Supplement

Mood Symptom Dimensions and Developmental Differences in Neurocognition in Adolescence

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Supplementary Method

Supplementary Participants

The sample includes data from studies at two sites (University of Colorado Boulder, University of California Los Angeles). Recruitment at both sites was aimed at adolescents; the University of Colorado site included participants ages 13 to 24 and the University of California site included participants ages 15 to 24. Eligibility requirements included either current or past mood diagnosis, or familial risk for mood disorders (first-degree relative with a diagnosed mood disorder), or no history of mood disorders, to maximize variance in mood symptoms. Participants were excluded if unable to abstain for 48+hours prior to the research session from stimulant medications, beta blockers, benzodiazepines, or anxiolytics, or for recent (past six weeks) changes in any other medications. Participants were excluded who reported another diagnosis primary to mood disorder. Comorbid psychiatric disorders secondary to mood disorders were allowed (except for secondary psychotic disorders); however, analyses were repeated excluding individuals with a history of moderate or severe substance use disorders, any recent (past year) substance use disorders, recent (past two years) eating disorders, or for whom secondary diagnostic data were incomplete (Table 2). In addition, analyses were repeated covarying use of any psychoactive medications. These exclusions did not significantly alter the nature or magnitude of effects, changes in standardized estimates <0.01 to 0.19, changes in ps< 0.01 to 0.09, therefore we retained the full sample for analyses.

A larger pooled sample of n=636 was available for simple confirmatory factor analyses (i.e., included the current sample of n=419, along with an additional n=217 adolescents who completed the same behavioral testing but not clinical evaluation). The pooled sample was demographically comparable to the primary (clinical evaluation) sample (Table S1).

Supplementary Procedures

Studies at both sites included an in-person research session at the time of enrollment, during which the same series of behavioral tests and surveys were administered. Participants also completed clinical measures, and additional research procedures conducted after the procedures described here (neuroimaging and follow-up evaluations). Other experimental questions related to other procedures, that are distinct from the hypotheses reported in this investigation, will be tested and reported elsewhere.

Clinical Evaluation

Structured Clinical Interview for the Diagnostic and Statistical Manual 5th Edition – Research Version (SCID5, (First et al., 2015). The SCID5 interview was performed by an advanced professional research assistant or pre-doctoral graduate student in psychology, under the supervision of a licensed clinical psychologist. We chose to administer the SCID5 because this interview measure shows good psychometric properties and can be administered in both adolescent and adult samples (First et al., 2015).

Supplementary Analyses

Primary Performance Parameters

See below and Tables S2-S3.

Secondary Performance Parameter: Probabilistic Reward Task

In addition to the discriminability parameter, we also computed a second performance parameter reflecting changes in response bias from the first (block 1) to the second (block 2) trial block. Response bias was calculated with the equation:

$$\text{RB} = \frac{1}{2} log\left(\frac{(Rich_{correct} + 0.5) * (Lean_{incorrect} + 0.5)}{(Rich_{incorrect} + 0.5) * (Lean_{correct} + 0.5)}\right)$$

In this equation, $Rich_{correct}$ is the number of correct responses, and $Rich_{incorrect}$ is the number of incorrect responses, to the rich stimuli; $Lean_{correct}$ is the number of correct responses, and $Lean_{incorrect}$ is the number of incorrect responses, to the lean stimuli. Following prior published studies using this task, 0.5 was added to each of the raw response variables, making it possible to calculate response bias when one of the raw variables was equal to zero (Santesso et al. 2008; Vrieze et al. 2013).

Confirmatory Factor Analyses

Neurocognitive factors were estimated with confirmatory factor analysis that modeled both the reward learning performance and the executive functioning factors. Confirmatory factor analysis was performed in a pooled sample of adolescents with available behavioral task data (Table S1).

Site Checks

Analyses were performed to check for potential site differences. First, model comparisons were performed to test invariance in the factor structures across sites. Second, site was included as a covariate in all models. Third, site was included as a moderator to test whether the direct or interactive effects of developmental and symptom measures on cognitive factors differed by site.

Structural Equation Model Covarying Gender

The SEM was repeated including self-reported gender. Gender was inconsistently associated with specific indicators (Table S3), consistent with prior work using these executive function tasks (Friedman et al., 2016). Therefore, we modeled gender effects at the indicator level, allowing it to predict only the indicators that showed gender differences in performance (antisaccade accuracy and probabilistic reward discriminability).

