THE MODERATING ROLE OF THE SYMPATHETIC NERVOUS SYSTEM IN THE INTERGENERATIONAL TRANSMISSION OF SUBSTANCE USE

by

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(Under the Direction of Assaf Oshri)

ABSTRACT

Youth of parents who abuse substances are at significant risk for the development of alcohol or other drugs (AOD) use problems. Despite this intergenerational risk for substance use problems (SUPs), not all youth exposed to substance use develop SUPs. The autonomic nervous system (ANS) has a central bioregulatory role in regulating behaviors that reliably forecasts substance abuse. Yet, the protective effect of the ANS system on the intergenerational effect of AOD use problems is unknown. This study aimed to examine a psychophysiological pathway that underlies the intergenerational transmission of parental substance use behavior and the development of ADHD in young adult offspring using a community sample of 225 low-SES young adults (M_{age} = 21.56; 52.9% female) in a two-wave design (12-18 month time interval between waves). A second aim was to test the mediating role of ADHD and the moderating role of ANS functioning (i.e., tonic pre-ejection period; PEP-b) on the intergenerational transmission of SUPs. Results indicated that the direct effect of parental substance use on young adult AOD use problems was mediated by ADHD, but only among youth with blunted self-regulation (i.e., high PEP-b).

INDEX WORDS: Alcohol use problems, Drug use problems, Autonomic nervous system, Sympathetic nervous system, ADHD, Substance use problems

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DEDICATION

This thesis is dedicated to my parents who instilled within me that anything worth having does not come easy. Thank you both for your continued love and support throughout the writing process. I would also like to dedicate this thesis to my sister and godparents whose unwavering support and encouragement did not go unnoticed or unappreciated. Thank you for always believing in me, even when I didn't believe in myself. I love you all very much.

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CHAPTER 1

INTRODUCTION AND LITERATURE REVIEW

Children of parents with substance use problems are significantly more likely to use drugs themselves during youth and adulthood. This effect has been referred to as the intergenerational transmission of substance use problems and is well-established in the literature (Handley & Chassin, 2009; Kerr & Capaldi, 2020; Saha et al., 2018; Van Gundy, 2002). In particular, children of parents with substance use problems (SUPs) are at significant risk for SUPs, such as alcohol and other drugs (AOD) use problems in young adulthood (King & Chassin, 2004). Less is known about the pathways that underlie this intergenerational link. Extant literature suggests this association may be mediated by child behavioral dysregulation, such as attention problems (Zoloto et al., 2012). For example, some studies have found that children of parents with SUPs are more likely to develop attention problems (Biederman et al., 1992; Biederman et al., 1990; Milberger et al., 1998).

Further, a large body of work purports that children with attention-deficit/hyperactivity disorder (ADHD) symptoms are significantly more likely to develop SUPs than those without ADHD symptoms (Lee et al., 2011). However, many children of parents with SUPs do not develop SUPs, potentially because of understudied individual differences in regulatory characteristics that may moderate this association. The autonomic nervous system (ANS) is increasingly identified as a promising transdiagnostic biomarker for emotion regulation (Beauchaine, 2015b; Beauchaine & Bell, 2020; Beauchaine & Thayer, 2015; Chalmers et al., 2016) . Growing recent research highlights the bioregulatory role of the sympathetic nervous

system (SNS) in the development of risk factors for psychopathology (Brenner & Beauchaine, 2011) and drug use risk (Oshri et al., 2018). The current study aimed to test whether ADHD symptoms mediated the link between parental SUPs and youth AOD use problems. Further, we investigated tonal pre-ejection period (PEP-b), a well-validated biomarker for the SNS, as a protective factor in linking young adult ADHD and young adult AOD use problems. Given the clinical and public health significance of substance disorders and the need to inform prevention programing, there is a need to further examine the indirect effect of parental SUPs from parents to children via ADHD symptoms in youth, and the potential moderating role of bioregulatory abilities in this link.

1.1 Parental Substance Use and Young Adult Substance Use Risk

Parents with SUPs are often burdened with comorbidities such as physical and psychological problems (Kendler et al., 1997). Further, children in such contexts are likely to observe substance use first-hand, which could possibly result in the normalization of such behavior (Bouchard et al., 2018). Consequently, extant research suggests children exposed to parental SUPs are at significant risk for substance use disorders (SUDs) throughout the lifespan, including AOD use problems (Lieb et al., 2002; Merikangas & Avenevoli, 2000). Indeed, a large body of research has documented the intergenerational effect (i.e., parent to child) of multiple types of parent SUPs on the development of SUDs in their offspring. For example, findings suggest that the offspring of parents who smoke cigarettes are more likely to smoke themselves (Chassin et al., 2002). The offspring of parents who smoke marijuana are more likely to use marijuana (Bailey et al., 2006; Merikangas & Avenevoli, 2000). In addition, children of parents with alcohol use problems were found to be at heightened risk for alcohol use during adolescence (Chassin et al., 1991; Lieb et al., 2002), earlier alcohol use than their peers

(Merikangas & Avenevoli, 2000), and alcohol abuse and dependence throughout the life course (Bailey et al., 2006; Lieb et al., 2002; Merikangas & Avenevoli, 2000). Taken together, these studies provide evidence that children reared by parents with more severe levels of SUPs are at increased risk for developing SUPs.

