Polygenic risk scores and substance abuse comorbidity in patients with schizophrenia and bipolar disorders

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Introduction

Cannabis is the most widely used illicit drug in the world. It is well established that substance abuse comorbidity i.a. cannabis use is much higher among patients with schizophrenia (SCZ) and bipolar disorders (BD) than in the general population. However, the relationship between SCZ, BD and cannabis use might be more complicated than it initially seems. Previous studies have revealed that a genetic predisposition to SCZ might be associated with increased use of cannabis in healthy individuals. Given this relationship, we intended to study whether polygenic risk scores (PRS) for SCZ predict cannabis use in patients with SCZ and BD. In addition we want to test whether cannabis PRS have an impact on cannabis use in these two subgroups.

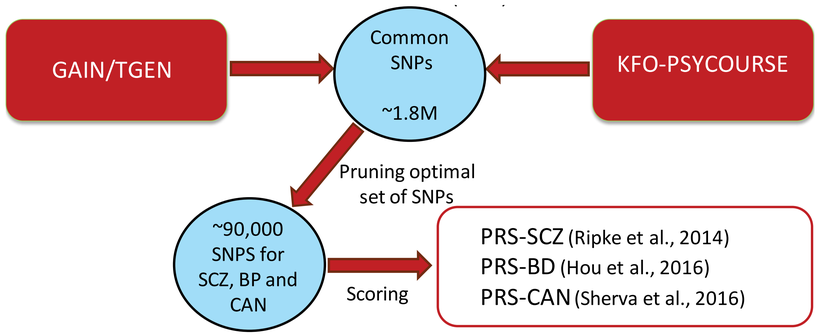
Methods

In the GAIN/TGEN sample of BD patients (N= 1.150):

1. We tested whether SCZ PRS predicts cannabis use in patients with BD
2. We tested whether BD PRS predicts cannabis use in patients with BD
3. We tested whether cannabis use PRS calculated according to a recent GWAS from the International Cannabis Consortium (ICC) explains cannabis use in patients with BD in our cohort
4. We tested the replicability of our results in an independent sample from the KFO/PsyCourse N=630 individuals (N= 367 SCZ, and N= 263 BD)

PRS analysis as regards *cannabis use ever vs. never*

- GAIN/TGEN and KFO-PsyCourse samples analyzed
- GAIN/TGEN sample best-guess genotypes (~2M)
- KFO-PsyCourse sample dosage genotypes (~7M)



- Logistic regression analysis: PRS(s) as independent variable(s)
- Covariates: age, sex, age2, sex*age, 10 principal components population structure
- Pseudo-Nagelkerke R2, as a measure of effect size.

Results

1. GAIN/TGEN sample: SCZ PRS showed positive associations for “use” versus “never use” of cannabis in BD over most of the P-value thresholds. The best estimate shows an R2 around 1%.
2. KFO/PsyCourse sample: This finding replicated in an independent sample of BD patients, where higher PRS were also associated with a higher probability of cannabis use.
3. No association was found in the same analyses for SCZ patients. Further, no association was found in none of the samples in the analyses based on BD PRS and cannabis PRS PRS.

Conclusion

First results suggest that individuals with BD and an increased polygenic risk for SCZ are more likely to use cannabis. The association between BD and cannabis use might be not simply one of an environmental risk factor, but rather involves gene–environment interaction, as individuals choose and shape their own environment according on their own innate preferences.

