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Does exposure to parental substance use disorders increase offspring risk for a substance use disorder? A longitudinal follow-up study into young adulthood

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ABSTRACT

Objective: The main aim of this study was to examine the risk of exposure to parental substance use disorders (SUD; alcohol or drug abuse or dependence) on the risk for SUD in offspring with and without attention deficit hyperactivity disorder (ADHD) followed into young adult years.
Methods: Subjects were derived from two longitudinal case-control studies of probands of both sexes, 6–17 years, with and without DSM-III-R ADHD and their parents. Probands were followed for ten years into young adulthood. Probands with a parental history of non-nicotine SUD were included in this analysis. Exposure to SUD was determined by active non-nicotine parental SUD while the parent was living with their child after birth. Cox proportional hazard models were used to calculate the risk of non-nicotine SUD in offspring.
Results: 171 of the 404 probands reassessed at ten-year follow up had a family history of parental SUD. 102 probands were exposed to active parental SUD. The average age of our sample was 22.2 ± 3.5 years old. Exposure to maternal but not paternal SUD increased offspring risk for an alcohol use disorder in young adulthood independently of ADHD status (OR: 2.7; 95% CI: 1.1, 6.9; p = 0.04).
Conclusion: Exposure to maternal SUD increases the risk for an alcohol use disorder in offspring ten years later in young adult years irrespective of ADHD status.

1. Introduction

A growing literature supports a strong bidirectional association between attention deficit hyperactivity disorder (ADHD) and substance use disorders (SUD). The available literature clearly documents that individuals with ADHD are at increased risk for SUD (Lee et al., 2011) and individuals with SUD are at increased risk for ADHD (Van Emmerik-Van Oortmerssen et al., 2012).

A recent familial risk analysis of youth with and without ADHD of both sexes followed into young adulthood provides strong evidence supporting a familial influence for the risk for SUD in ADHD youth (Yule et al., 2017). While these findings support the hypothesis that genetic influences are operant in mediating the risk for SUD in ADHD, this risk could also be driven by environmental influences, such as exposure to a parent with an active SUD (Newlin et al., 2000). Indeed, previous research has shown that exposure to parental substance use through parental modeling of substance use increases the risk for substance use in offspring (Arria et al., 2012; Chassin et al., 1996; Coffelt et al., 2006; Ennett et al., 2008; GiL et al., 2002; Ohannessian et al., 2004; Li et al., 2002; Shorey et al., 2013; Yu, 2003).

We previously reported on the impact of exposure to parental SUD in samples with and without ADHD followed into adolescence (Biederman et al., 2000; Yule et al., 2013) and found that exposure to parental SUD predicted SUD in the offspring. These studies also found that the timing of exposure during adolescent years was particularly impactful (Biederman et al., 2000; Yule et al., 2013). However, since follow up was limited to adolescent years, a longer follow up period is needed to evaluate the full extent of the environmental risk as the sample transitions into young adult years, a period of peak risk for developing SUD (Compton et al., 2007; Hingson et al., 2006).

Further understanding of whether exposure to parental SUD is a risk factor for SUD in young adults with and without ADHD has important implications, given the substantial morbidity and mortality associated with SUD (Whiteford et al., 2015). If exposure to parental SUD is a moderator in the relationship between ADHD and SUD, this knowledge can support the development of appropriate intervention strategies to mitigate this problem. Parents with active SUD may be motivated to change their substance use if they know that their behavior puts their

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children at higher risk to develop a SUD. This knowledge would also support clinical and public health efforts to screen for SUD in parents of ADHD youth, which could help decrease later development of SUD in their children.

The main aim of this study was to re-examine the risk of exposure to parental SUD (alcohol or drug abuse or dependence) on the risk for SUD in offspring with and without ADHD followed into young adult years during the peak age of risk to develop a SUD. To this end, we used data from longitudinal studies of psychiatrically and pediatrically referred youth of both sexes with and without ADHD at ten-year follow-up attending to the moderating effects of sex of the parent and offspring. Based on the literature, we hypothesized that exposure to parental SUD will increase the risk for SUD in young adult offspring and that the risk will be larger in offspring with ADHD. To the best of our knowledge, this study is the most comprehensive examination of the risk of exposure to SUD in older ADHD youth.

2. Methods

2.1. Subjects

Detailed study methodology has been previously described (Biederman et al., 2006; Biederman et al., 2010). Briefly, subjects were derived from two identically designed, longitudinal, case-control family studies of ADHD. These studies recruited male and female probands aged 6–17 years with DSM-III-R ADHD (N = 140 boys, N = 140 girls) and without ADHD (i.e., Controls, N = 120 boys, N = 122 girls) from pediatric and psychiatric clinics. These groups had 552 parents and 472 parents, respectively. Potential subjects were excluded if they had been adopted, their nuclear family was not available for study, if they had major sensorimotor handicaps, psychosis, autism, inadequate command of the English language, or a Full Scale IQ less than 80. ADHD subjects met full DSM-III-R diagnostic criteria for ADHD at the time of the clinic referral and were subsequently reassessed for DSM-IV criteria. Parents and adult offspring provided written informed consent to participate, and parents provided consent for offspring under the age of 18. Children and adolescents provided written assent to participate. The human research committee approved the initial assessments as well as all aspects of the follow up of this study. The current sample includes data collected from subjects 10 years after their initial assessment.