1.2 The Effect of Parental Substance Use on Young Adult ADHD

Extant literature suggests children of parents with SUPs are at elevated risk for attention problems (Biederman, Faraone, et al., 2000; Stanger et al., 1999). Parents with more severe SUPs are more likely to foster disorganized and unstable home environments, a significant risk for the development of ADHD problems in youth. Indeed, Earls et al. (1988) found elevated rates of ADHD in the children of alcoholics compared to a control group, findings that were supported by multiple studies (Cantwell, 1972; Morrison & Stewart, 1971, 1973; Stewart et al., 1979; Wilens et al., 2005). Children of parents who abuse alcohol are more likely to use alcohol while pregnant, which places their child at heightened risk for fetal alcohol spectrum disorder development. Fetal alcohol spectrum disorder has been positively linked to the development of ADHD (Burd, 2016; Popova et al., 2012) and could explain the higher prevalence of ADHD in the children of parents with SUPs. However, the exposure of vulnerable ADHD adolescents to active parental SUDs also increases the risk for subsequent ADHD (Biederman, Faraone, et al., 2000), suggesting a greater likelihood for the intensification of ADHD symptoms for affected children growing up in homes in which a parent has SUPs.

1.3 ADHD Symptoms and Substance Use Risk in Young Adults

Youth with ADHD are at significant risk for SUDs (Barkley et al., 2004; Chang et al., 2012; Charach et al., 2011; Galéra et al., 2013; Lee et al., 2011; Wilens, 2004; Wilens et al., 2011). For example, in a meta-analysis by van Emmerik-van Oortmerssen and colleagues, 23%

of treatment-seeking primarily young adult substance abusers had ADHD (van Emmerik-van Oortmerssen et al., 2012). In addition, the International ADHD in Substance Use Disorders Prevalence cross-sectional study sought to determine the prevalence of ADHD in adult treatment-seeking patients with SUDs in different countries with SUD populations. Among 3,000 patients from 10 countries, 40% of the subjects screened positive for ADHD (van de Glind et al., 2013). Indeed, some studies suggest that the risk for developing SUDs may be twice as high among those with ADHD than those without (Ercan et al., 2003; Wilens et al., 2011). For instance, Chang and colleagues (2012) found that individuals with symptoms of ADHD were at increased risk for early onset-tobacco use and alcohol use (Chang et al., 2012). Furthermore, one meta-analysis demonstrated a substantially higher likelihood of cigarette smoking and SUDs in youth with ADHD than those without ADHD (Charach et al., 2011). While ADHD symptoms and diagnosis is a risk factor for later AOD use problems, a growing body of research has been accumulating evidence for the mechanism that underlies this link.

1.3.1 The Underlying Mechanism Between ADHD and Alcohol Use Problems in Young Adults

A key context that has been shown to be part of the connection between ADHD and AOD problems is youth neuroregulatory problems. The ADHD to alcohol use hypothesis (Baker et al., 2012; Luderer et al., 2021; Mesman, 2015; Vollstädt-Klein et al., 2020) suggests that youth with ADHD are at significant risk for drug or alcohol use due to lack of self-regulation. This lack of self-regulation has been shown to increase impulsivity, a core symptom of ADHD (Luderer et al., 2021). Increased impulsivity can be attributed to reduced dopaminergic activity in the brain (Volkow, Wang, Newcorn, et al., 2007). This reduction in dopamine receptor availability in individuals with ADHD indicates reduced reward sensitivity, which is prevalent among adults with alcohol use disorders (Volkow, Wang, Telang, et al., 2007). Changes in the dopaminergic

neurotransmission in the striatum have also been associated with the transmission of intermittent binge drinking into a drinking habit, where continuous rewarding alcohol use leads to less sensitivity to other usually rewarding activities (Luderer et al., 2021). Additionally, glutamatergic neurotransmission in the anterior cingulate cortex has been associated with ADHD symptoms, especially hyperactivity and impulsivity (Bauer et al., 2018; Huang et al., 2019). The glutamatergic system appears to be relevant for craving induced by alcohol-related cues (Koob & Volkow, 2016). Lastly, the literature shows that those who use alcohol are also more likely to use other substances, including tobacco, marijuana, opiates, and other drugs (Degenhardt & Hall, 2003), suggesting that alcohol may be a gateway drug for the initiation of additional substance use. Taken as a whole, a host of neuroregulatory deficits are associated with ADHD, which may place individuals at heightened risk for alcohol use problems, and subsequent substance use.

1.4 Autonomic Nervous System Role in Substance Abuse Risk

The autonomic nervous system (ANS) is composed of the parasympathetic nervous system (PNS) and the sympathetic nervous system (SNS), which generally have opposing functions. The PNS facilitates the rest and digest function and is thought to serve as the "brake" that decelerates the heart via the vagus nerve and enables regulation of emotion and social engagement during non-stressful circumstances (Berntson et al., 1997; Hinnant et al., 2015; Porges, 2007). Alternatively, the SNS fosters mobilization through the fight or flight response in the context of an environmental challenge, promoting vigilance, increasing heart rate and sweat gland secretion, and simultaneously decreasing the activity of systems that may take away from the energy resources necessary for immediate mobilization (El-Sheikh et al., 2013). Well-validated, transdiagnostic biomarkers are increasingly used in studies to test for the role of the ANS, particularly the SNS, in emotion regulation. A promising cardiac biomarker of SNS

activity is pre-ejection period (PEP)—the time between the depolarization of the left ventricle of the heart-opening of the aortic valve. PEP indexes cardiac sympathetic activity by influencing ventricular contractility. Therefore, PEP is negatively correlated with SNS activation, such that lower values represent increases in sympathetic activity, whereas higher values indicate decreased sympathetic activity (Goedhart et al., 2008; Hinnant et al., 2021; Newlin & Levenson, 1979).

