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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 17.
 - 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., 2009) and greater risk of early alcohol use in adolescents who were maltreated children (Kaufman 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.
 - Number of repeats that result in Low MAOA activity have been linked to increased rates of delinquency and violence (Guo et al., 2008).
 - 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).

Current Study

- Previous studies of GxE interactions in childhood abuse and externalizing behaviors tend to collapse across the broad range of childhood maltreatment.
- We explored moderation of the effect of MAOA and 5-HTTLPR genotypes on alcohol dependence symptoms at age 25 by type of childhood abuse experienced (Physical and/or Sexual) prior to age 18.

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,
- 1203 (45.1% female) were genotyped for 5-HTTLPR,
- 978 (27.4% female) were genotyped for and homozygous on MAOA.
 - Females who were heterozygous for the High-Low activity genotype (N=227) were dropped from our genetic analyses due to uncertain MAOA activity level (see Kim-Cohen et al., 2006).

Measures

- Abuse status:** Childhood Physical and Sexual abuse were assessed at either age 21 or age 29.
 - 54.2% of those assessed for abuse were asked two Yes/No questions about physical and sexual assault respectively as part of a broader Life Events Inventory, as well as the first age at which they experienced that type of assault.
 - 74.1% received a more extensive abuse assessment, including:
 - 4 items on severe Physical abuse (if they were ever hit leaving a mark, hit with an object, assaulted with a weapon, or injured in another way by an adult responsible for them), and
 - 9 items on Sexual abuse (ranging from being propositioned to intercourse, whether in an unwanted situation prior to age 18 or with anyone more than 5 years older prior to age 13).
- For those assessed on both measures (N=551) reliability was good as indicated by cross-measure correlations of $r=0.27$ for Physical abuse and $r=0.73$ for Sexual abuse. Discrepancies tended to favor abuse endorsement on the second, more specific measure.
- Abuse status was aggregated across measures separately for Physical and Sexual abuse.
- Proportion reporting Physical abuse was 22.4%, while 6.2% reported Sexual abuse.
- For each abuse type, exposure before age 18 was coded as '1', while non-exposure was coded '0'.

Measures, continued

- 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 Anchordoquy 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%.
 - 5-HTTLPR was in Hardy-Weinberg Equilibrium, with a Minor Allele (S) Frequency of 0.43, $\chi^2(1)=0.02, p=0.87$.
 - Individuals were coded for number of Short alleles they possessed (0, 1, or 2).
- 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 High activity indicated by 3.5 or 4 repeats of the MAOA gene and Low activity indicated by 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 '0' 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

Model: $AD_Sx^A = \beta_0 + \beta_1 Sex^B + \beta_2 Physical^C + \beta_3 Sexual^D + \beta_4 genotype^{EF} + \beta_5 Physical^C * Sexual^D + \beta_6 Physical^C * genotype + \beta_7 Sexual^D * genotype + \beta_8 Physical^C * Sexual^D * genotype$

	β	Z	p		β	Z	p
MAOA				5-HTTLPR			
Sex^B	-0.858	-3.341	0.001	Sex^B	-0.462	-3.715	<0.001
Physical ^C	0.257	1.948	0.051	Physical ^C	0.311	2.063	0.039
Sexual ^D	-0.656	-1.931	0.053	Sexual ^D	-0.227	-1.053	0.292
MAOA ^E	-0.003	-0.026	0.980	5HTT ^F	-0.064	-0.911	0.362
Physical ^A				Physical ^A			
Sexual ^A	0.879	1.863	0.063	Sexual ^A	0.269	0.713	0.476
Physical ^A				Physical ^A			
MAOA	-0.085	-0.345	0.730	5HTT	-0.060	-0.438	0.661
Sexual^A				Sexual^A			
MAOA	1.110	2.514	0.012	5HTT	0.515	3.438	0.001
Physical ^A				Physical ^A			
Sexual ^A				Sexual ^A			
MAOA	-0.057	-0.991	0.321	5HTT	-0.153	-0.545	0.585

^ACount of alcohol dependence symptoms

^BSex: male=0, female=1

^CPhysical abuse before age 18: 0=no, 1=yes

^DSexual abuse before age 18: 0=no, 1=yes

^EMAOA activity: 0=high, 1=low

^F5-HTTLPR genotype: 0=LL, 1=LS, 2=SS

References

- Anchordoquy, et al. (2003). Genotyping of three candidate genes after whole-genome preamplification of DNA collected from buccal cells. *Behavior Genetics*, 33, 73-33.
- Brody et al. (2009). Parenting moderates a genetic vulnerability factor in longitudinal increases in youths' substance use. *Journal of Consulting and Clinical Psychology*, 77, 1-11.
- Caspi, et al. (2002). Role of genotype in the cycle of violence in maltreated children. *Science*, 297, 851-854.
- Guo, et al. (2008). The VNTR 2 repeat in MAOA and delinquent behavior in adolescence and young adulthood: Associations and MAOA promoter activity. *European Journal of Human Genetics*, 16, 628-634.

Figure 1. Moderation of 5-HTTLPR effect by sexual abuse status

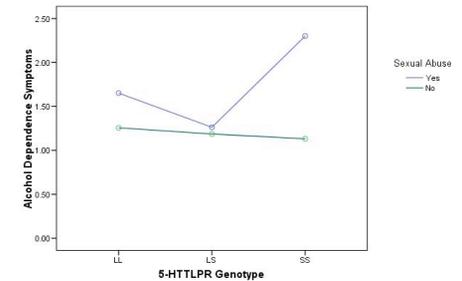
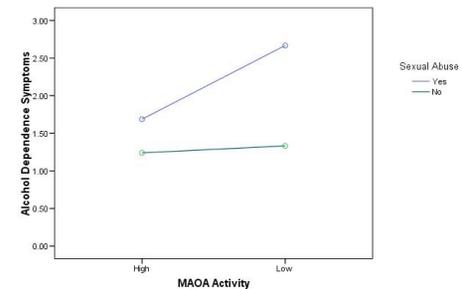


Figure 2. Moderation of MAOA effect by sexual abuse status



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 ($p \leq 0.001$) covariate in each model, although the current models did not examine interactions separately by sex.

- Haberstick, et al. (2005). Monoamin Oxidase A (MAOA) and antisocial behaviors in the presence of childhood and adolescent maltreatment. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, 135B, 59-64.
- Kaufman, et al. (2007). Genetic and environmental predictors of early alcohol use. *Biological Psychiatry*, 61, 1228-1234.
- Kim-Cohen, et al. (2006). MAOA, maltreatment, and gene-environment interaction predicting children's mental health: New evidence and a meta-analysis. *Molecular Psychiatry*, 11, 903-913.

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