

S92. REASONS TO START SMOKING CANNABIS: A CASE CONTROL-ANALYSIS FROM THE EUGEI STUDY

Edoardo Spinazzola^{*1}, Victoria Rodriguez², Diego Quattrone³, Giulia Trotta², Marta Di Forti³, Robin Murray²

¹King's College London, IoPPN; ²Institute of Psychiatry, Psychology & Neuroscience, King's College London; ³SGDP, Institute of Psychiatry, Psychology and Neuroscience, King's College London

Background: Studies have shown that cannabis can increase the risk of psychosis from 1.7 to 3.9 times. Both frequency and potency seem to contribute to differences in the incidence of psychosis across Europe. Despite this evidence, sceptics argue that the association between cannabis use and psychotic disorders could be explained by: (a) subjects who start experiencing psychosis use cannabis as a form of self-medication; (b) the co-morbid effect of other psychotogenic drugs (e.g., amphetamines); or (c) there is a common genetic vulnerability between cannabis use and psychosis. Thus, we aim to analyse: 1) reported reasons to start using cannabis, 2) if these predict differences in patterns of use (frequency and potency), 3) the association of both reasons to start and pattern of use with PRS for Schizophrenia, as it can explain whether patients with a higher genetic burden also start smoking cannabis after experiencing a higher psychological discomfort.

Methods: Using data from the multicentric EUGEI First-Episode Psychosis (FEP) case-control study we examined differences in reasons to start using cannabis between cases and controls. Data were obtained from the Cannabis Experiences Questionnaire modified version. Logistic regression models were used to test if reason to start predicted different patterns of use. Finally, we used regression to test if Polygenic risk scores for schizophrenia (SZ PRS) explained variance in reasons to start.

Results: Up to 85% of controls compared to 68% of FEP started using cannabis because either friends or family were using it. Instead, 18% of cases started using cannabis to feel better compared 5% of controls, reporting the 13.4% of cases and 10.3% of controls having start due to "other reasons". Regression models showed that being a case was positively associated with starting use in order to feel better (RRR 4.67, $z=7.58$, $p<0.001$), remaining significant after adjusting for gender, age, ethnicity or site. We did not find evidence of an association between start using cannabis "to feel better" and potency nor in cases or controls. We found an association for both cases and controls between those who started smoking to feel better and the frequency of use following a gradient from "more than once a week" to "daily". Using cannabis "to feel better" was associated with a 4 times increase in the risk (RRR=4.45 95% CI 1.85 – 10.72) of using it daily in controls and 3 times increase (RRR= 3.11 95% CI 1.81 – 5.35) in FEP. Multinomial regression showed that reasons to start did not change according to Schizophrenia PRS, with those starting because a family member was using cannabis (RRR = 1.05 95% CI 0.38 – 2.62) and those starting to feel better (RRR = 1.05 95% CI 0.47 – 2.33) not being at higher polygenic risk compared with those starting because their friends were using cannabis.

Discussion: These preliminary findings show that a higher proportion of patients with psychosis than controls start using cannabis as a way to make them feel better, although they are a minority. Furthermore, both cases and controls that started smoking "to feel better" presented higher chances to start smoking more frequently. Lastly, PRS did not predict the reasons to start smoking cannabis.

S93. ADHD SYMPTOMS AND DAILY SMOKING AT AGE 15–16 YEARS AND PSYCHOTIC DISORDER IN EARLY ADULTHOOD. FINDINGS FROM THE NORTHERN FINLAND BIRTH COHORT 1986 STUDY

Solja Niemelä^{*1}, Teemu Peltonen², Jari Koskela¹, Antti Mustonen³, Jouko Miettunen⁴, Tuula Hurtig³

¹University of Turku, Finland; ²City of Helsinki, Finland; ³University of Oulu, Finland; ⁴Center for Life Course Health Research, University of Oulu, Finland

Background: Association between smoking with both ADHD(1) and psychosis(2) has been explained by self-medication of ADHD and psychotic symptoms with nicotine use(3). Persons with psychosis also share impairments with persons with ADHD: e.g. inattention is a feature of both of these disorders(3).

Aim of this study was to investigate the association between ADHD symptoms and adolescent smoking in relation to psychotic disorder in young adulthood.

Methods: The Northern Finland Birth Cohort 1986 Study includes 99% of all births ($n=9432$) in the region. Participants with information on ADHD symptoms and daily smoking at age 15–16 years were included ($n=5858$, 48.7% male, 62.1% of the original study population). ADHD symptoms were evaluated by parents, who filled in the Strengths and Weaknesses of ADHD Symptoms and Normal Behaviors (SWAN) questionnaire. SWAN comprises ADHD symptoms (inattention, hyperactive-impulsive, combined) rated from 3 (far below average) to -3 (far above average). Information on psychiatric diagnoses was collected from four national registries until the end of year 2016. Associations between daily smoking and ADHD symptoms were analyzed using multiple linear regression. Sex, family structure, frequent alcohol intoxication, illicit drug use, and psychotic experiences at age 15–16 years were used as covariates. Analyses were done separately according to the psychiatric diagnosis status at age 30–31 years: no psychiatric diagnosis; any psychiatric diagnosis other than psychosis; any psychotic disorder.

