Striatal Activity to Reward Anticipation as a Moderator of the Relation Between Early Behavioral Inhibition and Changes in Anxiety and Depressive Symptoms from Adolescence to Adulthood

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Key Points

Question: How does reward processing in the brain modify trajectories of anxiety and depression among individuals with an inhibited childhood temperament, who are at greater risk for both forms of psychopathology?

Findings: This three-decade cohort study showed that the association between early childhood inhibition (14-24 months) and worsening depressive, but not anxiety, symptoms across ages 15-26 was observed only among those who showed blunted activity in the ventral striatum to reward anticipation in adolescence.

Meaning: These findings suggest that temperamental and neurocognitive risk factors play a role in the etiology and long-term development of different forms of internalizing psychopathology.

Abstract

Importance: The early childhood temperament of Behavioral Inhibition (BI), characterized by inhibited and fearful behaviors, has been associated with heightened risk for anxiety and depression across the lifespan. Although several neurocognitive correlates underlying vulnerability to the development of anxiety among inhibited children have been identified, little is known about the neurocognitive correlates underlying vulnerability to the development of depression.

Objective: To examine whether blunted striatal activation to reward anticipation, a well-documented neurocognitive vulnerability marker of depression, moderates the relation between early BI and the developmental changes in depression and anxiety from adolescence to adulthood.

Design, Setting, and Participants: Participants (*N*=165; 50% female) in this prospective longitudinal study were recruited at 4 months of age between 1989-1993 in the US. Follow-up assessments extended into 2018 (age 26). Data were analyzed between September 2021 to March 2022.

Main Outcomes and Measures: BI was measured through an observation paradigm in infancy (ages 14 and 24 months). Neural activity to anticipated rewards during a Monetary Incentive Delay Task was measured using fMRI in adolescence (between ages 15-18, *n*= 83 had usable data). Anxiety and depressive symptoms were self-reported across adolescence to young adulthood (ages 15 and 26, *n*=108). A latent change score model, accounting for the interdependence between anxiety and depression, tested the moderating role of striatal activity to reward anticipation in the relation between early BI and changes in anxiety and depressive symptoms. A region of interest approach limited statistical tests to regions within the striatum (i.e., nucleus accumbens, caudate head, caudate body, putamen).

Results: Preliminary analyses revealed significant increases in anxiety and depressive symptoms across ages 15-26, as well as individual variation in the magnitude of changes. Main analyses showed that reduced activity in the nucleus accumbens to reward anticipation moderated the relation between early BI and increases in depressive (β= -.32, *b*= -4.23, *CI*= -7.70, -.76, *p*= .017), but not anxiety, symptoms. Activity in the caudate and putamen did not moderate these relations.

Conclusions and Relevance: Blunted reward sensitivity in the ventral striatum may be a developmental risk factor connecting an inhibited childhood temperament and depression over the transition to adulthood. Future studies should examine the efficacy of prevention programs, which target maladaptive reward processing and motivational deficits among anxious youths, in reducing risks for later depression.

Keywords: Anxiety; Depression; Temperament; Behavioral inhibition; Striatum

Anxiety and depression are the most prevalent psychiatric disorders among young adults ages 18-25 years in the US, estimated in recent years at 22% and 15%, respectively[1 2]. The developmental courses of anxiety and depression are distinct, as anxiety typically emerges in adolescence whereas the full syndrome of depression typically emerges in young adulthood[3]. However, the two forms of psychopathology show considerable sequential comorbidity[4-10], with as many as half of adolescents with an initial diagnosis of anxiety eventually meeting criteria for a diagnosis of depression[3-7 9 10]. To examine antecedents of anxiety and depression, the present longitudinal study examined whether temperament and maladaptive neural processing of reward in concert relate to the developmental courses of anxiety and depression across adolescence and young adulthood.

One child temperament that is associated with significant risk for anxiety and depression is Behavioral Inhibition (BI). BI in infancy is characterized by cautious and fearful responses to unfamiliar people, objects, and situations[11 12]. Meta-analytic evidence suggests that BI is associated with a 4- to 6-fold increased risk for anxiety disorders in childhood and adolesence[13-15]. Additionally, cohort studies following BI children into young adulthood have found greater risk for depression[16-18], consistent with the patterns of comorbidity reported in psychiatric epidemiology[4-10 19 20]. To date, research has largely focused on identifying neurocognitive markers, such as attention biases to threat[21] or heightened cognitive control[16 22 23], associated with risk for anxiety amongst BI children. Few studies have examined neurocognitive markers of depression in relation to temperament[24-26], and none have considered their contributions to anxiety and depression together over time.

