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2020

GABRA2 and Alcohol Dependence in College-Aged Students

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African ancestry.

GABA2 and Alcohol Dependence in College-aged Students
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Introduction
Alcohol dependence is uncontrolled alcohol consumption despite consequences.
• Alcohol dependence defined in DSM-IV based on seven criteria such as tolerance and withdrawal.

GABRA2 encodes for the α2 subunit which is one of five subunits that make up the GABA_A receptor.
• GABA binds to the GABA_A; GABA is an inhibitory neurotransmitter that reduces neuronal activity (Roh et al., 2010).

Genetic variants (single-nucleotide polymorphisms) in the gene GABRA2 have been shown to be associated with alcohol dependence in older adults (Trucco et al., 2014).
• The association is not studied nearly enough in the college-aged population, a high-risk period for the development of alcohol-related problems.

This study uses longitudinal survey as well as genetic data, from Spit4Science, to focus on this association between alcohol dependence and the GABRA2 gene.

Past literature emphasized that GABRA2 shows association with alcohol dependence, so it will be hypothesized that GABRA2 is associated with alcohol dependence symptoms in college-aged students, specifically those in European and African ancestry.

Methods
- Data was taken from Spit4Science, a longitudinal study at VCU.
  - Surveyed during freshman spring semester
  - The Spit4Science survey asked about 7 questions related to alcohol dependence; if individuals fit 3 or more of the criteria from DSM-IV, they were classified as alcohol dependent.
  - Participants who reported never having a drink of alcohol were set to missing.
  - Saliva samples were collected and DNA extracted
  - Affymetrix biobank array utilized to genotype individuals
  - 8 SNPs from GABRA2 extracted
  - Participants from two genetically determined ancestries included:
    - 2014 Students of European Ancestry
    - 816 Students of African Ancestry
  - Statistic run with PLINK
    - Chi-Square tests utilized to see GABRA2 association with alcohol dependence

Results
- European Ancestry: 16.75% of students were alcohol dependent
- African Ancestry: 9.93% of students were alcohol dependent

Table 1. Indicates the 8 SNPs tested for GABRA2 as well as their location on chr. 4. A p-value less than 0.05 signifies statistically significant results.

<table>
<thead>
<tr>
<th>SNP</th>
<th>Base Pair</th>
<th>European Ancestry</th>
<th>African Ancestry</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs116039536</td>
<td>46265176</td>
<td>0.6007</td>
<td>0.4383</td>
</tr>
<tr>
<td>rs17537359</td>
<td>46265712</td>
<td>0.2256</td>
<td>0.6348</td>
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<td>46274771</td>
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<td>0.3402</td>
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<td>0.5791</td>
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<td>2.0683</td>
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<tr>
<td>rs4506518</td>
<td>46345219</td>
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<td>0.3652</td>
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<tr>
<td>rs11503556</td>
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<td>0.5014</td>
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<tr>
<td>rs16393568</td>
<td>46368578</td>
<td>0.1422</td>
<td>0.7061</td>
</tr>
</tbody>
</table>

- In both ancestries, no statistically significant association was found with any of the 8 SNPs.

Conclusion
Our study found that the 8 SNPs studied were not statistically significant.
- This is similar to Ittwut et al. (2011), as they found no individual SNP associations to alcohol dependence.
- Research by Sakai et al. (2010), tested a different SNP (rs279871) in GABRA2 and they also did not find association between alcohol dependence and GABRA2.

In the college environment, the environment might be more influential on alcohol-related outcomes than genetics.

These results also looked specifically at freshmen and did not study them out longitudinally, though alcohol dependence symptoms may emerge later in their college career.

This study looked at two subgroups, European and African ancestry, so it is possible that other groups may show significant results.

This study had a primary look at the SNPs in college-aged individuals, and it can guide future researchers into looking at either of these SNPs or other SNPs on GABRA2 so we can learn more about alcohol dependence as it relates to genetics and environment.

Future Direction
- Looking at other college campuses would help, as college campuses have their own atmosphere, and results could vary from one college to another.
- Studying other SNPs, ancestries, and other GABA receptors such as GABBR may yield different results.
- Additional genetic analyses such as using polygenic risk scores might be more informative.

References

Acknowledgements
Special thanks to Dr. Amy Adams, Dr. Sally Kuo and all Spit4Science participants, data collectors, and research assistants!