Results: Among participants with psychotic disorder ($n=119$), daily smokers had higher inattention mean scores compared to non-smokers (-6.5 vs. 0.03, p -value=0.001, effect size (es)=0.8). Among those without psychiatric disorders ($n=4618$), daily smokers had higher scores in all SWAN domains compared to non-smokers: inattention (-8.9 vs. -3.6, p -value<0.001, es =0.6); hyperactive-impulsive (-13.3 vs. -8.8, p <0.001, es =0.5); and combined (-22.2 vs. -12.5, p <0.001, es =0.6). Respectively, also daily smokers with any psychiatric disorder other than psychosis ($n=1121$) had higher scores in all SWAN domains: inattention (-7.0 vs. -2.1, p <0.001, es =0.5); hyperactive-impulsive (-11.6 vs. -7.0, p <0.001, es =0.5); and combined (-18.6 vs. 9.1, p <0.001, es =0.5). Within psychosis group, daily smoking associated only with inattention symptoms (standardized beta-coefficient (sbc)=0.38 p =0.004) in the multiple linear regression. Among those without psychiatric disorders, and among those with psychiatric disorders other than psychosis, daily smoking associated with all SWAN symptom domains. The respective figures were for inattention (sbc =0.14, p <0.001; sbc =0.12, p =0.001); for hyperactive-impulsive (sbc =0.11, p <0.001; sbc =0.12, p =0.001); and for combined (sbc =0.14, p <0.001; sbc =0.13, p <0.001).

Discussion: In adolescence, the relationship between inattention problems and daily smoking was remarkable among participants with subsequent psychotic disorder. Vulnerability to smoking among adolescents at risk for psychosis may be explained by self-medication related to inattention problems.

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S94. PREDICTION OF CANNABIS RELAPSE IN CLINICAL HIGH-RISK INDIVIDUALS AND RECENT ONSET PSYCHOSIS - PRELIMINARY RESULTS FROM THE PRONIA STUDY

Nora Penzel^{*1}, Rachele Sanfelici¹, Linda Betz², Linda Antonucci³, Peter Falkai¹, Rachel Uptegrove⁴, Alessandro Bertolino⁵, Stefan

Borgwardt⁶, Paolo Brambilla⁷, Rebekka Lencer⁸, Eva Meisenzahl⁹, Stephan Ruhrmann², Raimo K.R. Salokangas¹⁰, Christos Pantelis¹¹, Frauke Schultze-Lutter⁹, Stephen Wood¹², Nikolaos Koutsouleris¹, Joseph Kambeitz², ... the PRONIA group¹³

¹Ludwig Maximilian University, Munich; ²Faculty of Medicine and University Hospital of Cologne, University of Cologne, Germany;

³University of Bari Aldo Moro, Italy; ⁴University of Birmingham, UK; ⁵University of Bari; ⁶University of Basel, University of Lübeck; ⁷University of Milan, Milan, Italy; ⁸University of Muenster; ⁹Heinrich-Heine University Düsseldorf; ¹⁰University of Turku, Finland; ¹¹Melbourne Neuropsychiatry Centre, University of Melbourne, Australia; ¹²Orygen, the National Centre of Excellence in Youth Mental Health; ¹³EU Consortium

Background: Evidence exists that cannabis consumption is associated with the development of psychosis. Further, continued cannabis use in individuals with recent onset psychosis (ROP) increases the risk for rehospitalization, high symptom severity and low general functioning. Clear inter-individual differences in the vulnerability to the harmful effects of the drug have been pointed out. These findings emphasize the importance of investigating the inter-individual variability in the role of cannabis use in ROP and to understand how cannabis use relates to subclinical conditions that predate the full-blown disease in clinical high-risk (CHR). Specific symptoms have been linked with continued cannabis consume, still research is lacking on how different factors contribute together to an elevated risk of cannabis relapse. Multivariate techniques have the capacity to extract complex patterns from high dimensional data and apply generalized rules to unseen cases. The aim of the study is therefore to assess the predictability of cannabis relapse in ROP and CHR by applying machine learning to clinical and environmental data.

Methods: All participants were recruited within the multi-site, longitudinal PRONIA study (www.pronia.eu). 112 individuals (58 ROP and 54 CHR) from 8 different European research centres reported lifetime cannabis consume at baseline and were abstinent for at least 4 weeks. We defined cannabis relapse as any cannabis consume between baseline and 9 months follow-up reported by the individual. To predict cannabis relapse, we trained a random forest algorithm implemented in the mlr package, R version 3.5.2. on 183 baseline variables including clinical symptoms, general functioning, demographics and consume patterns within a repeated-nested cross-validation framework. The data underwent pre-processing through pruning of non-informative variables and median-imputation for missing values. The number of trees was set to 500, while the number of nodes, sample fraction and mtry were optimized. All hyperparameters were tuned with the model-based optimization implemented in the mlrMBO R package.