One neural system that has shown maladaptive functioning in depression and anxiety is the reward system. Mounting evidence using functional magnetic resonance imaging (fMRI)

suggests that healthy individuals show robust activation during the anticipation of rewards in striatal structures (i.e., nucleus accumbens [NAcc], caudate, and putamen)[27-29]. However, striatal activity during the processing of reward is often blunted in depression: adults[30-33] and adolescents[34 35] with depression display reduced activation in the NAcc during reward anticipation. Blunted reward processing among youths may relate to vulnerability for later depression[36-38]. In support of this idea, blunted neural sensitivity to rewards has been observed in children with familial risk for depression[39 40]. Additionally, prospective studies examining adolescents have shown that reduced striatal activation precedes the onset of depression[41-43], although the effect size is small[44]. Unlike this pattern of blunted reward sensitivity observed in depression, increased striatal activity during the anticipation of incentives has been associated with anxiety[45 46] and children with BI[24-26], possibly reflecting heightened performance monitoring[47]. Amongst BI individuals who are at risk for developing both anxiety and depression, it remains unknown whether blunted striatal activity to reward anticipation would moderate increases in depressive symptoms or whether heightened striatal activity would moderate increases in anxiety.

To address this question, the present study followed a cohort of infants with varying levels of temperamental BI for three decades to examine whether neural processing of reward during adolescence modifies the link between early BI and changes in anxiety and depressive symptoms from adolescence to adulthood. This is a critical transition period for increases in symptoms as individuals face new challenges in establishing independence. Considering the history of psychopathology linked to an inhibited temperament, we expected individuals with higher BI to show worsening anxiety and depressive symptoms. As part of the larger study, participants as adolescents (ages 15-18) underwent fMRI while completing a widely-used

Monetary Incentive Delay (MID) task to measure neural sensitivity to rewards[25]. That prior study showed that children with BI displayed increased activation in the caudate and putamen in anticipation of incentives across rewards and losses[25]. We extended that study to test the hypothesis that reduced striatal activation to reward anticipation, reflecting a vulnerability marker of depression, would moderate the relation between early BI and increases in depressive, but not anxiety, symptoms, into adulthood. Also, we tested the hypothesis that heightened striatal activation to reward anticipation would moderate anxiety, but not depressive, symptoms[45]. The analyses focused on the anticipation phase, because the relation between maladaptive neural responses during anticipation and depression has been well-replicated[30-35 41-43]. Several other studies, including prior studies from the current sample, also suggest that the anticipation phase is related to anxiety and BI in adolesence[24-26]. To test these hypotheses, we modeled interdependent developmental changes in anxiety and depressive symptoms across ages 15 and 26 and examined neural activation in four a priori regions of interest (ROIs) within the striatum, including the NAcc, caudate head, caudate body, and putamen.

Methods

Participants

This prospective longitudinal study was designed to examine the influence of infant temperament on socioemotional development (Supplemental Figure S1). One hundred and sixty-five infants (*N*=165; 50.1% female) were recruited at 4 months of age between the years 1989 to 1993 in the Washington, D.C. metropolitan area. This sample is predominately White (98%) and the parents were primarily from middle to upper-middle-class families (Table 1). To recruit families, hospital birth records were used to obtain the mailing addresses of families with infants. Interested families completed a brief survey and were excluded if the infants were born preterm,

showed any significant developmental problems or were on any long-term medications, and if either parent was left-handed.