Although the regulatory role of the ANS has most often been modeled exclusively by the PNS (Beauchaine, 2012, 2015b; Beauchaine & Bell, 2020; Beauchaine & Thayer, 2015; Chalmers et al., 2016; Young & Benton, 2018), research increasingly demonstrates that the SNS has a critical role in developmental outcomes. Typically adaptive in the face of danger, frequent or extreme SNS activation is metabolically costly, may result in excessive wear and tear on the body (McEwen, 1998), and has been linked to more adverse and impulsive behaviors. Therefore, increased sympathetic activity at rest may represent chronic states of arousal, which may be maladaptive (Cappadocia et al., 2009; Raine, 1997). Indeed, chronic and higher SNS activity has been linked to aggression (Hubbard et al., 2002) and externalizing behaviors (El-Sheikh, 2005). Further, more PEP reactivity, the shortening of PEP in response to stimuli, has been linked to delinquent and risky behaviors in childhood and adolescence. For example, Brenner and Beauchaine (2011) found that greater PEP reactivity was positively associated with an increased likelihood of future alcohol use in young adults. Moreover, the findings of several studies indicate that children with externalizing disorders also exhibit compromised SNS-linked cardiac activity and reactivity (Beauchaine, 2001; Beauchaine, 2015a; Bell et al., 2018). The lack of studies that model the neuroregulatory role of the SNS represents a significant gap in the literature.

1.5 The Current Study

The current study aims to examine a pathway that underlies the intergenerational transmission of parental substance use behavior and the development of ADHD in young adult offspring. The specific hypotheses and aims of the current study are as follows. First, we examine the link between parental substance use and AOD use problems in youth. We hypothesize that parental substance use will positively predict young adult AOD use problems such that young adults who have more parental substance use will have more AOD use problems. Second, the study investigates whether ADHD symptoms mediate the pathway between parental substance use and young adult AOD use problems. We hypothesize that parental substance use will positively predict offspring ADHD symptoms during young adulthood. Lastly, the final aim of the study is to determine whether self-regulatory abilities (PEP-b) moderate the pathway between offspring ADHD symptoms and AOD use problems. We hypothesize that low PEP-b will exacerbate the relationship between young adult ADHD symptoms and AOD use problems. In contrast, high PEP-b will buffer the connection between ADHD symptoms and AOD use problem risk.

CHAPTER 2

METHODS

2.1 Participants

Participants (N = 225) between the ages of 18 and 25 were recruited from a rural community in the Southeastern United States. To distinguish the sample from college-seeking young adults who are often less racially/ethnically diverse and come from higher SES backgrounds, young adults who are not in college or have college education were recruited. Further, rural young adults are at increased risk for socioeconomic adversity and substance use (Mack et al., 2017). Participants self-identified as male (n = 105, 46.7%), female (n = 119, 52.9%), and transgender (n = 1, 0.4%). The average age of the participants was 21.56 (SD = 2.24). The sample was racially/ethnically diverse, with 59.6% self-identifying as White, 30.7% as Black/African American, 5.8% as Hispanic/Latino, and 3.6% as Other. The majority of the participants came from economically impoverished backgrounds and reported making less than $20,000 annually ($n$ = 173, 76.9%). Exclusion criteria included being enrolled in a high school or in college, having a four-year college degree, or the presence of pregnancy or cardiovascular condition.

2.2 Procedure

The study and procedures were approved by the University of Georgia Institutional Review Board. Participants were recruited by community liaisons and trained research assistants via in-person and online advertisements. To connect with community liaisons, the research team recruited the help of a local community organization whose goal is to promote the well-being

among the youth and families and has many well-established relationships with community leaders. The organization worked with the research team to identify community members who lived in the community of interest and were socially influential and could act as study liaisons to help recruit study participants. Those who agreed to serve as liaisons were fully informed of the purpose and procedures of the study.

Data collection was obtained by particpants in a private laboratory setting on the University's campus. Prior to arriving in the laboratory, participants were reminded not to use any alcohol or other drugs for at least 24 hours before their participation in the study. Once participants arrived at the laboratory, informed consent and assent were obtained prior to any study activities. Once consent and assent were obtained, participants were attached to an electrocardiogram (ECG) via dermal electrodes for the entirety of the survey. One electrode was placed at the bottom of the ribcage, on each side of the clavicle, under the sternum, on the upper spine, as well as the lower spine. Female participants were intentionally paired with female research assistants to enhance their comfortability with electrode placement. Biometric data were obtained using the BioLab software provided through Mindware Technologies. Once the electrodes were attached, participants were instructed to use headphones to listen and watch a 3-minute video of neutral landscapes to establish baseline HRV based on recommendations for obtaining HRV (Malik, 1996).

