cases of CIAPP have a distinct phenomenological presentation including equivalent scores of psychosis, marked affective symptoms, lower schizophrenia-typicality, and better performance on some cognitive tasks. Furthermore, CIAPP have reduced connectivity but preserve gamma band power. At the time of discharge, and 4–6 months later, CIAPP cases have fewer residual symptoms. Two cases have relapsed after resuming the consumption of cannabis, supporting a role for cannabis in the expression of psychosis.

Conclusions: If these results are confirmed in a larger sample, it would suggest that CIAPP may represent a distinct subtype of psychotic disorder that has characteristic behavioral, cognitive and psychophysiological features. Longer longitudinal studies are warranted to understand the course and prognosis of CIAPP.

20.2 CANNABINOID 1 RECEPTOR AVAILABILITY AND MEMORY FUNCTION IN FIRST EPISODE PSYCHOSIS: A MULTI-MODAL PET AND FUNCTIONAL MRI IMAGING STUDY

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Background: The neurobiology of memory deficits in psychosis remains poorly understood and unaddressed by current treatments. The cannabinoid 1 receptor (CB1R) modulates memory, and cannabinoids drugs can both induce psychotic symptoms and impair memory encoding. In view of this, we investigated memory and CB1R availability in first episode psychosis (FEP).

Methods: Sixty-eight volunteers (33 FEP and 35 controls) completed the Sternberg working memory paradigm during an fMRI scan. A subset of these volunteers (20 FEP and 20 controls) underwent a [11C]MePEP PET scan to measure CB1R availability in vivo using a full arterial input function. The patients were antipsychotic naïve/ free.

Results: There was a significant main effect of group on CB1R availability (F(3, 40)=4.123, p<0.05), with moderate to large effect size reductions in the patient group in the hippocampus, (Hedge’s g=0.85), anterior cingulate (ACC) (Hedge’s g=0.81) and orbitofrontal cortex (OFC) (Hedge’s g=0.67). Volunteers showed significantly greater BOLD signal in the anterior cingulate cortex during encoding as working memory load demands increased (Pcorr=0.05), consistent with the role of this region in encoding. Relative to healthy volunteers, first episode psychosis patients showed significantly greater functional activation in the anterior cingulate cortex during memory encoding (MN1 coordinates: x=-8, y=44, z=0); T=4.36, Z=3.88, pcorr=0.013; voxel size=92). Mean fMRI activation during encoding positively correlated with CB1R availability in the anterior cingulate (R=0.509, p<0.05).

Conclusions: We show for the first time as far as we are aware in untreated first episode patients that CB1R availability is reduced, and that this is linked to altered cortical activation during memory encoding in patients. These findings are consistent with evidence that CB1R regulate synaptic transmission and plasticity involved in memory and identify the CB1R as a potential therapeutic target.

20.3 DNA METHYLATION PROFILING MIGHT SHED LIGHT ON THE BIOLOGY OF CANNABIS ASSOCIATED PSYCHOSIS

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Background: Epigenetic mechanisms are emerging as potential important players that underlie the interactions between genetic and environmental risk factors in the aetiology of psychiatric disorders. Cannabis is the most widely used recreational drug and its use, with a dose relationship pattern, has consistently been associated with an increased risk to develop Psychotic Disorders. Consistent with animal data, it has been shown that regular cannabis users show higher levels of CB1 mRNA expression and promoter methylation status in peripheral blood cells than non-users. We are the first to investigate if cannabis use leaves a distinct DNA methylation signature across the genome and if this overlaps with biological pathways already associated with Psychotic Disorders.

Methods: Genome-wide DNA methylation (EWAS) profiling using the Illumina Infinum MethylationEPIC array in human peripheral blood tissue from 413 First episode Psychosis and 521 healthy population controls part of the EUGEI (European network of national schizophrenia networks studying Gene-Environment Interactions) study. Samples were randomized with respect to phenotypic status, age, sex and study site to avoid batch effects.

Stringent QC pipeline checks (i.e. signal intensity, duplicates, sex, bisulphite conversion, genotypes) with cross-reactive and non-reliable probes removed. Our analyses focused on probes with a minimum range of methylation values of 5% within the middle 80% of samples, resulting in 618,048 probes5.

Covariates: 1) tobacco smoking score; 2) age; 3) cell type proportions and 4) study sites

Linear model was used to compare across the DNA methylation profiling of a) Lifetime cannabis users (YES) and b) daily cannabis users with never users.

Results: Our preliminary analyses revealed regular cannabis use-associated dysregulation of DNA methylation at multiple loci across the epigenome that also include CpGs previously associated with Schizophrenia. Downstream pathway analysis revealed enrichment of genomic regions that are highly disease relevant.

Conclusions: Our preliminary findings in a sample of healthy controls suggest:

Difference in DNA Methylation profiling between individuals who have tried cannabis at some point in their life and more significantly so in daily users compared to never users; 2) these differences were detected taking into account important confounders including the epigenetic tobacco scoring.

Most of these DMS are in protein coding genes including BDNF, SHANK2 and CACNA2D2, which are involved in important neurodevelopmental processes. BDNF and CACNA2D2 have also been indicated as susceptibility genes for Schizophrenia and Bipolar Disorders.

Finally, our pathway analysis indicated significant enrichment for these DMs in pathways involved in biological processing such as neuronal migration and development and glutamate receptor binding, a possible hint towards the unravelling of the biology linking adolescence cannabis use with psychosis.

20.4 EXAMINING THE ASSOCIATION BETWEEN CANNABIS USE AND PSYCHOSIS ACROSS THE SPECTRA OF EXPOSURE AND PHENOTYPE

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