BI was assessed at 14 and 24 months using a behavioral observation paradigm; 143 participants had behavioral observations of BI across the two time points. Between ages 15 to 18 years (*M age*= 15.05; *SD*= 0.82), 91 participants completed a Monetary Incentive Delay task[48] in an MRI scanner, of whom 83 were included in the analysis; 8 participants were excluded because of medication at the time of the scan (*n*=4), motion artifacts (*n*=2, motion ≥ 3mm on any axis), and technical difficulties (*n*=2). Individuals who participated in the fMRI component was a random subset of the cohort, who passed the MRI safety screening and were not on psychotropics. Prior psychiatric diagnoses were not a selection criterion. Moreover, prior reports in this cohort in adolescence found no consistent associations between mood or anxiety symptoms and blunted reward-related brain activation[25 49]. Internalizing psychopathology symptoms were self-reported through questionnaires at age 15 (*M age*=14.70; *SD*= 1.10; *n*=107) and age 26 (*M age*= 26.56; *SD*=1.44, *n*=108). The institutional review boards at the University of Maryland and National Institutes of Mental Health approved all procedures. Parents and participants provided written consent and assent, respectively, prior to age 18; Participants provided written consent at age 26.

Behavioral Inhibition (14 and 24 months)

BI was observed at 14 and 24 months of age in the laboratory. Infants were exposed to three episodes, including a free-play session in an unfamiliar playroom, an adult stranger, and a novel toy robot[12]. Infants' behaviors were videotaped and observers coded eight indicators of BI (see Supplement for full description and reliability). At each age, a composite measure of BI was calculated by standardizing and summing the scores of the behavioral codes. BI across 14 and 24

months was correlated, r=.30, p< .001; the average of the two BI assessments was used in analyses.

fMRI Task and Analysis: Striatal Activity to Reward Anticipation (15-18 years)

Participants completed an MID task[50] to assess fMRI blood oxygen level dependent (BOLD) signal during the anticipation of monetary gains, losses, and a neutral condition (i.e., no incentive). See Supplement and Supplemental Figure S2 for a full description of the task and image acquisition. Here, we note that participants were scanned in two different scanners, though the same acquisition sequences and GE head coil were used. The two scanning groups did not differ on the key predictor (i.e., BI), nor demographic characteristics (i.e., sex and parent's education level), *p's* > .05, though participants' age at the time of scanning was related to a change in the scanner, $p < .001$. As such, scanner type was used as a covariate in main analyses to account for potential differences. Images were analyzed in Analysis of Functional NeuroImages (AFNI)[51] using the same preprocessing method as our prior reports[25 49] (see Supplement for details about the pipeline, average motion, and correlations with measures of interest). Consistent with an ROI approach in our prior study[25], ROIs were defined by anatomical boundaries provided by AFNI after spatial normalization[52]. Individual BOLD contrast values to reward and loss anticipation (i.e., gain/loss vs neutral) across incentive magnitudes were extracted and averaged across the bilateral sites for each of the four ROIs (i.e., NAcc, caudate body, caudate head, and putamen). Supplemental analyses testing task conditions support averaging across incentive magnitudes and bilateral sites (Supplemental Figure S3 and Table S2). The averaged BOLD contrasts were used as moderators in the main analyses.

Anxiety and Depressive Symptoms (15 and 26 years)

Anxiety and depressive symptoms were assessed across time using subscales of anxiety and depressive problems from the Achenbach System of Empirically Based Assessment. At age 15, participants completed the Youth Self Report[53]. At age 26, participants completed the Adult Self Report[54]. Examples of items include, "I worry a lot" and "I am unhappy, sad, or depressed". Responses ranged on a 3-point scale (0=*not true*; 2=*very true/often true*). The summed raw scores at each time point were used in analyses. These symptoms were consistently reported on the same scale and by the same informant over time, which allowed us to model developmental changes.

Data Analysis

Main analyses were performed in the R package "lavaan"[55]. In preliminary analyses, an unconditional latent change score model[56] was used to measure changes in and interdependence between depressive and anxiety symptoms across ages 15 to 26 (Supplemental text and Figure S4). Subsequent to defining the latent change scores, predictor variables were added to test main and interactive effects of BI and striatal activation to reward anticipation. In the main model testing the interaction (Figure 1), the latent change scores for both anxiety and depressive symptoms, as well as symptom levels at the last time point (at age 26) were regressed on BI, NAcc activation to reward anticipation, and their interaction term. Predictor variables were mean-centered before generating the interaction term. All analyses adjusted for participants' sex, age at adult assessment, scanner type, and parents' education level. Also, residual covariances among predictor variables were included. These models were repeated for the other ROIs (i.e., caudate body, caudate head, and putamen). Significant interactions were probed with simple slope tests at high and low (± 1 *SD*) levels of striatal activation using the R package "semTools"[57]. To correct for inflation in Type I errors due to multiple tests across ROIs, we

applied a .05 false positive discovery rate[58] to p-values testing two sets of eight interactions between BI and four ROIs for depression and anxiety.