Exploratory Analyses Considering Diagnoses

The dimensional approach of this study was motivated by prior work showing that mood pathology may be best conceived on a continuum, and that subclinical symptoms are associated with neurocognitive dysfunction and subsequent mood disorders (Ayuso-Mateos et al., 2010; Carlson & Kashani, 1988; Cuthbert & Insel, 2010; Klein et al., 2013; Lewinsohn et al., 1995; Widiger & Samuel, 2005). However, we also repeated structural equation models replacing symptom dimensions with contrast codes for lifetime, full-criteria psychiatric disorders, *code1*: no diagnosis = +2, unipolar or bipolar diagnosis = -1, *code 2*: no diagnosis = 0, unipolar diagnosis = -1, bipolar diagnosis = +1.

Supplementary Results

Primary Performance Parameters

Task performance descriptive statistics and simple associations among parameters are reported in Tables S2-S3.

Secondary Performance Parameter

Change in response bias was not significantly correlated with learning rate on the bandit task, r=0.03, p=0.51, and was not significantly correlated with accuracy on the instrumental learning task, r=0.02, p=0.62. Therefore, given superior covariance between the discriminability parameter and reward parameters from other tasks, discriminability was selected as the primary performance parameter for latent variable modeling.

Confirmatory Factor Analysis

Confirmatory factor analyses modeled a reward learning performance factor and an executive functioning factor in a pooled sample of n=636 (all adolescents for whom behavioral task data were available). The model showed adequate fit, χ^2 (8) = 17.42, *p*<0.05, RMSEA = 0.04 [90% CI 0.01 to 0.07], CFI = 0.96. Reward learning performance and executive functioning were highly correlated (Figure S2 and Table S3).

Site Checks

To check for potential site differences, we first tested invariance in the factor structures across sites. The chi-squared difference test failed to show better fit for the unconstrained model relative to the constrained model, $\chi^2_{diff}(6) = 1.53$, *p*>0.10, supporting the same factor structure across sites. Second, site was included as a covariate in all models. The inclusion of this covariate did not alter the nature or significance of any effects, (changes in standardized estimates <0.015, changes in *p*s< 0.02). Third, site was included as a moderator to test whether the direct or interactive effects of developmental and symptom measures on cognitive factors differed by site. This analysis failed to show significant site differences in experimental effects, *p*s>0.49. Together, these checks indicate that there were no significant differences in factor structure or experimental effects between sites.

Structural Equation Model Covarying Gender

The structural equation model testing *a priori* hypotheses was repeated including self-reported gender. The model showed adequate fit, χ^2 (76) = 87.56, *p*>0.05, RMSEA = 0.02 [90% CI 0.00 to 0.04], CFI = 0.95. Developmental and psychopathology effects were not significantly altered by the addition of gender (changes in standardized estimates <0.06, changes in *p*s<0.02).

Exploratory Analyses: Diagnoses

An exploratory model was performed in which contrast codes for mood diagnoses were included in place of symptom dimensions (all covariates were retained). Model fit, χ^2 (72) = 117.73, *p*<0.05, RMSEA = 0.04 [90% CI 0.03 to 0.06], CFI = 0.80. The chi-square difference test indicated this model was superior to the constrained model in which paths were fixed at zero, $\chi^2_{diff}(20) = 69.45$, $p<0.05$. Diagnostic contrast codes did not moderate pubertal differences in reward learning performance, *p*s>0.39, but participants without any mood diagnosis exhibited better reward learning performance overall, (standardized) estimate =0.39 [90% CI 0.17 to 0.61], p=0.004. Diagnostic codes did not moderate age differences in executive functioning, *p*s>0.24, and there were no significant differences in executive functioning between groups, although there was a trend-level difference in which participants without any mood diagnosis exhibited better executive functioning overall, (standardized) estimate =0.16 [90% CI 0.00 to 0.31], p=0.098. Therefore, only symptom dimension models revealed interactions between mood and developmental differences in neurocognition, which may be a consequence of better statistical power with dimensional variables that capture the full range of symptom severity.

