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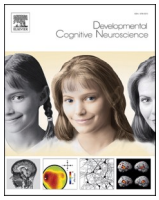

Neural cognitive control moderates the longitudinal link between hedonia and substance use across adolescence

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ABSTRACT

Hedonic dysregulation is evident in addiction and substance use disorders, but it is not clearly understood how hedonic processes may interact with brain development related to cognitive control to influence risky decision making and substance use during adolescence. The present study used prospective longitudinal data to clarify the role of cognitive control in the link between hedonic experiences and the development of substance use during adolescence. Participants included 167 adolescents (53% male) assessed at four time points, annually. Adolescents participated in a functional magnetic resonance imaging (fMRI) session where blood-oxygen level dependent (BOLD) response was monitored during the Multi-Source- Interference Task to assess cognitive control. Substance use and hedonia were assessed using self-report. A two-group growth curve model of substance use with hedonia as a time-varying covariate indicated that higher levels of hedonia predicted higher substance use, but only in adolescents with higher activation in the frontoparietal regions and in the rostral anterior cingulate cortex during cognitive control. Results elucidate the moderating effects of neural cognitive control on associations between hedonia and adolescent substance use, suggesting that lower cognitive control functioning in the brain may exacerbate risk for substance use promoted by hedonia.

1. Introduction

Adolescence is a vulnerable neurodevelopmental period as it involves physical, emotional, social, cognitive, and behavioral changes with implications for increases in sensation seeking and risk-taking behaviors, including substance use (Casey et al., 2008; Steinberg, 2008). Research suggests that earlier initiation of substance use in adolescence leads to poorer adjustment outcomes and further increases risk for substance use disorders and addiction (Castellanos-Ryan et al., 2017; Squeglia and Gray, 2016). Further, substance use during adolescence may increase vulnerability to the neurotoxic effects of these substances, especially in neurocognitive functioning related to risky decision making (Kim-Spoon et al., 2021; Schweinsburg et al., 2008). As such, it is important to understand risk and protective factors contributing to the development of substance use to inform prevention and intervention approaches during this developmentally salient period. The current prospective study investigates how two systems of research domain criteria (RDoC; Insel et al., 2010) focusing on hedonia (positive valence systems) and cognitive control (cognitive systems) jointly contribute to the development of substance use throughout adolescence.

1.1. Hedonia and substance use

Hedonia is characterized by the experience of pleasure. Hedonic feelings (e.g., positive affect, high intensity pleasure, and behavioral activation) can be influential in motivating behavior and decision making, which can lead to both maladaptive and adaptive functioning (Becker et al., 2019). Two competing theoretical perspectives suggest dual roles of hedonia in substance use initiation and progression. First, the reward deficiency theory suggests that hypofunction of the reward system predicts substance use escalation (Blum et al., 2000). Specifically, hypohedonia (i.e., low levels of hedonia, or anhedonia) promotes substance use, because substance use behavior is initiated to compensate for the reward deficiency and stimulate brain reward systems (Blum

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et al., 2000). Most prior empirical research has focused on anhedonia, or impaired hedonic processes evidenced by altered reward functioning and motivation in adolescents (Forbes and Dahl, 2012), and has shown the positive link between anhedonia and adolescent substance use (Christodoulou et al., 2020; Luby et al., 2018). Alternatively, the impulsivity theory suggests that addiction vulnerability is related to a hyperfunctioning reward system, such that substance use is the result of an impulsive response to cues predicting potential rewards (Luijten et al., 2017). Prior research suggests that hedonic dysregulation is evident in addiction processes and substance use disorders, implying that hedonia plays a role in the initial pleasurable feeling derived from substances that drive addictive processes (Koob and Le Moal, 1997; Monterosso and Ainslie, 2009). The role of hedonic dysregulation in the development of substance use behavior during adolescence has not been clearly understood. However, hedonics are particularly relevant to substance use during adolescence not only because this period is characterized by significant brain development related to reward seeking, but also because adolescents tend to engage in more risk-taking behaviors than children or adults (Dahl, 2004; Steinberg et al., 2008).

Research on sensation seeking and reward processing in adolescence provide important insight into the role of hedonic processes in substance use behaviors. Specifically, there is a normative peak in reward seeking behavior that occurs around the time of the onset of puberty (Dahl, 2004). It is important to note that the increased sensation for novelty and reward is adaptive during this period as adolescents seek out new environments and social experiences and thus, develop more knowledge and skills to use later in adulthood (Geier and Luna, 2009; Spear, 2012). However, heightened reward sensitivity coupled with immature or impaired top-down cognitive control may lead to bias in decision making resulting in risky behaviors (Kim-Spoon, Deater-Deckard et al., 2017). A recent meta-analysis examined neural evidence of vulnerability to problematic substance use and found support for hyperactivation of the striatum, a brain region involved in reward processing and motivation, predicting later problematic substance use during adolescence (Tervo-Clemmens et al., 2020). More empirical work is needed to clarify how hedonic processes influence risky decision making and the substance use during this vulnerable neurodevelopmental period.

1.2. Cognitive control

In addition to the increases in sensation seeking during adolescence, there is significant maturation in cognitive control during this period. Though previous research has demonstrated that substance use during adolescence affects brain development and is associated with poorer cognitive functioning (Lees et al., 2020; Squeglia and Gray, 2016), it remains unclear whether cognitive control functions as a risk or protective factor for later substance use during this period. Recent longitudinal studies found that better performance during cognitive control is a protective factor against adolescent substance use (Kim-Spoon et al., 2021), whereas impaired performance during cognitive control is a risk factor to adolescent substance use (Morin et al., 2019). Prospective longitudinal studies that involve both behavioral and neuroimaging assessments are needed to enhance mechanistic understanding of the role that cognitive control plays in the development of substance use.