Missing data analysis and solutions. Full information maximum likelihood estimation (FIML) was used to handle missing data. This estimation reduces potential bias in parameter estimates due to missing data and uses all available data in the analysis[59]. Participants with missing data did not differ from participants without missing data on BI, p= .133, anxiety and depressive symptoms, p's= .530 to .948, nor demographic variables, including participant's sex and parent education level, p's= .314 to .881. This suggests that the resulting cohort is representative of the original cohort.

Complementary whole-brain voxel-wise multivariate modeling was performed in AFNI (Supplement).

Results

Preliminary Analyses

Sample characteristics. Table 1 shows the sample characteristics. Correlations among variables of interest are in Supplemental Table S3. Anxiety and depressive symptoms were concurrently correlated at ages 15 and 26 (r's= .69 to .78, p's< .001); however, there was low temporal stability across ages 15 to 26 (r's= .13 to .19), suggesting that levels of symptoms changed among individuals over time. 5.6% and 20.4% of participants met the clinical cut-off for anxiety and depression at age 26, respectively (Supplemental Table S4).

Developmental changes in anxiety and depressive symptoms. The unconditional latent change score model showed significant developmental increases in anxiety and depressive symptoms between ages 15 and 26 (latent change in depressive symptoms: *mean*= 3.96; *95% CI*= 2.99, 4.94; p<.001; latent change in anxiety symptoms: *mean*= 3.54; *95% CI*= 2.92, 4.71;

p<.001). Also, variances in latent change scores were significantly different from zero (latent change in depressive symptoms: *variance*= 26.24; *95% CI*= 18.93, 33.54; *p*<.001; latent change in anxiety symptoms: *variance*= 10.46; *95% CI*= 7.43,13.49; *p*<.001), indicating that individuals varied in the magnitude of symptom change. Likewise, there was significant individual variation in symptom levels at age 26 (Supplemental Table S5).

Main effects of BI and ROIs in the striatum to reward anticipation on latent changes in depressive and anxiety symptoms, and symptom level at age 26 are shown in Supplemental Table S6. BI was associated with increases in depressive symptoms between ages 15-26 and more depressive symptoms at age 26, though no associations were found for the ROIs.

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Table 2 shows results testing interactions between the ROIs and BI. There was a significant interaction between early BI and activity in the bilateral NAcc to reward anticipation associated with greater increases in depressive symptoms across age (β= -.32, *b*= -4.21, *95% CI*= -7.70, -.71, *p*= .018) and more depressive symptoms at age 26 (β= -.47, *b*= -5.09, *95% CI*= -7.74, -2.43, *p*<.001). However, there were no significant interactions associated with latent changes in anxiety across age nor anxiety at age 26. Figure 2 shows the interaction plots. Follow-up simple slope tests indicated significant relations between early BI and greater increases in depressive symptoms across age at low (-1 *SD*) levels of NAcc activation (*b*=1.89, *SE*= .57, *p*< .001), but not at high (+1 *SD*) levels of activation (*b*= - .08, *SE*= .37, *p*= .832). Similarly, significant relations between early BI and more depressive symptoms at age 26 was observed at low levels of NAcc activation (*b*=1.95, *SE*= .44, *p*< .001), but not at high levels (*b*=- .39, *SE*= .28, *p*= .164). Similar results emerged when using the Johnson-Neyman technique to probe the interaction

(Supplemental Figure S6). After correcting for multiple testing, the interaction associated with depressive symptoms at age 26 remained statistically significant (*p-adjusted* <.001), though the interaction associated with change in depressive symptoms did not (*p-adjusted*= .072).

There were no interactions between BI and activation in the caudate body, caudate head, or putamen on depressive or anxiety symptoms (Table 2).

In the additional whole-brain voxel-wise analyses, no regions survived the whole-brain correction using a family-wise error correction of $p<.05$ for the interaction between BI and anxiety or depressive symptom changes (Supplement). Supplemental Table S7 and Figure S7 present additional results showing the left/middle frontal gyrus using a less stringent activation threshold at $p< .001$.

