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Moderation of 5-HTTLPR and MAOA effects on alcohol dependence differs by type of childhood abuse

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Background

- 5-HTTLPR is a variable-number-of-repeats region in the gene SLC6A4 located on chromosome 11.
  - The two versions are Long and Short, with the Short allele associated with reduced transcription of serotonin transporter mRNA.
  - Previous gene-environment interaction (GxE) studies indicated the presence of one or two Short alleles to be related to greater increases in substance use in adolescents from families low on involved-supportive parenting (Brody et al., 2005) and greater risk of early alcohol use in adolescents who were maltreated as children (Kauffman et al., 2007).

- MAOA is a variable-number-of-repeats gene on the X-chromosome that codes for an enzyme (also MAOA) which degrades neurotransmitters.

- The relationship between Low MAOA and violence, conduct disorder, and antisocial personality disorder is especially strong in individuals who experienced childhood maltreatment or physical abuse (Caspi et al., 2002; Kim-Cohen et al., 2006).

Participants

- Minnesota Twin and Family Study (MTFS) community-sampled twin participants who were assessed for alcohol dependence at age 25 (N=2093, 44.9% female) were included in our sample.
- Of these, 1949 (44.1% female) had childhood abuse status data, which included in our sample.
- 1203 (45.1% female) were genotyped for 5-HTTLPR, and/or age 29.
- Of these, 1949 (44.1% female) had childhood abuse status data, which included in our sample.

Measures

- Alcohol dependence symptoms: Participants were assessed for DSM-IV criteria alcohol dependence symptoms at age 25 covering approximately the past 4 years.
  - Each individual received a count of symptoms which had definitely been met.
  - The sample mean was 1.3 symptoms, with a standard error of 0.12 and a range of 0 to 10.

- 5-HTTLPR was assessed from participants’ peripheral blood samples or buccal swabs as described in Anchorduko et al. (2003).
  - Number of repeats was coded into Short (S, 484bp) and Long (L, 528bp).
  - Proportions of each genotype were: LL = 32.3%, LS = 48.9%, SS = 18.9%.

- MAOA was assessed from participants’ peripheral blood samples or buccal swabs as described in Haberstick et al. (2005).
  - Individuals were dichotomized for MAOA activity level, with 2, 3, or 5 repeats (as described in Caspi et al., 2002).
  - The Low activity genotype was less frequent (31.4% of the sample), which is similar to previous reports (e.g. 43.3% males, 19.7% females, Guo et al., 2008).

- MAOA was coded as ‘O’ for High activity, ‘1’ for Low activity.

Analyses

- Multiple regressions were conducted in Mplus (Muthén & Muthén, 1997-2008), taking into account the non-independent nature of the twin data.
- Alcohol dependence symptom counts were modeled on a zero-inflated Poisson distribution.

Table 1. Regression Results

<table>
<thead>
<tr>
<th>Measure</th>
<th>β</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical*</td>
<td>5HTT</td>
<td>-0.153 (0.637)</td>
<td>0.713</td>
</tr>
<tr>
<td>Sexual*</td>
<td>5HTT</td>
<td>0.269 (0.713)</td>
<td>0.04</td>
</tr>
<tr>
<td>Physical*</td>
<td>MAOA</td>
<td>0.515 (3.438)</td>
<td>0.001</td>
</tr>
<tr>
<td>Sexual*</td>
<td>MAOA</td>
<td>0.515 (3.438)</td>
<td>0.001</td>
</tr>
<tr>
<td>Physical*</td>
<td>MAOA</td>
<td>0.060 (0.483)</td>
<td>0.681</td>
</tr>
<tr>
<td>Sexual*</td>
<td>MAOA</td>
<td>0.060 (0.483)</td>
<td>0.681</td>
</tr>
</tbody>
</table>

Conclusions

- There was a significant interaction between exposure to childhood Sexual abuse and genetic status in predicting adult alcohol dependence symptoms for both 5-HTTLPR and MAOA. Similar to previous findings (Caspi et al., 2002, Kim-Cohen et al., 2006, Kaufman et al., 2007, Brody et al., 2009), the Short allele in 5-HTTLPR (p=0.001) and Low MAOA activity (p=0.01) increased number of alcohol dependence symptoms in individuals who had experienced childhood Sexual abuse.

- Physical abuse did not interact with either gene in predicting alcohol dependence symptoms, though there was a significant main effect in the 5-HTTLPR model (p=0.04) and a suggestive main effect in the MAOA model (p=0.05), indicating that physical abuse in childhood is predictive of increased alcohol dependence symptoms in adulthood regardless of genetic status on MAOA or 5-HTTLPR.

- Sex was a significant (p<0.001) covariate in each model, although the current models did not examine interactions separately by sex.

References


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