Previous research has established that brain regions within the prefrontal cortex are important for cognitive control development during childhood and adolescence (Crone and Steinbeis, 2017). Longitudinal studies examining trajectories of cognitive control-related brain activation across adolescence have found developmental changes in frontoparietal regions (involved in interference inhibition), the dorsal and rostral anterior cingulate cortex (involved in error-processing), and the dorsolateral prefrontal cortex (involved in executive control; Kim-Spoon et al., 2021; Ordaz et al., 2013; Sebastian et al., 2013; Van Leijenhorst et al., 2010). Our conceptual framework focuses on the *interaction* between the reactive system (i.e., reward sensitivity) and the regulatory system (i.e., cognitive control) to understand the etiology of individual differences in adolescent risk-taking behaviors (see Kim-Spoon, Kahn et al., 2017 for a review). We propose that cognitive control *modulates* the operation of reward sensitivity in the service of goal directed behavior, which for some may result in substance use, resulting from difficulty in inhibiting behaviors that pursue reward seeking. In this paper, we suggest that hedonia may be linked to substance use behaviors depending on the developmental trajectory of cognitive control during adolescence.

The current prospective study investigated the moderating role of cognitive control, using both behavioral and neural measures, in the link between hedonic experiences and substance use using longitudinal data measured repeatedly over four years. We hypothesized that substance use would increase across adolescence and that the effects of hedonic levels on substance use would be weaker in adolescents with higher cognitive control (i.e., high cognitive control would be protective). There were two alternative hypotheses regarding the role of hedonia: First, consistent with the reward deficiency theory, lower levels of hedonia paired with lower cognitive control would be related to higher substance use. Second, consistent with the impulsivity theory, higher levels of hedonia paired with lower cognitive control would predict higher substance use.

2. Methods and materials

2.1. Participants

The sample included 167 adolescents (53% male) from a southeastern state in the United States. Adolescents participated in annual assessments across four years and were 13–14 years of age at Time 1 ($M = 14.07$, $SD = 0.54$ for Time 1, $M = 15.05$, $SD = 0.54$ for Time 2, $M = 16.07$, $SD = 0.56$ for Time 3, and $M = 17.01$, $SD = 0.55$ for Time 4). About 78% of adolescents identified as White, 14% African American, 2% other, and 6% as more than one race. The median annual family income was in the $35,000-$50,000 range. Inclusion criteria included being age 13 or 14 at Time 1. Exclusion criteria were claustrophobia, history of head injury resulting in loss of consciousness for $>$ 10 min, orthodontia impairing image acquisition, severe psychopathology (e.g., psychosis) and other contraindications to magnetic resonance imaging (MRI). At Time 1, 157 families participated, and at Time 2, 10 families were added for a final sample of 167 parent-adolescent dyads. At Time 2 data from 150 participants, at Time 3 data from 147 participants, and at Time 4 data from 150 participants were collected. Not all participants participated in all possible assessments for reasons including ineligibility for tasks (i.e., brain abnormality, not meeting MRI safety criteria), declined participant, and lost contact. Rate of participation was not significantly predicted by income, sex, race or study variables ($p = .80$).

2.2. Procedures

Data included in the present study were collected as part of a larger project. Adolescent participants were recruited via email announcements, flyers, and snowball sampling (word-of-mouth). Data collection was administered at university offices where participants completed self-report questionnaires, behavioral and neuroimaging tasks, and were interviewed by trained research assistants. On average, the study duration was five hours long and participants were compensated monetarily for their time. All procedures were approved by the institutional review board of the university and written informed consent or assent was received from all participants.

2.3. Measures

2.3.1. Hedonia

A hedonia factor score was created based on three measures that capture this construct according to theoretical work (Becker et al.,

2019). First, positive affect (10 items) was assessed via The Positive and Negative Affect Schedule at Times 1–4 (PANAS; Watson et al., 1988). Adolescents rated (1 = not at all to 5 = extremely) on various emotions or feelings in the past week (e.g., interest, enthusiasm). Mean scores were calculated, with higher scores indicating more positive affect (α = .82 ~.86 at Times 1–4). Second, high intensity pleasure (7 items) was captured via the Early Temperament Questionnaire-Revised Short Form.

(EATQ-R; Capaldi and Rothbart, 1992) which assesses adolescent's temperament at Times 1–4 (from 1 = almost always untrue to 5 = almost always true). Mean scores were calculated across 7 items (e.g., "I enjoy going places where there are big crowds and lots of excitement"), with higher scores indicating higher intensity pleasure (α = .62 ~.70 at Times 1–4). Third, behavioral activation (12 items) was assessed via the Behavioral Inhibition System and Behavioral Activation System Scale (BIS/BAS: Carver and White, 1994) at Times 1–4. Adolescents rated (1 = very true for me to 4 = very false for me) on statements reflecting tendency to search for novel, potentially rewarding experiences, sensitivity to reward, and pursuit of appetitive goals (α = .81 ~.83 at Times 1–4).