Following the baseline task, participants were asked to complete a five-minute mental arithmetic stress task shown in prior research to produce a significant physiological reaction (Berntson et al., 1997) to stimulate the participants' autonomic response to a stimulated acute social-cognitive stressor. During the task, participants were asked to answer a series of increasingly difficult arithmetic problems aloud quickly and accurately in front of an audience of

research assistants. Task difficultly was adjusted from easier to more difficult based on the accuracy and response time of participants' answers to account for differential math abilities. Research assistants were trained to remain neutral and refrain from giving feedback throughout the duration of the task. After completing the arithmetic task, participants were instructed to report how stressful the arithmetic task was for them (1 = "not stressful at all", 2 = "not very stressful," 3 = "somewhat stressful," 4 = "stressful," and 5 = "very stressful"). 84.3% of participants rated the task as being somewhat to very stressful. The mean response was 3.57 with a standard deviation of 1.08. Then, participants were once again instructed to view a 3-minute relaxing video then answer a series of questionnaires.

Research assistants followed up with consenting participants 9 to 12 months after the initial baseline laboratory visit (T1) via text message or email with a brief follow-up survey. Participants provided additional informed consent through an online form then completed a brief online questionnaire. The rate of attrition for the study was moderate, with 65.3% of participants returning at T2.

2.3 Measures

2.3.1 Parental Substance Use (T1)

Parental substance use was assessed using three different scales to measure cigarette, alcohol, and drug use. Parents were also asked to respond to the 10 items included on the Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001) to assess their level of alcohol use and dependence. Frequency of alcohol use was assessed by summing the response scores to questions 1-3. Alcohol problems were assessed by summing responses to questions 4-10. The total score for alcohol use and problems was calculated by summing responses from questions 1-10 (α = .766). Drug use was assessed using the Drug Use Disorders Identification

Test (DUDIT; Bergman et al., 2003). Responses to each of the 11 items included on the DUDIT were summed to find the total score of drug use frequency and problems. Parents were asked questions to determine whether they used cigarettes. Specifically, cigarette use was defined as an affirmative response to the following questions: *Do you currently smoke tobacco daily, less than daily, or not at all? Do you currently use smokeless tobacco daily, less than daily, or not at all?* Parents were also asked to respond to the following open-ended question: *During the past 30 days, how many cigarettes have you smoked on an average day?*

2.3.2 Young Adult AOD Use Problems (T1 and T2)

Young adult AOD use problems was measured using the participants' own report of their own alcohol use and dependence on the Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001). Frequency of alcohol use was assessed by summing the response scores to questions 1-3. Alcohol problems were evaluated by computing the responses to questions 4-10. The total score for alcohol use and problems was found by summing responses from questions 1-10. The internal reliability of the AUDIT scale was satisfactory (α = .766).

2.3.3 Young Adult ADHD Symptoms (T1)

Participants completed the SWAN ADHD Rating Scale to report on their child's ADHD symptoms over the previous six months. The SWAN ADHD Rating Scale contains 18 reworded items to measure ADHD. Based on the previous Swanson, Nolan, and Pelham (SNAP) scale (Swanson, 1992), items were reworded from the categorical approach of ATBRS (This child: Has trouble following through on instructions and finish schoolwork, chores or duties?) to a dimensional approach (Does this child: Follow through on instructions and doesn't finish schoolwork, chores or duties?). On the SWAN scale, caregivers rated items on a 4-point scale ranging from 0 *(not at all)* to 3 *(very much).* The total score on inattention and hyperactivity-

impulsivity dimensions of the SWAN scale were then averaged from 0 to 3, with a high score closer to 3 indicating a higher level of ADHD symptoms or problem behaviors. A score closer to 0 on the SWAN scale indicates that the young adult has better average attention behaviors. The internal reliability of the SWAN ADHD rating scale was satisfactory (α = .73).

2.3.4 PEP-b (T1)

Basal sympathetic nervous system reactivity, proxied by basal PEP, was collected using a mobile impedance cardiograph (Mindware Technologies, Ltd., Gahanna, OH). To measure PEP, impedance cardiography analysis was conducted by isolating the time interval between the initial electrical stimulation of the heart (the onset of the R peak) and the opening of the aortic valve (B point of the dZ/dT wave; Lozano et al., 2007). Using the MindWare IMP 3.1.4 Software module, impedance data were ensemble-averaged in 30-second epochs and combined with R waves that were obtained from the electrocardiogram. Research assistants were extensively trained to cross-inspect and correct abnormal R-R intervals such as severe fluctuations, inadvertent cardiac fluctuations, and ectopic beats due to physical movement or breathing. Mean values of PEP across the 30-second epochs were calculated for the baseline.