Comment

Our findings focusing on ROIs in the striatum related reduced activation in the NAcc to increases in depressive symptoms across ages 15 to 26 among individuals who began life with higher levels of temperamental BI. Notably, these results, adjusted for multiple covariates, support blunted neural sensitivity to reward anticipation as a risk pathway to adult depression in the context of early temperament.

Considerable research highlights comorbidities between depression and anxiety, particularly social anxiety. Some evidence suggests that heightened overall levels of early anxiety symptoms relate to later risk for depression[4 5], whereas other evidence suggests specific associations with social anxiety symptoms[6]. This connection may be partly mediated by low social involvement and approach motivations[60-62], behaviors which are related to BI. Converging with these findings, prior work in this cohort had linked stable BI across childhood to adolescent anxiety disorders[15], which could carry risk for adult anxiety and depression[16]. The finding that

early BI related to worsening depressive, but not anxiety, symptoms across adolescence and adulthood, supports theories asserting that BI should show stronger relations with anxiety in adolescence. But as the expression of psychopathology changes over time, BI should be more strongly related to depression in adulthood[63]. Nevertheless, the lack of relation between BI and anxiety could be masked by a relatively low prevalence of anxiety disorders in the current cohort. Alternatively, the inconsistent relations could reflect the probabilistic, rather than deterministic, nature of risk linked to temperament, as specific developmental contexts and other risk factors (e.g., continuity of BI across childhood[15 64], negative peer experiences[65 66], over-intrusive parenting[67], and heightened inhibitory control) may be needed for psychopathology risk to manifest among BI children.

Our current results indicate that only children with higher BI who showed blunted striatal sensitivity to reward anticipation as adolescents developed more depressive symptoms into adulthood. Such blunted activation may reflect core features of depression, such as anhedonia and maladpative prediction of rewards[35], and might explain different trajectories of psychopathology among inhibited children. Results based on ROIs extend prior studies showing that blunted activation in ventral striatal regions, rather than the caudate and putamen, to reward anticipation is a correlate of depression in adults[30-33], and a marker of vulnerability for later depression in prospective studies of youths[41-43]. Likewise, altered neural sensitivity to reward recorded by EEG have been associated with depression as early as preschool[68]. Considering the developmental context into adulthood, blunted neural sensitivity might interfere with inhibited individuals' motivations to seek positive experiences, and such missed opportunities could be associated with worsening depressive and socially withdrawn symptoms. Future research on

inhibited and/or anxious youths could examine these processes and alterations in the development of reward circuitry and interactions with networks implicated in anxiety.

Notably, the pattern of blunted ventral striatal activation to reward anticipation contrasts with prior work examining other neurocognitive processes in BI[16 21 23 69-72]. This includes work on executive and attentional control networks that moderate risk for anxiety among BI children. Studies using behavioral and neural methods to examine performance monitoring have found that inhibitory control—a component of executive functions—plays a paradoxical role in BI children such that heightened inhibitory control moderates greater risk for the development of anxiety[16 23 69 70]. In contrast, BI children with less inhibitory control in certain contexts are less likely to be at risk for anxiety. Similarly, studies have found that neural and behavioral indices linked to attention bias toward threat moderate BI children's risk for anxiety[21 71 72]. Together, the current and prior findings highlight different neurocognitive mechanisms as they demonstrate who is at greater risk for the development of different forms of internalizing psychopathology. Furthermore, by providing knowledge on the histories of psychopathology, risk, and pathophysiology, the results could inform the development of prevention-oriented treatments tailored to different individuals[73].

Strengths of the present study include the use of (a) early behavioral assessments of temperament through blinded observers, (b) neuroimaging data reflecting incentive processing, and (c) a life-course perspective. There were several limitations. First, the sample size is modest for a longitudinal study and due to limited resources, only a subset of the cohort completed the MID task. Considering recent recommendations for sample sizes that might be required to obtain reliable brain-behavior relations[74], we note that our power to detect complex associations may be insufficient. Additionally, our reported estimates could be influenced by sample variability.