2.3.2. Substance use

Substance use (3 items) was assessed using a substance use index adapted from Wills et al. (2003) at Times 1–4. Adolescents reported typical frequency (i.e., which is the most true for you about using alcohol/smoking cigarettes/using marijuana?) using a 6–point response scale ranging from 1 (*never used*), 2 (*Tried once- twice*), 3 (*Used three-five times*), 4 (*usually use a few times a month*), 5 (*usually use a few times a week*), to 6 (*usually use every day*). A max score was calculated across cigarette, alcohol, and marijuana use, with higher scores indicating greater substance use (α = 0.61~.75 at Times 1–4). Intraclass correlation (ICC) values were assessed using two-way mixed effects models with absolute agreement in SPSS (ICC =.81; CI:0.656 −0.882).

2.3.3. Cognitive control

Adolescents completed the Multi-Source Interference Task (MISIT; Bush et al., 2003) while undergoing a functional MRI scan at Times 1–4. In each trial, adolescents were presented with three digits and were tasked with reporting the identity of the different digit (unlike the other two) by pressing a button. In neutral trials, the target's identity matched

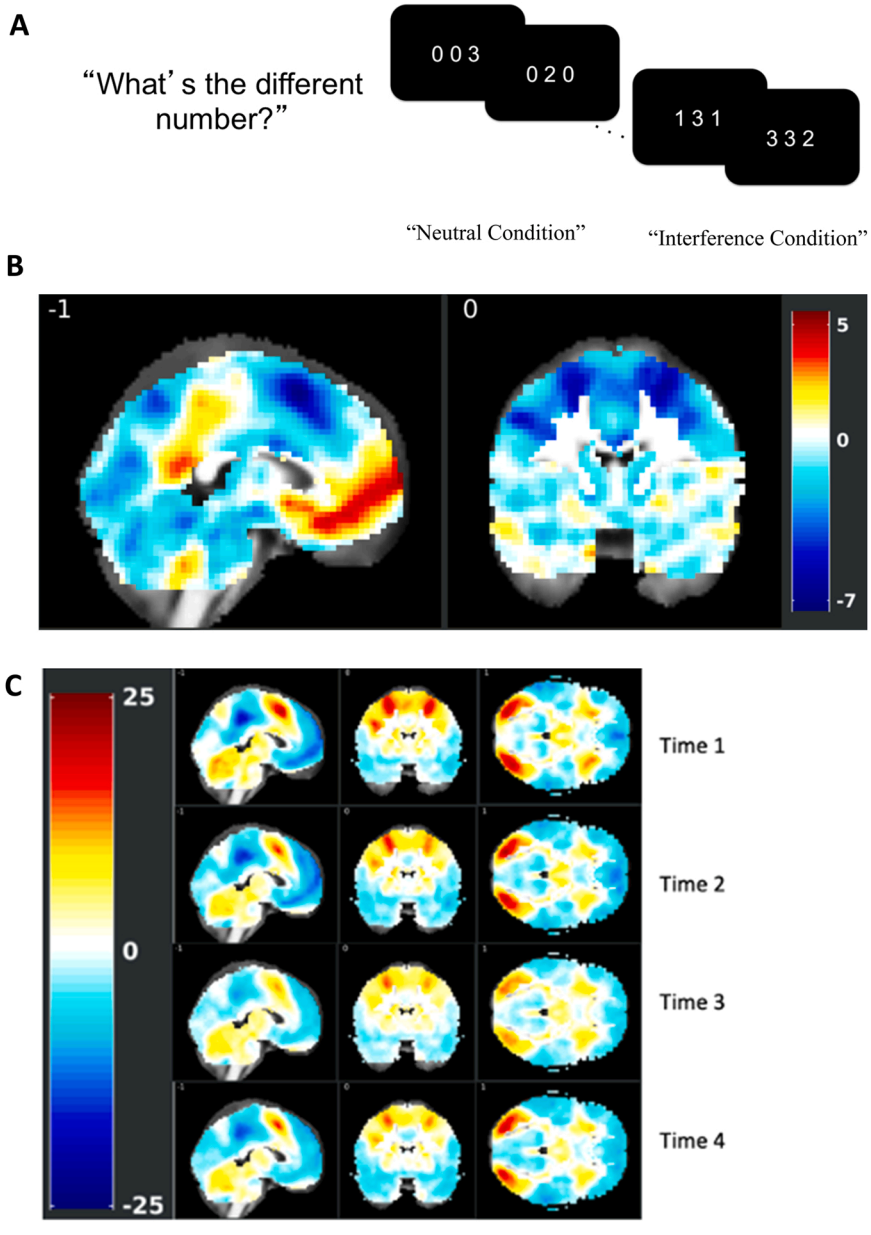

Fig. 1. A-C. Schematic Display of the Multi-Source Interference Task (MSIT) and Activation Maps Showing Significant Activation for the Interference-Neutral Contrast, Note: A) Adolescents were instructed to identify the different digit while ignoring its position. B) Statistical T map showing regions of positive and negative linear change in the interference effect on BOLD responses with time point using the Sandwich Estimator Toolbox after applying a gray matter mask. C) Statistical T maps showing regions of positive (interference > neutral) and negative (neutral > interference) interference effect for each time point after applying a gray matter mask. Figure reprinted from Kim-Spoon, J., Herd, T., Brieant, A., Elder, J., Lee, J., Deater-Deckard, K., & King-Casas, B. (2021). A 4-year longitudinal neuroimaging study of cognitive control using latent growth modeling: Developmental changes and brain-behavior associations. Neuroimage, 237, 118134.

the digit's presented location, whereas in interference trials, the target's identity was not congruent with the digit's presented location (see Fig. 1A-1 C). To assess task performance, we used intraindividual variability in response time, indexed as intraindividual standard deviations (ISD; MacDonald et al., 2012) for correct responses in the interference condition. Lower ISD scores represented higher cognitive control (ICC =.72; CI:0.478 −0.833).