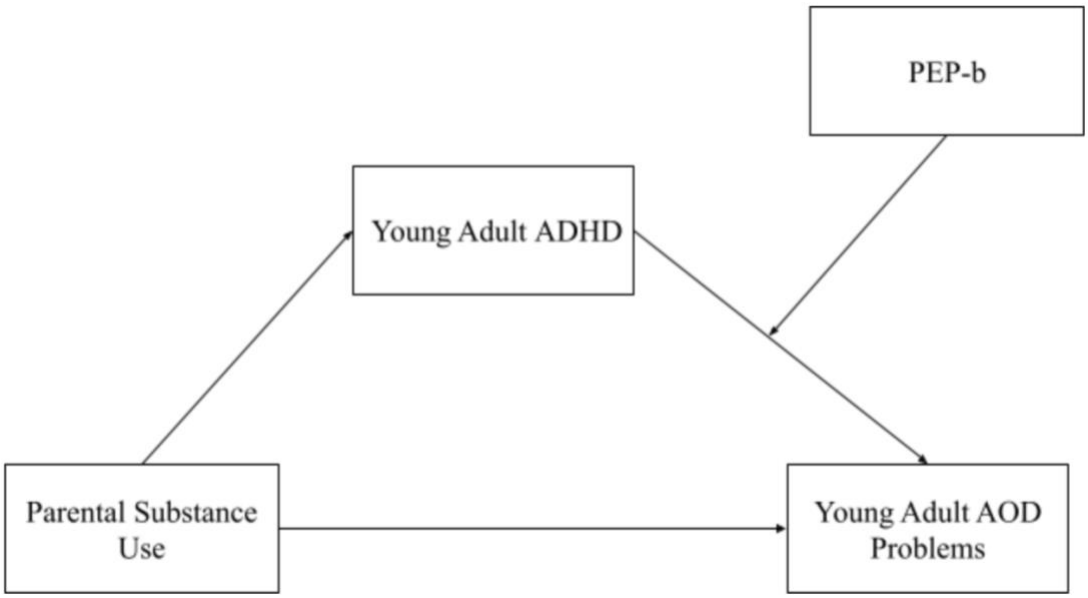
2.4 Analytic plan

The hypotheses were tested within a structural equation modeling (SEM; Figure 1) framework using the Mplus version 7.4 statistical software (Muthén & Muthén, 2009). First, I investigated the direct effect of parental substance use on young adult AOD use problems. Then, young adult ADHD symptoms was be examined as a mechanism in the indirect link between the intergenerational transmission of parental substance use and young adult AOD use problems. Third, a moderated mediation was tested on the impact of youth's PEP-b at T1 on the indirect link. Moderation was tested by creating interaction terms (i.e., PEP-b x ADHD) and regressing

the outcome variable on the interaction term. Last, the Johnson-Neyman plot was be generated to probe significant interaction effects (Johnson & Neyman, 1936).

Figure 1.

SEM Model for the Current Study.



CHAPTER 3

RESULTS

3.1 Preliminary Analyses

Table 1 presents descriptive statistics and bivariate correlations for the study variables. Among the 225 participants, 42.7% at T1 and 40.8% at T2 reported levels that met or exceeded the AUDIT threshold for hazardous alcohol use (Bohn et al., 1995).

Table 1.

Bivariate Correlations and Descriptive Statistics for Study Variables (N = 225).

	1	2	3	4	5	6	7
1. Biological sex	–	-.058	-.279**	-.084	.175	.194*	.195*
2. Age	-.058	–	-.012	-.142	-.081	.158	.030
3. Alcohol Use Frequency & Problems Scale (All Alcohol Items)	-.279**	.257*	–	.565**	.005	-.255**	.083
4. Follow-up Alcohol Use Frequency & Problems Scale (All Alcohol Items)	-.084	-.142	.565**	–	.155	-.201	-.365**
5. Screening scores of adult ADHD	.175	-.081	.005	.155	–	.049	.282**
6. IMP Math Task -- Baseline	.194*	.158	-.255**	-.201	.049	–	-.214
7. Parental Substance Use_Total	.195*	.030	.083	.365**	.282**	-.214	–
Mean	1.56	21.56	6.06	5.92	2.25	106.44	4.31
SD	.51	2.24	5.32	5.99	1.56	29.92	4.52

***. Correlation is significant at the 0.01 level (2-tailed).*

**. Correlation is significant at the 0.05 level (2-tailed).*

3.2 Initial Model

A moderated mediation (i.e., conditional indirect effect) SEM model was used to concurrently test the indirect effect of parental substance use on young adult AOD use problems via young adult ADHD symptoms, and the moderation of the path between parental substance use and young adult AOD use problems by baseline SNS activity (PEP-b). Age and gender were adjusted for in all the subsequent models. The results of the SEM model are presented in Table 2 and Figure 2. The model fit the data well: $\chi^2(8) = 15.507$, $p = 0.05$; CFI = 1.000, RMSEA = 0.000, standard root mean square residual (SRMR) = 0.024.

Table 2.

Moderated Mediation Model of the Associations Between Parental Substance Use, Young Adult ADHD, Young Adult AOD Use Problems, and PEP-b (N = 225).

