP) study.

**Results:** 110 (55%) smoked cannabis, eighty-nine were male and 21 female. We collected data on age at first use on seventy subjects, of whom 44 (62.8%) began their use before age 16. The mean age at first use of cannabis was 16.24 years. The mean age of onset of psychosis in the cannabis users group was 2 years earlier (mean 23.2; SD 4.575) than in the non cannabis users group (mean 25.3; SD 7.004), p = 0.014. However there was no significant difference in age of onset between genders. Among those who commenced cannabis use before age 16, the mean length of cannabis use was 9.5 years compared to 5.4 years among those whose use began after 17 years. We had data on frequency of cannabis use on sixty-three subjects. Forty-one began their use before age 16, and of these 33 (70.2%) used cannabis three or more times a week compared to the 14 (29.8%) of those who started after 16 years. Applying a multiple regression, we found that age at first use predicted years of cannabis use (p = 0.008) independent of age of onset of psychosis and showed a trend towards significance for frequency of cannabis use (p = 0.07). We had available data on level of education achieved on 81 patients, 55 (67.9%) male and 26 female (32.1%), mean age: 31.0 yrs, range 19–59 yrs (SD 7.7). Of these 81 cases 54 (66.7%) were cannabis users, with mean age of 29.2 yrs (SD 5.9) and 27 cases (33.3%) were not cannabis users, mean age 34.7 yrs (SD 9.5). Applying linear regression analysis using level of education as the dependent variable and frequency of use as the independent variable we found that frequency of cannabis use predicts level of education achieved (p = 0.03).

**Conclusion:** Early age at first use of cannabis is associated with longer and regular use in patients with their first episode of psychosis. Counterintuitively, our data also show that frequent cannabis use is associated with higher academic achievement in a first episode psychotic population. This is not due to the non-users being of lower age. Further analyses will be conducted to explore this interesting finding.

**TC2D**  
**THE ENDOCANNABINOID SYSTEM, ITS ROLE IN EARLY PSYCHOSIS AND THE INFLUENCE OF CANNABIS USE HEREON**

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The endogenous cannabinoid system has been identified in the late 1980s and represents the target for exogenous cannabinoids like the major psychoactive compound of herbal cannabis, Δ9-Tetrahydrocannabinol. It consists of naturally occurring endocannabinoid lipids (eCBs) – of which anandamide is the first characterized example – and their respective CB1 cannabinoid receptors, which are expressed in brain areas involved in the control of motor functions, cognition and motivation. Activation of cannabinoid CB1 receptors produces intense emotional and cognitive responses, suggesting that dysfunction in the endocannabinoid system may contribute to the pathogenesis of mental disorders.

We examined the role of endocannabinoid signalling in psychotic states by measuring levels of anandamide in cerebrospinal fluid (CSF) and serum of healthy volunteers (n = 84) and various groups of patients suffering from acute psychiatric disorders (n = 180). When compared to controls, the levels of anandamide in CSF were significantly elevated in acute, antipsychotic-naïve, first-episode schizophrenic patients (n = 47) and negatively correlated with psychotic symptoms. This was reversed by the administration of antipsychotics, which antagonize dopamine D2-like receptors (n = 37), but not by those, which preferentially antagonize 5HT 2A receptors (n = 34). In addition, a significant elevation of anandamide was already apparent in a sample of persons clinically at high risk for developing psychosis (prodromal states, n = 27). Furthermore, the levels of anandamide in CSF were found significantly lower in antipsychotic-naïve schizophrenic patients reporting more than 20 times of cannabis use in life when compared to those with no more than 5 times.

In conclusion, our results suggest that anandamide release in the central nervous system (CNS) may serve as an adaptive mechanism countering neurotransmitter abnormalities in acute schizophrenia. They indicate that frequent cannabis exposure may down-regulate CNS anandamide signaling in schizophrenia and thereby further impact the course of the disease.

**TC2E**  
**PSYCHOLOGICAL INTERVENTION FOR CANNABIS MISUSE IN PSYCHOSIS**

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**Introduction:** Rates of cannabis misuse amongst people presenting with recent onset psychosis are high and associated with negative outcomes including increased frequency of relapse. However, treatment for this client group is not well researched and there is a clear need for the development of effective interventions.

**Method:** The outcomes of studies to date will be reviewed. Outcomes will be considered in relation to the contextual issues contributing to treatment challenges.