2.2. Assessment procedures

Lifetime psychiatric assessments in parents were completed at baseline only using the Structured Clinical Interview for the DSM-IV (SCID; First et al., 1997; Spitzer et al., 1990) (supplemented with modules from the Schedule for Affective Disorder and Schizophrenia for Children (K-SADS-E; OrvascheL, 1994) to assess childhood diagnoses. Probands were assessed at baseline and at the 10 year follow up with the K-SADS-E for subjects younger than 18 years of age and the SCID for subjects 18 years of age and older. All diagnostic assessments were conducted by raters with Bachelor's or Master's degrees in psychology, who had been extensively trained and supervised by the senior investigators. Raters were blind to the ascertainment of the families. Direct interviews were conducted with subjects older than 12 years of age and indirect interviews were conducted with their mothers (i.e., mothers complete the structured interview about their offspring). We combined data from direct and indirect interviews by considering a diagnostic criterion positive if it was endorsed in either interview.

Board-certified child and adult psychiatrists and psychologists who were blind to the subject's ADHD status, referral source, and all other data resolved diagnostic uncertainties. To assess the reliability of our overall diagnostic procedures, we computed kappa coefficients of agreement by having experienced, blinded, board-certified child and adult psychiatrists diagnose subjects from audiotaped interviews made by the assessment staff. Based on 500 assessments from interviews of children and adults, the median kappa coefficient was 0.98. The kappa coefficient for ADHD was 0.88 and for SUD was 1.0. Interviewers assessed the degree of impairment on daily functioning associated with each disorder that subjects endorsed on a three-level ordinal scale: minimal, moderate, or severe. For SUD, we made the diagnoses only when associated with at least moderate impairment. Socioeconomic status (SES) was measured using the 5-point Hollingshead scale (Hollingshead, 1975).

2.3. Statistical analysis

We stratified our sample into two groups: probands with a parental history of non-nicotine SUD with and without exposure to their parent's SUD. Exposure was defined as active non-nicotine substance use meeting criteria for abuse or dependence to alcohol or drugs while the parent was living with their child, after birth.

We compared demographic characteristics between probands with a parental history of SUD who were exposed or not exposed to active parental SUD using the Student's T test for continuous outcomes, the Wilcoxon Rank Sum test for socioeconomic status (SES), and the Pearson $\chi 2$ tests for binary outcomes.

We used the Kaplan-Meier cumulative failure function to calculate survival curves and cumulative lifetime risk of non-nicotine SUD in offspring. Cox proportional hazard models were used to calculate the risk of non-nicotine SUD in offspring. We first looked at the effect that maternal use and paternal use may have separately had on offspring SUD. We subsequently looked at the effect of exposure to either parent's SUD on offspring SUD. We examined whether the timing of the exposure was related to offspring SUD using a multivariate logistic regression model (all time periods were included in the model). For this analysis, we used the age of the offspring at baseline in addition to the onset and offset of the parent's substance use to determine the time period in which the offspring were exposed.

To examine the impact of ADHD and sex on the associations between parental SUD exposure and offspring SUD, we examined the ADHD-by-exposure and the sex-by-exposure interaction terms. At any point, if either interaction term was significant, we estimated the effect of exposure to parental SUD separately by ADHD/sex. If either interaction was not significant, we removed it from the analyses and reran the model adjusting for ADHD and sex. All tests were two-tailed, and our alpha level was set at 0.05 for all analyses. We calculated all statistics using STATA, version 12.0. Data are expressed as mean ± standard deviation (SD) unless otherwise specified.

3. Results

As previously described, (Biederman et al., 2010; Biederman et al., 2012) with very few exceptions, there were no significant differences between those who were lost-to-follow-up and those who remained in the study on age, race, global assessment of functioning score, familial intactness, or psychiatric outcomes. There was a significant difference in SES in both ADHD and control probands in those who were lost-to-follow-up and had lower SES than those successfully reassessed (Biederman et al., 2011). The final sample, reassessed at ten-year follow-up, included 404 probands (ADHD: 112 boys and 96 girls; Control: 105 boys and 91 girls). Among their 800 parents, there were 404 mothers (age at baseline ± SD: 40.9 ± 5.4 years) and 396 fathers (43.3 ± 6.1 years). Twenty-seven percent of parents (N = 214) had a SUD: 22% (N = 174) with an alcohol use disorder, 13% (N = 106) with a drug use disorder, and 8% (N = 66) had both an alcohol and drug use disorder. The sample for this analysis included the 171 probands who had a family history of parental SUD (maternal SUD and/or paternal SUD).

As shown in Table 1, at the ten-year follow-up, the average age of our sample was 22.2 ± 3.5 years old. Offspring exposed to parental SUD had a lower SES and were older (both p values < 0.05) than those