Second, due to institutional changes in the neuroimaging facilities at the time, a small portion of the sample was scanned in a different MR scanner. We acknowledge there may be variability in brain responses linked to different scanners, although we adjusted for this in the analyses. Third, after correcting for multiple testing, the interaction results remained statistically significant for depressive symptoms at age 26 (*p-adjusted*< .001) but not changes (*p-adjusted*= .072). Interpretation of statistical significance should balance Type I and Type II errors due to a modest sample size and consider the fact that individuals exhibiting worsening symptoms over time often are the same individuals who subsequently report more symptoms. Fourth, the results are based on the anticipation component of reward processing. However, reward feedback, consummation, and learning have been implicated in the pathophysiology of depression and could be examined in future work. Fifth, the associations cannot untangle the contributions of BI from general low approach behaviors. Since few existing studies span toddlerhood to early adulthood, additional studies are needed to test whether avoidance of novelty is associated with reward function and internalizing psychopathology. Sixth, there was a low prevalence of anxiety disorders which could be related to why we failed to find significant temporal stability across time in some measures of depression and anxiety, though we found trends of stability (Supplemental Table 3). Anxiety at age 26 correlated with both anxiety at age 15 (r=.19) and depressive symptoms at age 15 (r= .13). Depressive symptoms at age 26 may not have tracked with previous symptoms, partly because of lower levels and variability in depressive symptoms at age 15 relative to age 26. However, this latter pattern fits with the idea that depression becomes increasingly prominent as adolescents reach adulthood. Lastly, the sample was primarily White. Future work should recruit samples that are more heterogenous in terms of race and ethnicity to ensure the generalizability of the findings.

In summary, this study advances etiological models of developmental psychopathology[75] by identifying early temperamental risk factors and neural processes that might shape different facets of internalizing psychopathology across the lifespan.