Results: After 9 months 50 individuals (48 % ROP, 52 % CHR) have relapsed on cannabis use. Relapse was over all timepoints associated with more severe psychotic symptoms measured by PANSS positive and PANSS general ($p < 0.05$) and a significant interaction between positive symptoms and time of measurement ($p < 0.05$). Our random forest classifier could predict cannabis relapse with a balanced accuracy, sensitivity, and specificity of, respectively, 66.5 %, 66.0 % and 67.0 %. The most predictive variables were a higher cumulative frequency of cannabis consumption in the last 3 months, worse general functioning in the last month, higher density of place of living, younger age and a shorter interval time since the last consumption.

Discussion: Our results using a state-of-the-art machine learning approach suggest that the multivariate signature of baseline demographic and clinical data could predict follow up cannabis relapse above chance level in CHR and ROP. Our findings revealing that cannabis relapse is associated with more severe symptoms is in line with previous literature and emphasizes the need for targeted treatment towards abstinence from cannabis. The information of demographic and clinical patterns might be useful in order to specifically address therapeutic strategies in individuals at higher risk for relapse. This might include special programs for younger patients and taking

into account the place of living, like urban areas. Further research is needed in order to validate our model in an independent sample.

S95. DIFFERENCES IN LIFETIME PATTERNS OF PSYCHOSTIMULANTS AND THEIR IMPACT ON THE PROPORTION OF PATIENTS WITH FIRST-EPISODE PSYCHOSIS ATTRIBUTABLE TO PSYCHOSTIMULANTS USE ACROSS EUROPE

Manuel Duran-Cutilla^{*1}, Elisa Rodríguez Toscano¹, David Fraguas², Gonzalo Lopez¹, Marta Rapado-Castro¹, Laura Roldan¹, Teresa Sanchez-Gutierrez³, Ana Calvo⁴, Covadonga Martinez-Caneja¹, Celso Arango¹

¹Institute of Psychiatry and Mental Health, Hospital General Universitario Gregorio Marañón, School of Medicine, Universidad Complutense, IISGM, CIBERSAM, Spain.; ²Hospital General Universitario Gregorio Marañón, IISGM, CIBERSAM; ³Faculty of Health Sciences, Universidad Internacional de La Rioja (UNIR); ⁴Faculty of Health Sciences, Universidad Internacional de La Rioja

Background: Substance use may be a risk factor for the onset of schizophrenia. Almost 50 % of people with first episode psychosis (FEP) have a history of cannabis or alcohol use. Smaller but significant proportions of this population have a history of psychostimulants (PS) use. Cross-sectional studies have shown a link between recreational and regular use of PS and psychotic symptoms, particularly among individuals with PS dependence, that usually revert after drug withdrawal. Nevertheless, some PS users suffer not just spontaneous relapse of the symptoms but also persistent psychosis in the absence of the drug. European data are not available for a large sample of the prevalence of consumption and its relation to the severity of symptoms in FEP. For this purpose, we described the differences in patterns of use of PS current and lifetime between FEP and healthy controls (HC) and their impact on the severity of the clinical symptomatology.

Methods: This analysis is based on data from the case-control study work package of the EUropean network of national schizophrenia networks studying Gene-Environment Interactions (EU-GEI), which took part between 2010 and 2015 across six countries.

901 FEP patients (M age=30.76, SD= 10.51; 38.1% females) and 1235 HC (M=36.15, SD=13.30; 53% females) were included in the present case-control study. Data related to amphetamine use were obtained through CEQUEU-GEI. To assess psychopathology the OPERational CRITeria (OPCRIT) system was used.

Group comparisons were made using t-test or Chi square, and ANCOVA or logistic regression controlling for age, sex and cannabis use when appropriate.

Results: FEP subjects displayed a trend for higher use of PS in the last year ($B = -0.18$, $p = 0.055$: 81 (9%) FEP and 56 (4.5%)) and a significant higher lifetime use ($\chi^2 = 37.33$, $p < 0.001$: 196 (21.8%) FEP and 149 (12.1%) HC) than HC, but the frequency of PS use did not differ between groups.

Lifetime FEP PS-users showed higher scores, thus is, more severe symptoms in the Mania ($t = -3.69$, $p < 0.001$) and the general ($t = -3.47$, $p = 0.001$) factors compared to FEP non-PS-users. Current FEP PS-users showed higher scores in the Mania factor ($t = -2.52$, $p = 0.012$) than FEP non-PS-users. However, these results were not significant when the comparisons were adjusted for age, sex and cannabis use. FEP PS-users displayed lower scores than the non-users in the negative factor both in the last year ($t = 2.10$, $p = 0.038$ and: $F_{1,866} = 4.27$, $p = 0.039$ when adjusted for age, sex and cannabis use) and lifetime ($t = 1.99$, $p = 0.046$ and $F_{1,869} = 1.37$, $p = 0.243$ when adjusted for age, sex and cannabis use).

Discussion: As previous studies, we confirmed the higher rates of PS use in FEP than HC in a European study with a big sample. PS use was related to severity of clinical symptomatology. PS-users presented more severe general symptoms and, specifically, in the mania factor. Otherwise, FEP non-PS-user showed higher scores in the negative factor which might be related to the usual course of the psychosis without exposure to PS use.