Acknowledgements

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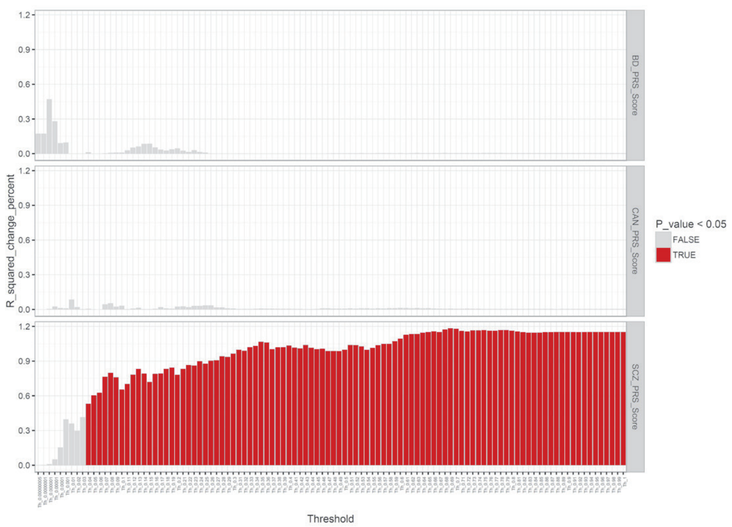
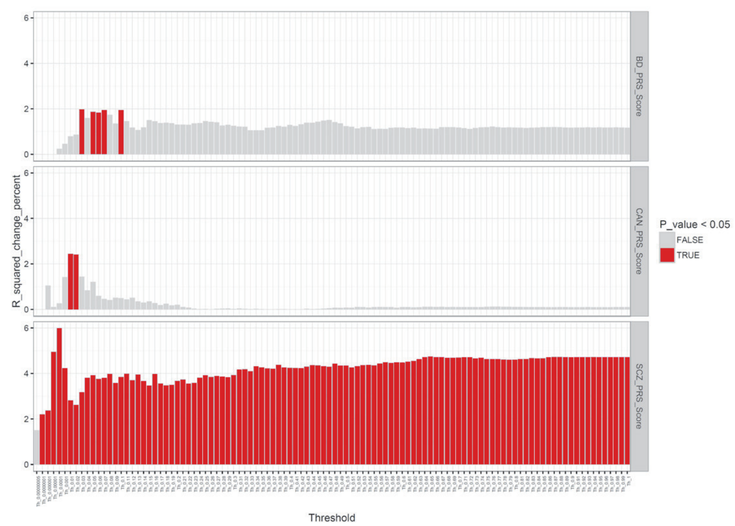
Effects of SCz, BD and cannabis PRS in GAIN/TGEN sample (BIP)



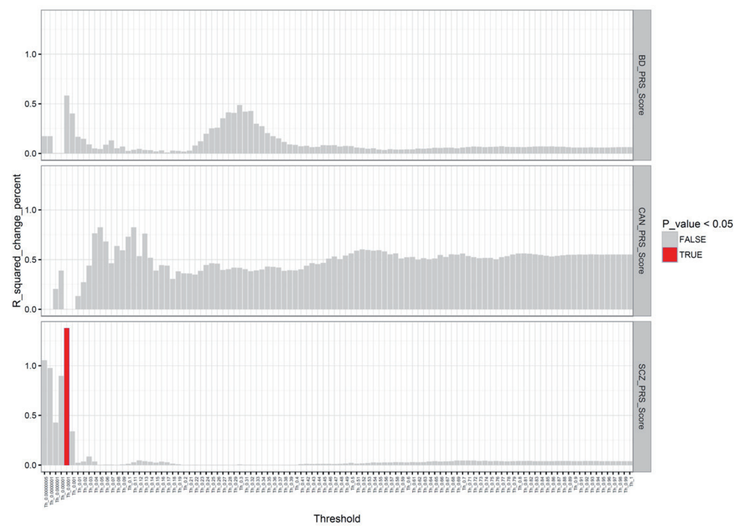
SCZ-PRS consistently higher in those subjects who ever tried cannabis over all thresholds

Effects of SCz, BD and cannabis PRS in KFO-BIP sample



SCZ-PRS consistently higher in those subjects who ever tried cannabis over all thresholds

Effects of SCz, BD and cannabis PRS in KFO-SCZ sample



No effect in the SCZ sample