Effect of D2R, NMDAR and CB1R genetic variants associated with cannabis use and childhood trauma in first-episode psychosis in a Brazilian population [abstract only]

LOUREIRO, C.M. <http://orcid.org/0000-0002-0239-5064>, CORSI-ZUELLI, F., FACHIM, H.A., SHUHAMA, R., MENEZES, P.R., DALTON, C.F., LOUZADA-JUNIOR, P., BELANGERO, S.I.N., COELI-LACCHINI, F.B., REYNOLDS, G.P., LACCHINI, R. and DEL-BEN, C.M.

Published version

LOUREIRO, C.M., CORSI-ZUELLI, F., FACHIM, H.A., SHUHAMA, R., MENEZES, P.R., DALTON, C.F., LOUZADA-JUNIOR, P., BELANGERO, S.I.N., COELI-LACCHINI, F.B., REYNOLDS, G.P., LACCHINI, R. and DEL-BEN, C.M. (2023). Effect of D2R, NMDAR and CB1R genetic variants associated with cannabis use and childhood trauma in first-episode psychosis in a Brazilian population [abstract only]. European Psychiatry, 66 (S1), S255-S255.

pathways' homeostasis) leading to an over-expression of pro-inflammatory cytokines. However, despite a higher prevalence of cannabis (THC) consumption in patients with psychosis, few studies have investigated the impact of this use on inflammatory markers.
Objectives: The objective of this study was to investigate the impact of cannabis use and its withdrawal on inflammatory markers in patients with psychosis and to explore the link between these inflammatory markers and clinical symptoms.
Methods: A retrospective study was performed including 102 patients with psychosis. White blood cell, hsCRP and fibrinogen levels were measured at baseline and after 4 weeks of cannabis cessation. Urinary THC was also measured at baseline and after 4 weeks of cannabis cessation. Comparisons, adjusted on age, gender, body mass index, smoking status and diagnosis, were performed between cannabis users (THC+) and cannabis nonusers (THC-). To assess the association between inflammatory markers and sociodemographic or PANSS scores, Spearman or Pearson correlations were computed.
Results: After cannabis cessation, a greater increase of leucocyte levels ($p < 0.01$), monocyte levels ($p = 0.05$) and a statistical trend to a higher increase of lymphocyte levels ($p = 0.06$) were found in the consumer group compared to the nonuser group. After 4 weeks of cannabis cessation, higher leucocyte ($p = 0.03$), lymphocyte ($p = 0.04$) and monocyte ($p < 0.01$) counts were found in the THC+ group whereas at baseline no difference was found. A positive correlation was found between monocyte count at 4 weeks and baseline PANSS negative subscore ($p = 0.045$) and between the variation of monocyte count between baseline and 4 weeks and the PANSS total score at 4 weeks ($p = 0.05$).
Conclusions: This study shows that cannabis cessation is associated with an increased inflammation depicted by an elevation of white blood cell, lymphocyte, and monocyte levels, which correlates with symptomatology of patients with psychosis. Studying the link between cannabis and inflammation could lead to a better understanding of the pathophysiology of psychosis.

Disclosure of Interest: B. Romeo: None Declared, V. Lestra: None Declared, C. Martelli: None Declared, A. Amirouche: None Declared, A. Benyamina Consultant of: Lundbeck, Mylan, Merck-Serono and Bristol-Myers Squibb , Speakers bureau of: member of board Indivior, N. Hamdani: None Declared

EPP0260

Effect of D2R, NMDAR and CB1R genetic variants associated with cannabis use and childhood trauma in first-episode psychosis in a Brazilian population

C. M. Loureiro[1,2]*, F. Corsi-Zuelli[1], H. A. Fachim[3], R. Shuhama[1,2], P. R. Menezes[2,4], C. F. Dalton[5], P. Louzada-Junior[6], S. I. N. Belangero[7], F. B. Coeli-Lacchini[6], G. P. Reynolds[5], R. Lacchini[8] and C. M. Del-Ben[1,2]

[1]Neuroscience and Behavior, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto; [2]Population Mental Health Research Centre, São Paulo, Brazil; [3]University of Manchester, Manchester, United Kingdom; [4]Preventive Medicine, University of São Paulo, São Paulo, Brazil; [5]Biomolecular Sciences Research Centre, Sheffield Hallam University, Sheffield, United Kingdom; [6]Internal Medicine, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto; [7]Morphology and Genetics, Universidade Federal de São Paulo, São Paulo and [8]Ribeirao Preto College of Nursing, University of São Paulo, Ribeirão Preto, Brazil
*Corresponding author.
doi: 10.1192/j.eurpsy.2023.584

Introduction: Gene-environment interactions increase psychosis risk (Gayer-Anderson *et al.* Soc Psychiatry Psychiatr Epidemiol 2020; 55(5):645-657). However, identifying the genetic variants involved and how they interact with environmental risk factors underlying psychosis remains challenging.
Objectives: To investigate whether there are gene-environment interactions in the relationships of childhood trauma, lifetime cannabis use, and single nucleotide variants (SNVs) of dopamine D2 receptor (D2R: *DRD2*), N-methyl-d-aspartate receptor (NMDAR: *GRIN1*, *GRIN2A* and *GRIN2B*) and cannabinoid receptor type 1 (CB1R: *CNR1*) with psychosis.
Methods: In a population-based case-control study nested in an incident study (STREAM, Brazil) (Del-Ben *et al.* Br J of Psychiatry 2019; 215(6):726-729), part of the EU-GEI consortium (Gayer-Anderson *et al.* Soc Psychiatry Psychiatr Epidemiol 2020; 55 (5):645-657), 143 first-episode psychosis patients and 286 community-based controls of both sexes aged between 16 and 64 years were included over a period of 3 years. Twenty-three SNVs of D2R (rs1799978, rs7131056, rs6275), NMDAR (*GRIN1*: rs4880213, rs11146020; *GRIN2A*: rs1420040, rs11866328; *GRIN2B*: rs890, rs2098469, rs7298664), and CB1R genes (*CNR1*: rs806380, rs806379, rs1049353, rs6454674, rs1535255, rs2023239, rs12720071, rs6928499, rs806374, rs7766029, rs806378, rs10485170, rs9450898), were genotyped from peripheral blood DNA using a custom Illumina HumanCoreExome-24 BeadChip. Environmental adversities were evaluated using the Cannabis Experience Questionnaire (Di Forti et al. The Lancet Psychiatry 2009; 6(5):427–436) and the Childhood Trauma Questionnaire (Grassi-Oliveira et al. Rev Saude Publica 2006; 40(2):249-55). Associations between SNVs and environmental risk factors were performed using the nonparametric multifactor dimensionality reduction software (version 3.0.2).
Results: Single locus analysis showed no association among the 23 SNVs with psychosis; however, gene-environment analysis was significant for the polymorphic loci rs12720071 and rs7766029 in *CNR1*. The best association models were the two-factor representing by the combination of *CNR1* rs12720071 with lifetime cannabis use ($p<0.001$), and *CNR1* rs12720071 with childhood trauma ($p<0.05$), both suggesting an increased risk of psychosis. Additionally, when considering the interaction of both environmental factors in the same model, we found *CNR1* rs7766029 to be associated with psychosis ($p<0.001$).
Conclusions: Our study supports the hypothesis of gene-environment interactions for psychosis involving the T allele carriers of *CNR1* SNVs (rs12720071 and rs7766029), childhood trauma and lifetime cannabis use in psychosis.

Disclosure of Interest: None Declared