2.3.4. Imaging acquisition and analysis

Neuroimaging data were obtained on a 3 T Siemens Tim Trio scanner using a 12-channel head matrix coil. Functional images were obtained with repetition time (TR) = 2 s, slice thickness = 4 mm, 34 axial slices, field of view (FoV) = 220 × 220 mm, echo time (TE) = 30 ms, flip angle = 90 degrees, voxel size = 3.4 × 3.4 × 4 mm, 64 × 64 grid, and slices were hyperangulated at 30 degrees from anterior-posterior commissure. Anatomical images were acquired with TR = 1.2 s, slice thickness = 1 mm, FoV = 245 × 245 mm, TE = 2.66 ms, flip angle = 8 degrees, and an isotropic 1 mm^3 voxel size across 192 slices.

SPM8 (Wellcome Trust Neuroimaging Center) was used to analyze the MSIT imaging data. A General Linear Model (GLM) was fit to each participant's preprocessed fMRI at each time point. The interference and neutral task conditions were modeled using a boxcar convolved with a canonical hemodynamic response function (HRF). For each GLM, we obtained a contrast-map by subtracting the Neutral beta-map from the Interfere beta-map. These contrast maps were entered into second-level GLMs at each longitudinal time-point, using root mean framewise displacement (FD) as a regressor of no interest. We assessed how the interference effect on BOLD changed with time-point by entering data from all four waves into a longitudinal group-level model using the Sandwich Estimator Toolbox, version 2.1.0 (SwE; Guillaume et al., 2014), with root mean FD as a no-interest regressor to account for age-correlated changes to in-scanner head motion (Satterthwaite et al., 2012).

We observed a significant interference effect on BOLD at each time point (see Fig. 1B). Our longitudinal model showed a significant linear change in the interference effect on BOLD in cognitive control regions identified by the MSIT. Using a cluster-defining false discovery rate (FDR) corrected threshold of p < 1e-5 and a gray matter mask, the SwE derived map of time-related changes in BOLD was used to identify nine clusters for an ROI analysis, including bilateral insula, bilateral middle frontal gyrus (MFG), left pre-supplementary motor area (pSMA), right pregenual anterior cingulate cortex (pACC), left inferior parietal lobule (IPL), right precuneus, and left middle occipital gyrus (see Fig. 1 C; for coordinates for peak regions within each time point, see Appendix A). From each time-point, the first eigenvariate was obtained, adjusting for the effect of interest. Two neural cognitive control scores were extracted based on longitudinal confirmatory factor analyses (see Appendix B): the "frontoparietal" factor scores (left and right insula, left and right MFG, left pSMA, left IPL, and right precuneus; ICC = 0.575; CI:0.400 −0.696) and the left rACC scores (ICC = .409 to .41; CI:0.176 −0.591). In a previous study, Kim-Spoon and colleagues (2021) reported that as adolescents' behavioral cognitive control improves with age, frontoparietal activation decreased and rACC activation increased, suggesting that lower frontoparietal activation and higher rACC activation may implicate better cognitive control. In addition, they demonstrated measurement invariance in longitudinal confirmatory factor analysis based on the multiple ROIs in the frontoparietal regions across four years, implying longitudinal reliability of ROI indicators during the MSIT task (Kim-Spoon et al., 2021).

2.4. Data analytic approach

Models were tested using Structural Equation Modeling (SEM) in M*plus* (Muthén and Muthén, 1998–, 2021). We first examined developmental trajectories of hedonia and substance use by testing growth curve models. In the no growth model (baseline model), non-significant change in the slope was assumed. In the linear growth model, a linear pattern of change was assumed with factor loadings fixed to 0, 1, 2, and 3 from Time 1 through Time 4. The latent basis growth model allowed the data to estimate the shape of growth by fixing the first and last time points (to 0 and 1, respectively) and freely estimating the second and third time points. Next, time-specific hedonia variables were introduced to the growth curve model of substance use as time-varying covariates to account for the influence of individual hedonic levels on substance use. To use longitudinal scores of cognitive control as a moderator, we performed growth mixture modeling to examine whether there were discrete latent classes based on longitudinal trajectory patterns. Then, to determine whether the effects of hedonia on developmental trajectories of substance use differed by the level of cognitive control, a two-group growth curve model was tested with low (lowest 50%) and high (highest 50%) cognitive control groups. Additionally, a Wald's test of parameter constraints was used to test whether imposing equality constraints significantly degrade model fit or not. Significant Wald's test suggested that the groups differed significantly with respect to the association between hedonia and substance use.

3. Results

3.1. Descriptive Statistics and Demographic Covariates Testing

Correlations and descriptive statistics for all study variables are presented in Table 1. There was one outlier for Time 1 and one outlier for Time 2 (> 3.29 SD). We tested using Winsorized data and found that the results are consistent. Thus, we decided to keep the models using the original (non-Winsorized) data. Multivariate general linear modeling analyses for testing demographic covariates indicated that sex ($p = .14$), race ($p = .13$), and family income ($p = .26$) were not significant predictors of study variables, and thus were not included in the hypothesized model testing.