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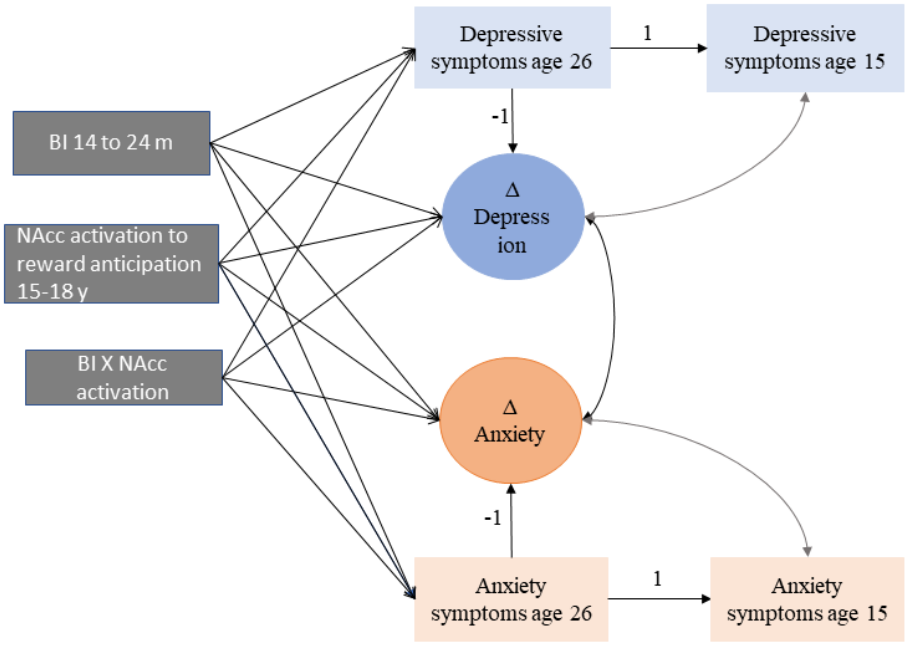
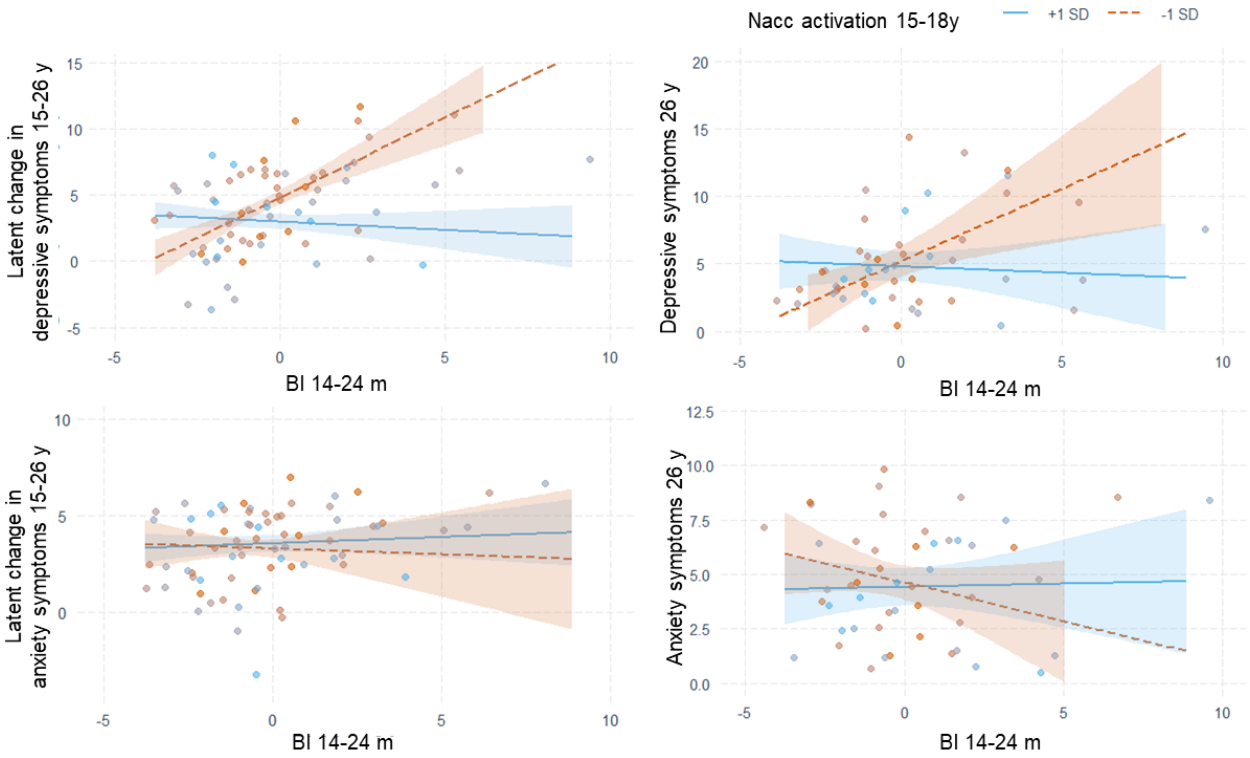
Figure 1. Conceptual diagram of the cross-domain model examining interactive effects between early BI and activation in the nucleus accumbens to reward anticipation in adolescence on latent change scores of anxiety and depressive symptoms across ages 15-26, and symptom levels at age 26



Note. BI=behavioral inhibition. NAcc= nucleus accumbens.
To measure developmental changes from adolescence to adulthood, the path from symptoms at age 26 to the latent factor was fixed to negative one (to allow the interpretation that changes are positive); the autoregressive path between symptoms at age 26 to symptoms at age 15 was fixed to one; and the intercept of symptoms at age 15 was set to zero (i.e., a baseline). As such, the variances of age 15 symptoms were not estimated. The covariance between symptoms at age 15 and the latent factors captured the degree to which change is dependent on initial levels at age 15. To account for relations between anxiety and depression, covariances between the two latent change score factors and residual covariances between symptoms at age 26 were included. The model also adjusts for sex, parent education, age, and scanner type, though they are not shown for simplicity. Residual covariances among predictors were also included but not shown for simplicity.

Figure 2. Adolescent ventral striatal activation to reward anticipation as a moderator of the relation between early BI and adult depressive and anxiety symptoms.



Note. Shaded region indicates 95% confidence intervals around the observed data. BI=behavioral inhibition. NAcc= nucleus accumbens.

Table 1. Characteristics of the sample.