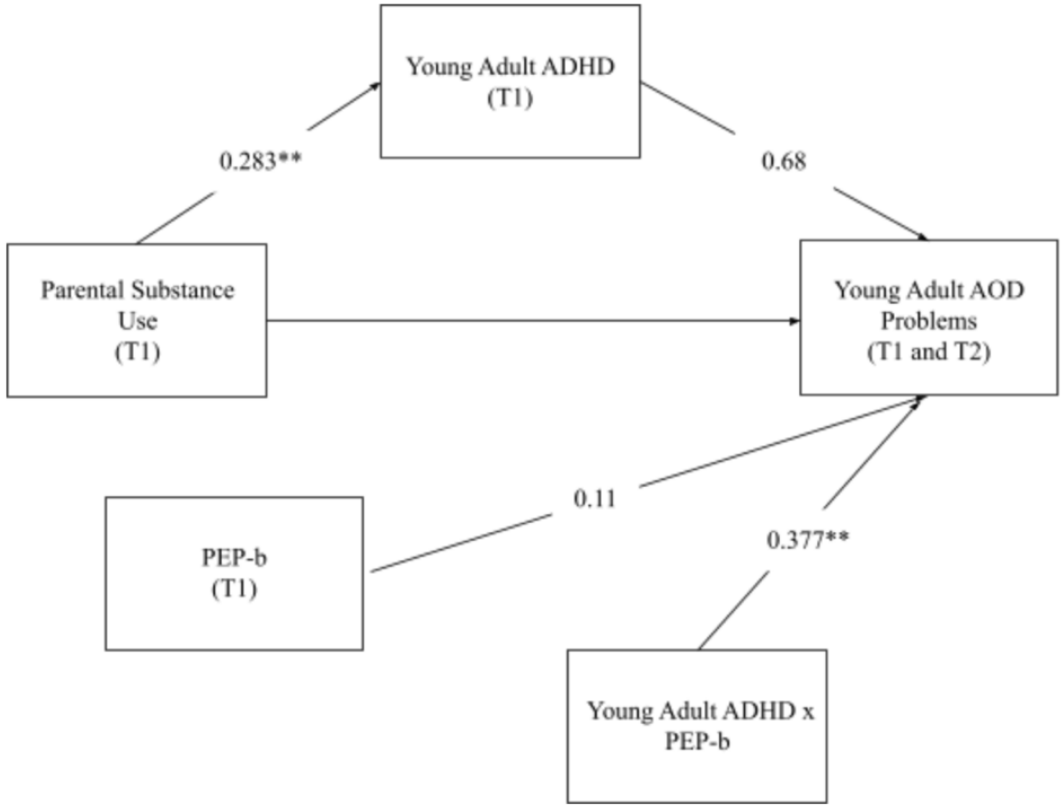
Paths	B(SE)	β	95% CI of B
Direct effects			
Parent substance use T1 → AOD use problems T2	.158(.213)	.122	[-.259, .575]
Parent substance use T1 → ADHD symptoms T1	.08(.032)	.231	[.016, .143]**
ADHD symptoms T1 → AOD use problems T2	.262(.401)	.07	[-.524, 1.047]
Covariates			
Sex T1 → AOD use problems T2	.192(1.153)	.017	[-2.067, 2.452]
Age T1 → AOD use problems T2	-.378(.207)	-.144	[-.784, .028]
Interaction effect			
ADHD symptoms × PEP-b → AOD use problems T2	.062(.02)	.09	[.13, .03]**
Conditional indirect effect			
Parent substance use T1 → ADHD symptoms × PEP-b → AOD use problems T2	1.669(.81)		[.384, 3.26]*

Notes. T1 = Time-point 1; T2 = Time-point 2. PEP-b = baseline pre-ejection period, AOD = alcohol or other drugs, SE = standard error, CI = confidence interval.

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

Figure 2.

Moderated Mediation Model of the Associations Among Parental Substance Use, Young Adult ADHD, Young Adult AOD Use problems, and PEP-b.



Notes. T1 = time point 1; T2 = time point 2. Age and gender at T1 were controlled in the analyses. The controlled paths are not displayed for clarity. Only standardized parameters of significant paths are presented in the figure.

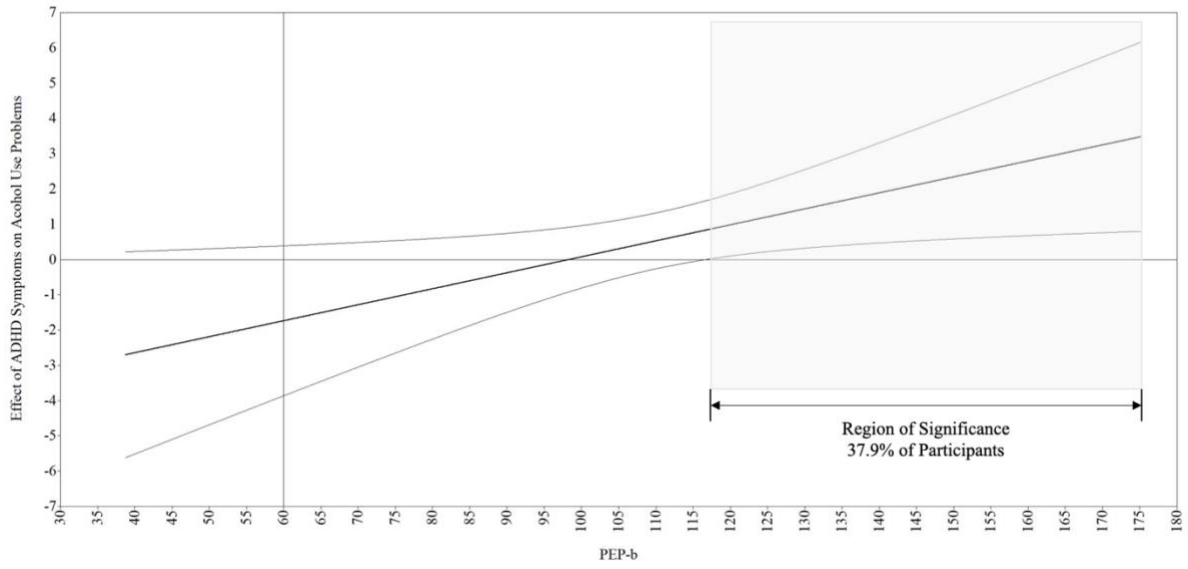
3.3 Mechanistic Analyses

Johnson and Neyman's (1936) technique was used to probe and interpret the moderating role of SNS reactivity on the associations between young adult ADHD and young adult AOD use problems (Figure 3). As Figure 3 suggests, for participants with lower levels of baseline SNS activity (i.e., higher PEP-b), ADHD was associated with more AOD use problems. Furthermore,

ADHD was associated with fewer AOD use problems for participants with higher levels of baseline SNS activity (i.e., lower PEP-b).