3.2. Confirmatory factor analysis and growth curve models of hedonia

To calculate composite variables of hedonia, assessed by positive affect, behavioral activation, and high intensity pleasure, we conducted confirmatory factor analyses with a single latent factor based on three indicators. The model was fully saturated ($\chi^2 = 0$, $df = 0$). All factor loadings were statistically significant (standardized $\lambda > 0.32$; all *ps* <0.05). After construct validation, an averaged composite at each time point was created using standardized scores of positive affect, behavioral activation, and high intensity pleasure (ICC = .89; CI: 0.854 −0.918).

We further estimated longitudinal trajectories of hedonia using growth curve models. Results indicated that the no growth model provided the best fit, indicating non-significant growth trajectories over time (see Appendix C). Therefore, we conceptualized hedonia levels at each time point as a time-varying covariate to examine within-person relations between hedonia and substance use.

3.3. Growth curve models for substance use

Three separate models were fit in order to determine the shape of the trajectories of substance use across four years (see Appendix D). The linear model provided best fit for the data compared to the no growth and latent growth models. The mean ($\mu = 1.47$, $SE = 0.06$) and variance ($\sigma^2 = .54$, $SE = 0.08$) of the intercept as well as the mean ($\mu = 1.21$, $SE = 0.10$) and variance ($\sigma^2 = .1.32$, $SE = 0.22$) of the slope were significant (all *ps* < 0.001), indicating significant increases in substance use over time with significant individual differences in starting points as well as trajectory patterns.

Table 1
Descriptive Statistics and Correlations of Study Variables.

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	M	SD	Min	Max
Hedonia														
1. Hedonia T1											3.47	0.47	1.96	4.62
2. Hedonia T2	.70 **										3.47	0.46	2.18	4.51
3. Hedonia T3	.61 **	.70 **									3.50	0.44	2.48	4.71
4. Hedonia T4	.64 **	.62 **	.70 **								3.48	0.49	1.73	4.70
Substance Use														
5. Substance Use T1	.11	.13	.12	.11							1.48	0.77	1	6
6. Substance Use T2	.14	.17 *	.19 *	.18 *	.70 **						1.75	1.06	1	6
7. Substance Use T3	.08	.04	.21 *	.18 *	.53 *	.67 **					2.19	1.22	1	6
8. Substance Use T4	-.02	.03	.14	.12	.49 **	.63 **	.78 **				2.69	1.39	1	6
Cognitive Control														
9. Frontoparietal	-.01	-.03	-.06	-.07	.09	.08	.16	.11			-0.58	0.54	-1.77	1.36
10. rACC	.06	.07	-.01	-.01	-.17 *	-.10	-.15	-.21*	-.14		-0.40	0.27	-1.58	0.26
11. Behavior	.05	.00	.00	.02	.07	.07	.15	.19 *	.19 *	-.16 *	0.21	0.04	0.12	0.35

Note: rACC= rostral anterior cingulate cortex; T1 = Time 1; T2 = Time 2; T3 = Time 3; T4 = Time 4; Behavior is indicated by ISD (intraindividual standard deviations) with lower scores suggesting better cognitive control. * $p < .05$; ** $p < .01$.

3.4. Growth mixture modeling of cognitive control

Given that we had cognitive control data assessed over four years, we explored whether cognitive control trajectory patterns vary significantly across adolescents and thus would need to be viewed as a time-varying moderator. We estimated discrete latent classes based on longitudinal trajectories of cognitive control using growth mixture modeling (Muthén and Muthén, 2000). Results indicated that, for the behavioral cognitive control, frontoparietal activation, and rACC activation, the one-class model provided the best fit, indicating that the pattern of growth trajectories was similar across adolescents (see Appendix F). Given the evidence indicating growth trajectories of behavioral cognitive control as well as frontoparietal activation and rACC activation during cognitive control were homogenous, we calculated a grand mean by averaging across four time points to represent each individual's general level of cognitive control.

3.5. Substance use with hedonia as a time-varying covariate moderated by cognitive control

We tested whether adolescents with high cognitive control showed weaker associations between hedonia and substance use, compared to those with low levels of cognitive control (i.e., high cognitive control as a protective factor). For testing group differences, we imposed equality constraints to test numeric invariance with respect to the effects of hedonia on substance use. If model fit was significantly degraded by imposing equality constraints, the results indicated significant differences between differing levels of cognitive control. We used longitudinal levels of cognitive control (moderator) to create groups for testing the moderator effect via a multiple group modeling method (e.g., Flora et al., 2006).

To test cognitive control as a moderator (i.e., grouping variable), we created two groups using a median split as low (n = 80) vs. high (n = 80) groups.[1] We tested whether adolescents with lower vs. higher scores of cognitive control showed different patterns of hedonia effects on substance use, separately for frontoparietal activation, rACC activation, and behavioral cognitive control (see Appendix E for correlations for low vs. high cognitive control groups). The effects of hedonia were equalized across time within each group, because freeing those effects did not improve the model fit significantly.

Regarding the frontoparietal region as the grouping variable, the model fit was acceptable ($\chi^2 = 54.52$, $df = 41$, $p = .077$, RMSEA = 0.07, CFI = .96). As shown in Fig. 2, hedonia significantly predicted substance use for adolescents with higher frontoparietal activation ($b = 0.34$, $SE = 0.13$, $p = .008$), but not for adolescents with lower frontoparietal activation ($b = -0.02$, $SE = 0.12$, $p = .891$). Results suggested that hedonia was positively associated with substance use only for adolescents exhibiting high levels of activation in frontoparietal regions.

