Cannabis. However, among healthy people who had not used compared with patients who had never or only occasionally used shown to reduce the elevation in anandamide levels in CSF, when Additionally, in patients with schizophrenia, cannabis use was times in a month were assigned to the ‘heavy’ use condition.

Thirty-three individuals were recruited from a database created during previous studies. Seven indexed acute psychotic response to naturally smoked cannabis on the Psychotomimetic States Inventory (PSI). These data were used for correlational analyses for all but three cannabis users who had not participated in the previous study. Non-parametric tests were used throughout because of non-normality of the data.

The whole sample comprised 15 males and 18 females. One-way analysis of variance (ANOVA) showed no significant group differences in age (22.1 years, s.d. = 2.45) or years of education (16.3 years, s.d. = 1.99). There were no significant group differences in the number of regular alcohol users or level of alcohol use. Urine tests revealed the presence of THC in urine of all heavy cannabis users (n = 10/10), all but one light cannabis users (n = 9/10) and no controls (n = 0/13). One heavy cannabis user and one light cannabis user tested positive for MDMA (3,4-methylenedioxyamphetamine).

The number of regular cannabis users and the number of years of cannabis use was not significantly different between the light

The endocannabinoid system is emerging as crucial to many regulatory functions in the brain. The known endocannabinoids are anandamide, 2-arachidonoylglycerol (2-AG), oleoylethanolamide (OEA) and palmitoylethanolamide (PEA). Anandamide levels have been found to be elevated in the cerebrospinal fluid (CSF) of patients with antipsychotic-naive first-break schizophrenic psychosis1,2 and in the initial prodromal states of psychosis.3 This elevation is reversed by treatment with typical, but not atypical, antipsychotics,2 leading to the suggestion that anandamide has an adaptive, if not protective, role in psychosis and has a homeostatic role in controlling, for example, excessive dopamine release.4

Repeated treatment with Δ⁹-tetrahydrocannabinol (THC), the major psychotomimetic compound of cannabis, has been shown to downregulate anandamide signalling in the central nervous system (CNS) of rats (see for example Di Marzo et al.5). Additionally, in patients with schizophrenia, cannabis use was shown to reduce the elevation in anandamide levels in CSF, when compared with patients who had never or only occasionally used cannabis.6 However, among healthy people who had not used cannabis significantly in their lives (<5 occasions in their lifetime) and those who were low-frequency users (<50 occasions in their lifetime) there were no differences in anandamide, suggesting that at least low-level cannabis use does not downregulate endocannabinoid signalling. No previous study had investigated levels of CSF endocannabinoids in heavy cannabis users and how these might relate to differences in the response to cannabis and associated risk of schizophrenia.

The number of regular cannabis users and the number of years of cannabis use were not significantly different between the light

The National Research Ethics Committee for National Health Service research. Participants were compensated £10 per hour (up to £50) for participation in the lumbar puncture procedure.

Participants were asked to abstain from recreational drugs and alcohol for 24 h before testing commenced. Each participant was tested at a single session lasting around 2 h. Urine tests were also administered where available to assess the presence of THC and other substances. Drug use histories were taken and demographic data collected from participants. Lumbar punctures were conducted, with the participants choosing between the lying and sitting position. The needle was inserted in the lumbar 4–5 interspace. An atraumatic Sprotte needle was used to collect CSF. A sample of blood was taken from each participant. Blood samples were centrifuged for 10 min at 500 rpm. Samples were stored at −80°C and then all samples were analysed at the Central Institute of Mental Health, Mannheim, Germany. To quantify fatty acid ethanolamides, 1 ml aliquots from CSF and serum samples were spiked with 25 pmol of [¹⁵N₂]anandamide, [¹⁴C]H₂2-AG, [¹³C]H₂ PEA and [¹⁴C]OEA to resemble the analytes and analyses were conducted by standard procedures reported elsewhere.7,8

Data from a previous study reported elsewhere7 indexed individual’s acute psychotic response to naturally smoked cannabis on the Psychotomimetic States Inventory (PSI). These data were used for correlational analyses for all but three cannabis users who had not participated in the previous study. Non-parametric tests were used throughout because of non-normality of the data.

Thirty-three individuals were recruited from a database created during previous studies.7 Individuals who used cannabis >10 times in a month were assigned to the ‘heavy’ use condition (n = 10), whereas individuals who used cannabis <10 times per month (n = 10) were assigned to the ‘light’ use condition. Controls were a group of 13 non-cannabis-using individuals. All controls had used cannabis less than eight times in their lifetime; two individuals had never used cannabis. All participants were free from any diagnosis of psychopathology or current medical problems according to DSM-IV criteria.8 All participants provided written, witnessed, informed consent. This study was approved by

Summary

Anandamide is a ligand of the endocannabinoid system. Animals show a depletion following repeated Δ⁹-tetrahydrocannabinol (THC) administration but the effect of cannabis use on central nervous system levels of endocannabinoids has not been previously examined in humans. Cerebrospinal fluid (CSF) levels of the endocannabinoids anandamide, 2-arachidonoylglycerol (2-AG) and related lipids were tested in 33 volunteers (20 cannabis users). Lower levels of CSF anandamide and higher levels of 2-AG in serum were observed in frequent compared with infrequent cannabis users. Levels of CSF anandamide were negatively correlated with persisting psychotic symptoms when drug-free. Higher levels of anandamide are associated with a lower risk of psychotic symptoms following cannabis use.

Declaration of interest

None.

Cannabispore fluid anandamide levels, cannabis use and psychotic-like symptoms

Celia J. A. Morgan, Emma Page, Carola Schaefer, Katharine Chatten, Amod Manocha, Sumit Gulati, H. Valerie Curran, Brigitta Brandner and F. Markus Leweke

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Cerebrospinal fluid anandamide levels,
Cerebrospinal fluid anandamide levels across the three groups.
Online supplement

Fig. DS1  Serum 2-arachidonoylglycerol (2-AG) levels across the three groups.
Cerebrospinal fluid anandamide levels, cannabis use and psychotic-like symptoms

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