Figure 3.

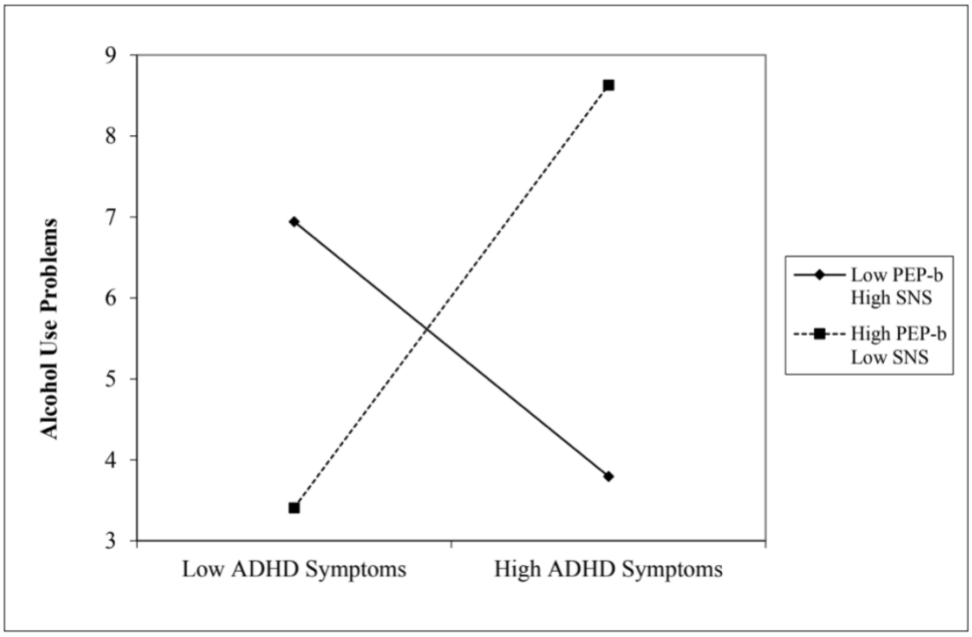
Interpretation of the Indirect Effect of Parental Substance Use on Young Adult AOD Use Problems via Young Adult ADHD Symptoms, Contingent on PEP-b.



To test for mediation analyses, I used the product coefficient approach with bootstrapping resampling (10K). The bootstrapping approach allows corrections for SE bias that are common in the abnormal distribution of the product coefficient, as well as enhances the power of the mediation test (Preacher et al., 2007). The moderation of the mediation by the SNS was examined using the conditional indirect effect procedure (Preacher et al., 2007). Results showed that the indirect effect of parental substance use on young adult AOD use problems through young adult ADHD symptoms, and conditional on PEP-b, was significant ($\alpha^*\beta = 0.157$, $p < 0.039$). Specifically, the indirect effect between parental substance use and young adult AOD use problems through young adult ADHD symptoms was positive among participants with high PEP-b but negative for participants with low PEP-b. These associations are presented in in Figure 4.

Figure 4.

Visualization of Two-way Interaction Between ADHD and PEP-b on Young Adult AOD Use Problems.



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CHAPTER 4

DISCUSSION

ADHD is significantly associated with neurophysiological vulnerabilities that are implicated in substance use behaviors among young adults (Baker et al., 2012; Luderer et al., 2021; Volkow, Wang, Newcorn, et al., 2007; Volkow, Wang, Telang, et al., 2007; Vollstädt-Klein et al., 2020), especially among those that grew up with a parent who has SUPs. The present study extended this line of inquiry by utilizing longitudinal data drawn from a sample of low-SES rural young adults and incorporating an experimental task for self-regulation to test the impacts on parental substance use on young adult AOD use problems through the mechanism of ADHD. The aim was to test whether the effect of parental substance use on the risk of AOD use problems during young adulthood is dependent on the interaction between young adult ADHD symptoms and psychobiological sensitivity to stress (Karpyak et al., 2014).

4.1 Parental Substance Use and Young Adult AOD Use Problems

In support of our first hypothesis, parental substance use was found to be significantly associated with a higher risk for AOD use problems during young adulthood. This finding corroborates research that has shown that youth in homes in which a parent uses substances are more likely to utilize substances and develop SUPs themselves as a result of parents modeling that behavior (Akers & Jensen, 2006; Kruis et al., 2020; Lee et al., 2004). Social learning theory (Bandura & Walters, 1977) purports that patterns of behavior (i.e., AOD use problems) can be acquired through direct experience or by observing the behavior of others (i.e., parental substance use). For example, Akers et al. (1995) suggested that social learning theory could be

generalized to account for involvement in substance use among adolescents, specifically alcohol use and marijuana. Khron and colleagues (1985) also found support for social learning theory in the context of adolescent drinking and drug use. Taken as a whole, our findings suggest that children are at significantly higher risk for SUPs such as AOD use during young adulthood if a parental figure has modeled substance use during their lifetime.

4.2 Parental Substance Use, AOD Use Problems, and Mediation by Young Adult ADHD

In contrast to the first hypothesis, our second hypothesis was only partially supported, as the direct effect of parental substance use on young adult AOD use problems was mediated by ADHD, but only among youth with blunted self-regulation (i.e., high PEP-b). This finding could reflect the ages and size of the population used in the present study. In fact, Biederman and colleagues (2000) found that the prevalence of ADHD is usually lower in young adults than in adolescents. Specifically, in the oldest age group in the study (18 to 20 years), the presence of syndromic ADHD remission was greater than 60% (Biederman, Mick, et al., 2000), suggesting that the current study warrants further investigation using a sample of adolescents rather than just young adults. In addition, the sample size of the present study is relatively small, consisting of only 225 young adults, which may not allow for much individual variation among those who reported having ADHD symptoms. Future investigations utilizing the line of inquiry for the present study should use a much larger population sample to determine whether the present finding persists.