Regarding the rACC as the grouping variable, the resulting model fit was acceptable ($\chi^2 = 46.66$, $df = 40$, $p = .218$, RMSEA = 0.05, CFI = .98). In Fig. 3, hedonia predicted substance use for adolescents with higher activation in the rACC ($b = 0.33$ $SE = 0.13$ $p = 0.011$), but not for adolescents with lower activation in the rACC ($b = .10$, $SE = 0.12$ $p = .410$), suggesting that hedonia was associated with substance use only for adolescents exhibiting high levels of activation in the rACC.

Regarding behavioral cognitive control as the grouping variable, the model fit was acceptable ($\chi^2 = 48.17$, $df = 41$, $p = .205$, RMSEA = 0.05, CFI = 0.98. However, as shown in Fig. 4, hedonia did not predict substance use regardless of the level of behavioral cognitive control ($b = 0.16$ $SE = 0.12$ $p = 0.180$ for the high ISD group; $b = .11$, $SE = 0.13$ $p = 0.407$ for the low ISD group). Results suggested non-significant associations between hedonia and substance use which did not vary by behavioral cognitive control levels.

Finally, for testing whether the magnitude of the hedonia-substance use link differed significantly between the high and low groups, we imposed equality constraints on the effects of hedonia on substance use. This numeric invariance tested whether we can assume that the effects of hedonia on substance use are numerically identical. Regarding frontoparietal activation, such constraints did significantly degrade model fit (Wald $\chi^2 = 4.12$, $df = 1$, $p = .042$). Thus, the results suggested that the two groups significantly differed with respect to the effects of hedonia on substance use, such that the magnitude of the association was significantly stronger for adolescents with higher frontoparietal activation than for adolescents with lower FP activation. Regarding rACC activation, such constraints did not significantly degrade model fit (Wald $\chi^2 = 1.63$, $df = 1$, $p = .202$), suggesting that the magnitude difference in the effects of hedonia on substance use between the two groups was not statistically significant. Similarly, regarding behavioral cognitive control, such constraints did not significantly degrade model fit, indicating non-significant group differences in the effects of hedonia on substance use on estimates (Wald $\chi^2 = .11$, $df = 1$, $p = .743$).

4. Discussion

This study aimed to investigate how two systems of RDoC—hedonia (positive valence systems) and cognitive control (cognitive systems)—interact to contribute to substance use behaviors across adolescence at both neural and behavioral levels. Our findings provide insight into the mechanistic understanding of key factors contributing to substance use

[1] [1] Total N (160) excluded seven adolescents whose neural cognitive control data were not available due to not meeting MRI safety criteria (n = 2), refusal to scan (n = 3) and movement greater than 3 mm (n = 2).

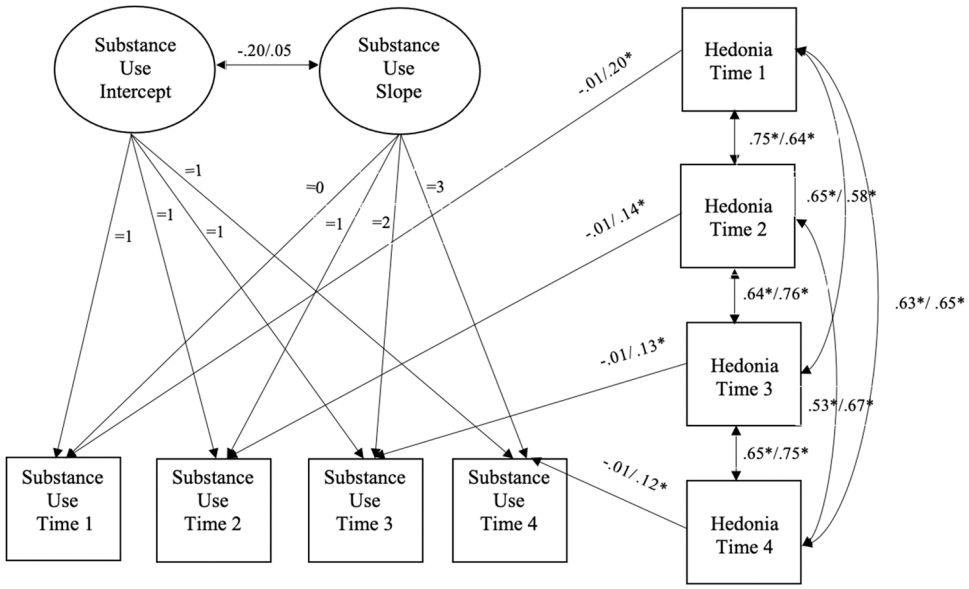

Fig. 2. *Growth Curve Model of Substance Use with Hedonia as a Time Varying Covariate, Moderated by Neural Cognitive Control (Frontoparietal Activation), Note.* Standardized estimates on the left are for the high cognitive control group, and estimates on the right are for the low cognitive control group. "= " indicates fixed parameters.

