Prediction of cannabis use disorder severity from genetic and behavioral data

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Team Interactions / Meetings
We have had multiple in-person and online team meetings:

Online	In-person
Mar. 7, 2017 – Ariel, Milind, Shikha	Mar. 9, 2017 – Ariel, Shikha
Mar. 16, 2017 – Ariel, Milind, Shikha	May 19, 2017 – Ariel, Shikha
May 12, 2017 – Ariel, Milind, Shikha	Sep. 14, 2017 – Ariel, Shikha
Aug. 29, 2017 – Ariel, Milind, Shikha	May 10, 2018 – Ariel, Milind, Shikha
Jan 5, 2018 - Ariel, Milind, Shikha	May 11, 2018 – Ariel, Milind, Shikha
Feb. 8, 2018 – Ariel, Milind, Shikha	May 12, 2018 – Ariel, Milind, Shikha
May 2, 2018 – Ariel, Milind, Shikha	
Aug 27, 2018 – Ariel, Milind, Shikha	

We have also had numerous online chat interactions.

Project Overview
Background: Problematic cannabis use, or cannabis use disorder (CUD) occurs in approximately 10% of cannabis users. With the shifting legal landscape and widespread public opinion that cannabis is "safe", the number of individuals with cannabis use disorder is likely to increase. As such, researchers need more accurate and more precise tools to identify risk factors for CUD. One tool that holds promise for characterizing the breadth and depth of susceptibility-factors for cannabis use disorder is genetics: genetic variability and alleles that encode it may help quantify susceptibility in cannabis users. However, exploratory genetic analyses require large sample sizes to overcome the volume and complexity of genetic variability. One common approach, the Multilocus genetic profile (MLGP) method, attempts to consider risk alleles for a disease as composite. MLGP scores infer the additive effect of these multiple alleles, but (1) these scores do not reflect allele interactions, and (2) multiple-comparison correction becomes prohibitive with a large, and therefore more likely phenotypically representative number of alleles in the model. Thus, our aim was to identify and apply a more sophisticated analysis method to overcome these challenges. With such a method, we aimed to identify risk alleles associated with CUD, that would allow us to develop a MLGP score using relatively small sample sizes (despite the curse of dimensionality) while accounting for interactions between alleles.
Methods: To achieve this, we employed the least absolute shrinkage and selection operator (LASSO) technique on GWAS data from 235 cannabis users and assessed their cannabis use-related problems (Marijuana Problems Scale; MPS), which closely mirrors CUD symptomatology as outlined in the Diagnostic Statistical Manual 5 (DSM-5) for Psychiatric Disorders. We began with a hypothesis-driven, literature-based approach to reduce the number of total SNPs to only those with a previous association with CUD. We optimized the LASSO algorithm with MPS score predictors for each SNP and interactions between SNPs as features.
Results: This method identified SNPs and allele interactions that contributed to the prediction of CUD severity. The number of risk alleles for each SNP correlated with MPS scores and subjective craving.
Conclusion: This method may serve as a powerful tool for identifying alleles and combinations thereof that contribute to CUD. As such, it could greatly benefit MLGP development to identify susceptible

cannabis users. This will facilitate better diagnostic criteria for, and biological understanding of, CUD in conjunction with the goals of the Research Domain Criteria.

Research Progress
We presented our project as a poster presentation at the Society of Biological Psychiatry Annual Meeting in New York in May 2018 (Abstract: https://www.sciencedirect.com/science/article/pii/S0006322318309867)

We received valuable feedback and positive comments for our poster at the conference. We are currently finalizing analyses (particularly the interactions between SNPs), and drafting a manuscript for publication.

List of presentations, posters, conferences, publications
- Presentation at the CSoI Annual Meeting in December 2016
- Presentation at the CSoI Virtual Brown Bag Series on March 16, 2017.
- Presentation at the Society of Biological Psychiatry Annual Meeting in May 2018.

Remaining Budget
Spent: $4041.20 for expenses related to attending the annual meeting of the Society of Biological Psychiatry.

Item	**Paid by**	**Amount**
Initial Budget	CSoI	6,000.00
Abstract Submission for the annual meeting of the Society of Biological Psychiatry	Ariel	40.00
Conference-related expenses - Shikha Prashad	Shikha	905.18
Conference-related expenses - Ariel Ketcherside	Ariel	2131.99
Conference-related expenses - Milind Rao	Milind	964.03
Total Spent		4041.20
Remaining		1958.80

We plan to spend the remaining balance toward publications costs for the manuscript.

Acknowledgements:
We are immensely grateful for the support from the National Science foundation, for allowing this project to develop. We would like to thank Brent Ladd, Robynne McCormick, and Kiya Smith for their continued support in the coordination of this project. We would like to thank our advisor, Dr. Francesca M. Filbey, for the use of her data and advice on project development, and our advisor Dr. Andrea Goldsmith, for her statistical input and support.