4.3 Parental Substance Use, AOD Use Problems, and Moderation by PEP-b

Our third hypothesis was partially supported as our findings indicated that high PEP-b exacerbated the relationship between young adult ADHD symptoms and AOD use problems, whereas low PEP-b did not buffer the connection between ADHD symptoms and AOD use

problem risk for youth. This finding corroborates that of Crowel and colleagues (2006) which found that children with ADHD were characterized by lengthened PEP (decreased sympathetic functioning) at baseline, suggesting that ADHD places youth at higher risk for AOD use problems. Polyvagal theory (Porges, 1995) could also serve as an explanation for why the offspring of parents with SUPs would be at increased risk for decreased SNS reactivity at baseline. For example, research suggests that, in the presence of a chronic stressor, the SNS may be activated, allowing for fight or flight behaviors while consequently being more metabolically costly (Porges, 1998). Research indicates that parental substance use is highly correlated with environmental stress and disruption for offspring (Chassin et al., 1991), indicating that the SNS may be chronically aroused for children raised in this context. Additionally, Brenner and Beauchaine (2011) found that low PEP reactivity in response to incentives positively predicted increases in alcohol use longitudinally. Since low PEP reactivity may suggest that an individual has higher levels of PEP at baseline, our findings add to considerable evidence for a central role of compromised SNS reactivity in the development of SUPs.

4.4 Implications for Policy and Preventative Intervention

The present findings bear important implications for policy and intervention efforts to prevent AOD use problems among rural low-SES young adults who report growing up in homes in which a parent uses substances. Recent research supports the need for parent- and family-centered intervention programs for young adults that specifically target self-regulation skills and psychobiological processes that bear important implications in the development of AOD use behaviors during youth (Dodge, 2001; Stormshak et al., 2009; Stormshak & Dishion, 2009). Additionally, research also suggests that there is a need to confront early life disparities of mental and physical health with policy initiatives (Shonkoff et al., 2009). For example, Anda

(2014) and Larkin et al. (2014) suggest utilizing a biopsychosocial approach to inform social policies that respond to early life adversity in order to achieve widespread improvements in the overall health and well-being of the population. Additionally, the authors stress the importance of focusing on multiple levels of at-risk individuals, including families, communities, and the larger society, when discussing prevention and intervention response strategies. The biopsychosocial perspective is supported by economic research involving human capital development which has suggested that the effective implementation of these strategies may result in significant cost savings (Mathur, 1999). Overall, there are significant mental health risk outcomes for youth exposed to childhood adversity (Afifi et al., 2008), including but not limited to the exposure to parental substance use problems. Introducing policy initiatives that address socioeconomic inequities as well as prevention efforts that reduce the exposure of youth to adverse childhood events could significantly reduce the prevalence of addiction psychopathology and associated mental problems in the overall population.

Those responsible for the development of intervention programs may benefit from considering the risk for parental substance use and its effect on the development of ADHD and AOD use risk for subsequent generations. Hülsheger and colleges (2013) found that intervention programs that utilize mindfulness activities can impact HRV and emotion regulation, possibly buffering the effect of parental substance use on offspring ADHD and AOD use problems. Additionally, a growing number of studies have found that mindfulness-based therapies can help those with externalizing disorders, including ADHD. For example, a meta-analysis conducted by Cairncross and Miller (2020) found that mindfulness-based therapies were effective in reducing the core symptoms of ADHD, including inattention and hyperactivity/impulsivity, irrespective of age. Further, recent research suggests that brain plasticity exists, especially in the

context of intense neurocognitive training. For example, working memory training was shown to mitigate the core symptoms of ADHD (Beck et al., 2010). This finding can be plausibly applied to the subsequent risk for addiction (Bickel et al., 2011). Therefore, it is possible that preventative intervention programs can tailor program content to effectively target self-regulation and working memory among at-risk youth, potentially reducing their levels of impulsivity as well as the risk for AOD use problems among these young adults.

4.5 Limitations and Strengths

Our present findings should be interpreted within the study's limitations. First, the targeted sample comprised rural low-SES young adults. To increase the generalizability of the present study, future research should test the current models in impoverished metropolitan samples. However, a strength of the present study is the use of an understudied sample of young adults that are at significant risk of AOD use problems. Additionally, the current study utilized psychophysiological data as a proxy for self-regulation and emotional regulation, in relation to AOD use problem risk for young adults. Last, in the present study, self-regulation was measured under the experimental condition of acute cognitive stress. This acute stress procedure aimed to measure self-regulation via HRV reactivity when under social stress evoked from being evaluated during performance in front of an audience of research assistants. However, other types of acute stressors could play a role in the mechanism that underlies young adult AOD use problems, such as the modeling of parental substance-using behaviors or consuming substances as a means of stress reduction. Overall, the present study carries important strengths that contribute to the confidence in the reported results. These include the use of a multi-method longitudinal follow-up design using an understudied sample consisting of young adults that are at high-risk for externalizing problems such as ADHD and AOD use problems.

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