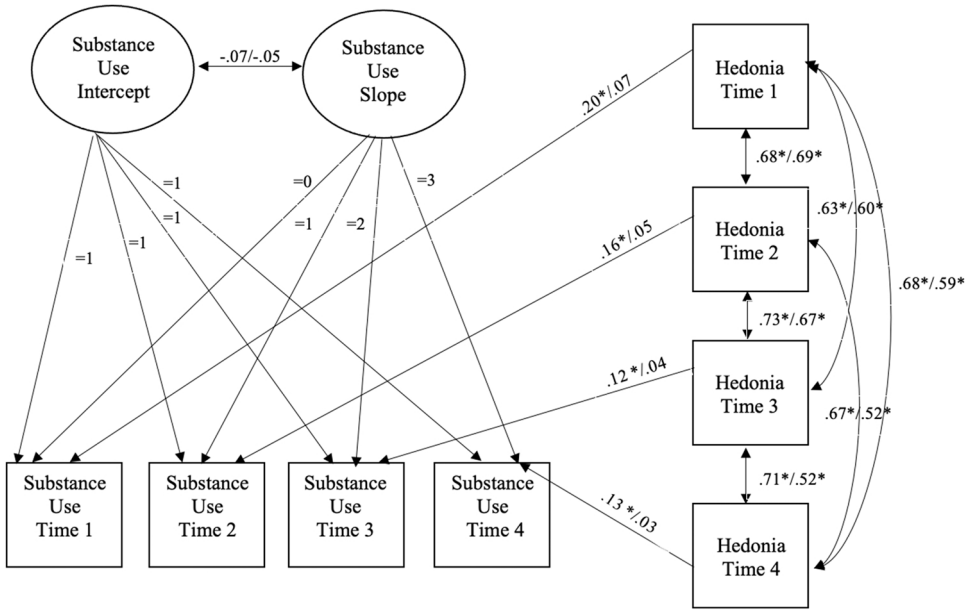

Fig. 3. *Growth Curve model of Substance Use with Hedonia as a Time Varying Covariate, Moderated by Neural Cognitive Control (rACC Activation), Note.* Standardized estimates on the left are for the high cognitive control group, and estimates on the right are for the low cognitive control group. "= " indicates fixed parameters.

development by revealing neuro-protective effects of cognitive control on the longitudinal associations between personality risk factors (hedonia) and the development of substance use.

Examining the within-person relation between the substance use growth functions and time-specific hedonia levels, we discovered that higher levels of hedonia were related to higher substance use. Our findings dovetail with previous research showing that elevated activation of positive valence functioning, such as reward responsivity and behavioral activation, predicts future substance use onset and substance use problems (Alloy et al., 2009; Stice et al., 2013). Further, our results support that higher levels of hedonia may facilitate substance use fueled by anticipated feelings of pleasure or gratification (Ainslie, 2000), rather than anhedonic feelings associated with higher substance use (Kwako et al., 2016). This finding highlights the role of reward or pleasure seeking as the motivation of using substances among adolescents, which is consistent with the observation that initial pleasure plays an important role at the start of the addiction process (Kennett et al., 2013). The highly rewarding substance use may set up heightened expectations of future reward (Monterosso and Ainslie, 2009) which could drive some adolescents to engage in problematic substance use.

Regarding cognitive control as a moderating factor for the effect of hedonia, we found that higher hedonia was significantly associated with higher substance use, only for adolescents with higher activation in frontoparietal regions during cognitive control. Research suggests that higher frontoparietal activation during cognitive control reflects less efficient neural functioning (Crone and Steinbeis, 2017; Kim-Spoon et al., 2021; Luna et al., 2010) and individuals with substance use dependence show inefficiency of frontoparietal cortical activity during

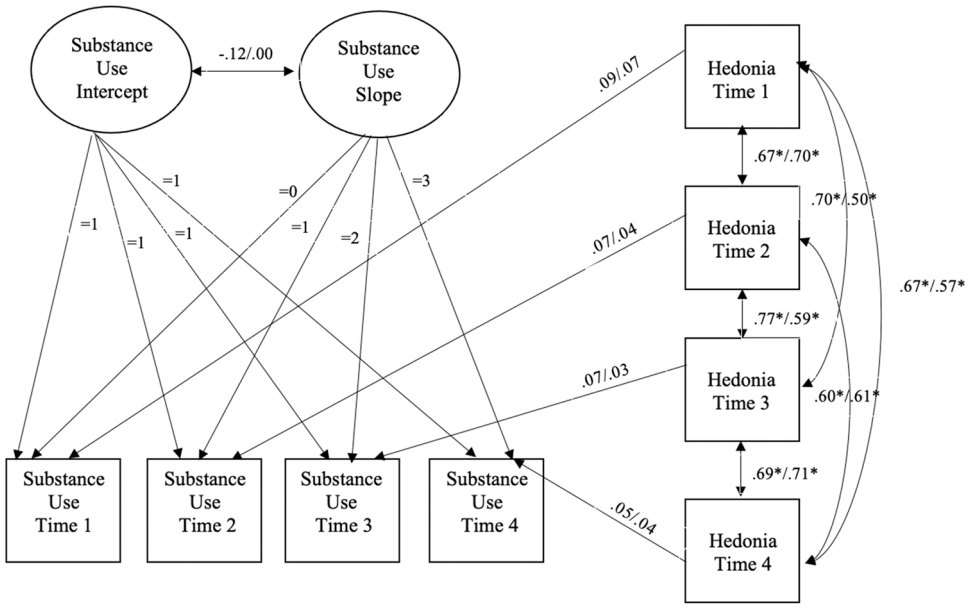

Fig. 4. *Growth Curve model of Substance Use with Hedonia as a Time Varying Covariate, Moderated by Behavioral Cognitive Control, Note.* Standardized estimates on the left are for the high cognitive control group, and estimates on the right are for the low cognitive control group. "= " indicates fixed parameters.

delay discounting (Monterosso et al., 2007). Importantly, our results demonstrate that hedonia can be a risk factor, particularly when it is coupled with inefficient cognitive processing. Although our measure of hedonia was heterogeneous, including measures of temperament, reward responsiveness, and positive affect, this moderation effect supports the theoretical perspective that the prefrontal regulatory system plays a modulating role on the reward system that contributes to adolescent health risk behaviors (Kim-Spoon, Deater-Deckard et al., 2017).