	M (SD)	*N (%)*
BI 14 to 24 months	.06 (2.35)	143 (86.7%)
Depressive symptoms age 15	1.93 (3.00)	107 (65.0 %)
Depressive symptoms age 26	5.85 (4.33)	107 (65.0 %)
Anxiety symptoms age 15	1.34 (2.17)	108 (65.5 %)
Anxiety symptoms age 26	4.83 (2.85)	108 (65.5 %)
Mother's level of education 4 months[a]		
Graduate school		14 (10.4%)
College		69 (51.1%)
High school or other		52 (38.5 %)
Father's level of education 4 months[b]		
Graduate school		22 (16.5%)
College		61 (45.9)
High school or other		50 (47.6%)
Child ethnicity/race (%White)		162 (98.0%)

Note. Total N in cohort at recruitment=165. [a]N in mother's education=135. [b]N in father's education =133. BI= behavioral inhibition.

Table 2. Interaction between early BI and activity in striatal regions to reward anticipation in adolescence and associations with changes in depressive and anxiety symptoms across adolescence to adulthood.

	Moderator: NAcc				Moderator: putamen				Moderator: caudate head				Moderator: caudate body			
	β	*b*	*95% CI*	*p*	*β*	*b*	*95% CI*	*p*	*β*	*b*	*95% CI*	*p*	*β*	*b*	*95% CI*	*p*
Associations with latent change in anxiety symptoms ages 15-26																
BI 14-24 m	.26*	.36	.06, .67	.021	.22*	.30	.01, .58	.042	.21*	.29	.02, .56	.038	.16	.22	-.17, .62	.266
ROI activation 15-18 y	-.14	-1.87	-5.68, 1.93	.335	-.06	-1.62	-8.99, 5.75	.666	-.15	-2.79	-8.39, 2.81	.329	-.03	-.91	-9.05, 7.24	.828
BI X ROI activation	-.20	-1.58	-3.84, .68	.170	-.12	-1.57	-4.88, 1.74	.352	-.21	-2.18	-5.23, .87	.162	.05	.50	-3.48, 4.48	.805
Associations with latent change in depressive symptoms ages 15-26																
BI 14-24 m	.40**	.89	.39, 1.39	<.001	.30*	.65	.17, 1.13	.008	.28*	.61	.15, 1.07	.010	.42*	.92	.25, 1.59	.007
ROI activation 15-18 y	-.27*	-5.99	-11.67, -.31	.039	-.10	-4.92	-17.27, 7.43	.435	-.20	-6.21	-15.57, 3.16	.194	-.27	-12.19	-25.42, 1.05	.071
BI X ROI activation	-.32*	-4.21	-7.70, -.71	.018[a]	-.14	-2.78	-8.63, 3.07	.352	-.14	-2.34	-7.88, 3.19	.407	-.24	-4.38	-11.15, 2.39	.205
Associations with Anxiety Symptoms age 26																
BI 14-24 m	.21	.25	-.01, .51	.062	.17	.20	-.04, .44	.109	.15	.18	-.05, .41	.129	.06	.08	-.28, .42	.675
ROI activation 15-18 y	-.05	-.64	-4.16, 2.88	.720	.02	.41	-6.31, 7.13	.906	.01	.22	-4.59, 5.03	.928	.11	2.72	-4.34, 9.79	.450
BI X ROI activation	-.20	-1.43	-3.38, .53	.152	-.17	-1.90	-4.91, 1.10	.215	-.19	-1.77	-4.49, .96	.204	.09	.89	-2.73, 4.51	.630
Associations with Depressive symptoms age 26																
BI 14-24 m	.42**	.78	.38, 1.17	.000	.28*	.51	.11, .92	.013	.24*	.44	.06, .83	.025	.31	.58	-.02, 1.18	.059
ROI activation 15-18 y	-.11	-2.01	-7.21, 3.18	.448	-.02	-.93	-12.07, 1.21	.869	-.01	-.18	-8.25, 7.89	.965	-.10	-3.89	-15.71, 7.92	.518
BI X ROI activation	-.47**	-5.09	-7.74, -2.43	<.001[b]	-.20	-3.42	-8.57, 1.73	.193	-.13	-1.79	-6.61, 3.04	.468	-.14	-2.11	-8.42, 4.20	.512

Note. ***p* <.001. **p* <.05. False positive discovery rate was also applied to correct for Type I error: [a]*p-adjusted*= .072. [b]*p-adjusted*= .001. BI= behavioral inhibition. NAcc= nucleus accumbens. ROI= region of interest. Models adjusted for sex, age, parent education, and scanner type.