We found that higher hedonia was associated with substance use only for adolescents with higher levels of rACC activation during cognitive control; however, given that group differences were not statistically significant, we interpret this finding with caution. These findings are also not what we expected, as higher rACC activation during cognitive control implicates better cognitive control (Kim-Spoon et al., 2021). The theory of expected value of control (EVC) proposes that the anterior cingulate cortex (ACC) integrates information pertaining to the value of expected outcomes, the amount of control to be invested to achieve the competing outcomes, and the cost of obtaining each outcome in terms of cognitive mental efforts (Shenhav et al., 2013). Taking this perspective, the significant associations between hedonia and substance use for adolescents with higher activation (or less deactivation) in the rACC (implicating higher cognitive control) may imply that these adolescents were actively engaging in evaluating outcomes and *chose* to use substances as a voluntary reward-seeking behavior (Ainslie, 2000). Importantly, the integrated pattern of brain activation during cognitive control—i.e., elevated activation of both frontoparietal regions and the rACC—may indicate the vulnerability that amplifies the hedonia effects on substance use. This neural pattern may reflect brain processes of adolescents who make impulsive choices in the face of anticipated appetitive reward, rather than controlled choices according to principle—i.e., active evaluation of appetitive reward prompt them to make decisions according to "particulars" instead of "universals" (Aristotle, 1984; pp. 1147; Monterosso et al., 2007).

In contrast to neural cognitive control, behavioral cognitive control levels did not moderate associations between hedonia and substance use. We found modest yet significant correlations between behavioral and neural indicators of cognitive control, which are consistent with previous findings using the MSIT in adolescent samples (Fitzgerald et al., 2010; Taylor et al., 2006). One explanation is that behavioral responses are more specific to the context of the task. Neural indicators of cognitive control appear to be more sensitive measures than behavioral indicators of cognitive control to capture vulnerability to making risky decisions in real-life situations, particularly driven by hedonic propensity.

Our findings have important implications for identifying adolescents who may be vulnerable to risky decision making, particularly regarding substance use. Our data suggest that higher levels of hedonia may motivate adolescents' initial responsiveness to reward during substance use decision making. This finding emphasizes the role of pleasure seeking (i.e., hedonia) in the initial use of substances (Kennett et al., 2013). However, the role of pleasure seeking may change according to progression of substance use, as suggested by the neurobiological disease model (Volkow, 2005). That is, initial substance use may release a large amount of dopamine in the brain causing intense feelings of pleasure, and then repeated substance use may result in tolerance for the substance (with less pleasure experienced) followed by the emergence of a negative emotional state—anhedonia—which may perpetuate substance-seeking (Koob and Le Moal, 1997). However, our analyses include adolescents from a community sample, not those with problematic substance use. Replications in clinical samples are warranted to clarify generalization of our findings. Notably, our findings demonstrate that the hedonia effects can be deterred by strengthening cognitive control during adolescence when the brain undergoes important developmental changes and substance use behavior emerges. A fruitful direction for future research is to examine how the roles of positive valence systems and cognitive systems may change in relation to the progression of substance use problems.

Despite the current study's strengths, there are limitations and future directions to be noted. First, although we used longitudinal data, their correlational nature prevents us from inferring causality. It is also important to note that we have not considered bi-directional associations between hedonia and substance use across waves, which limits our understanding of the bidirectional nature of these associations during this period. Second, we used a community sample of adolescents. Future work may benefit from investigating these associations in a clinical sample, which may show stronger effects of hedonia or cognitive control, to produce results that can be more directly applied to intervention efforts for youths with substance use disorders. If this study is replicated in older samples, it may also be beneficial to examine problematic

substance use, as opposed to general consumption. Additionally, it would be informative for future work to examine whether the effects of hedonia on substance use may vary depending on the type of substance. Finally, given prior research indicating distinctive factor structure and differential predictability of social anhedonia versus physical anhedonia (Olino et al., 2018), future work would benefit from considering distinctive nature of social versus physical hedonia (or anhedonia) experiences related to substance use behaviors.

This is the first prospective longitudinal study to clarify the role of hedonia in the development of substance use behaviors and to investigate theoretically informed moderating effects of cognitive control across adolescence. Our findings illustrate that cognitive control modulates the within-person effects of hedonia to predict longitudinal trajectories of substance use behaviors. This research is an important step towards identifying adolescents vulnerable to maladaptive pathways that may lead to problematic substance use. Furthermore, it provides implications for preventative intervention approaches, such as the promotion of cognitive control related to risky decision making in the presence of potential rewards, in attempt to mitigate cascading risk for substance use among adolescents with hedonic propensity.

Declaration of Competing Interest

There was no conflict of interest.

Data Availability

The datasets generated and/or analyzed during the current study are not currently publicly available but are available from the corresponding author on request.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.dcn.2022.101111.

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