MPLUS Commands for Confirmatory Factor Analysis

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ANALYSIS:  ESTIMATOR = MLR;
MODEL:
    EFF BY ANTACC CSSSWC S2BACC;
    RPF BY PRTDIS ILTACC BANLRN;
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Supplementary References

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Table S1. Demographics of Pooled and Clinical Evaluation Sample

Sample:	**POOLED**			**CLINICAL EVALUATION**		
Site:	CU Boulder	UCLA	**All**	CU Boulder	UCLA	**All**
	n = 264	*n* = 372	***n* = 636**	*n* = 264	*n* = 155	***n* = 419**
	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)
Age	17.37 (2.23)	20.36 (2.04)	19.09 (2.59)	17.37 (2.23)	20.34 (2.21)	18.46 (2.65)
PDS	3.56 (0.49)	3.82 (0.24)	3.66 (0.44)	3.56 (0.49)	3.82 (0.24)	3.66 (0.44)
GBI-MH	4.00 (4.22)	n/a	n/a	4.00 (4.22)	4.48 (5.90)	4.16 (4.85)
MASQ-AD	16.60 (6.65)	n/a	n/a	16.60 (6.65)	18.99 (8.63)	17.49 (7.53)
	%	%	%	%	%	%
Gender						
Cisgender Female	54.75%	70.97%	64.24%	54.75%	69.03%	60.03%
Cisgender Male	38.78%	26.34%	31.50%	38.78%	29.03%	35.17%
Other	6.46%	2.69%	4.25%	6.46%	1.94%	4.79%
Ethnicity						
Hispanic or Latinx	11.85%	21.11%	17.27%	11.85%	19.75%	14.77%
Non-Hispanic and Non-Latinx	84.44%	75.46%	79.19%	84.44%	75.93%	81.29%
Other	3.70%	3.43%	3.54%	3.70%	4.32%	3.93%
Race						
Asian	4.43%	28.23%	18.35%	4.43%	19.14%	9.87%
Biracial or More than One Race	9.96%	13.46%	12.01%	9.96%	14.81%	11.75%
Black or African American	1.84%	3.49%	2.81%	1.84%	3.10%	2.31%
Native Hawaiian	0.00%	0.27%	0.16%	0.00%	0.00%	0.00%
Native American	0.00%	0.53%	0.31%	0.00%	0.00%	0.00%
White	80.07%	37.47%	55.15%	80.07%	49.38%	68.72%
Other	3.69%	16.62%	11.25%	3.69%	13.58%	7.35%
Parent Education						
8th Grade or Less	0.00%	6.86%	4.01%	0.00%	6.17%	2.28%
Partial High School	2.95%	4.49%	3.85%	2.95%	3.09%	3.00%
High School/GED	8.49%	12.40%	10.78%	8.49%	10.49%	9.23%
Vocational/Trade	1.85%	0.79%	1.23%	1.85%	0.62%	1.39%
Partial College or 2-year Degree	12.55%	16.89%	15.09%	12.55%	17.90%	14.53%
College or 4-year Degree	30.63%	30.87%	30.77%	30.63%	35.80%	32.54%
Graduate Degree	39.48%	24.27%	30.58%	39.48%	21.60%	32.87%
Not reported	4.06%	3.43%	3.69%	4.06%	3.10%	3.70%
Family Income (yr)						
<10,000	5.54%	7.92%	6.93%	5.54%	10.49%	7.37%
~10,000-25,000	8.12%	9.23%	8.77%	8.12%	9.26%	8.54%
~25,000-50,000	12.18%	14.25%	13.39%	12.18%	12.96%	12.47%
~50,000-75,000	17.34%	17.15%	17.23%	17.34%	15.43%	16.63%
~75,000-100,000	18.82%	17.15%	17.84%	18.82%	14.20%	17.11%
>100,000	34.32%	30.87%	32.30%	34.32%	33.33%	33.95%
Not reported	3.69%	3.43%	3.54%	3.69%	4.32%	3.92%

Note: Age = age in years, CU = University of Colorado Boulder, GBI-MH = General Behavior Inventory, Mania/Hypomania subscale, MASQ-AD = Mood and Anxiety Symptom Questionnaire, Anhedonic Loss of Interest subscale, PDS = Pubertal Development Scale, UCLA = University of California Los Angeles. The pooled sample consisted of adolescents who completed behavioral testing and were eligible for confirmatory factor analyses. The clinical evaluation sample consisted of adolescents who completed behavioral testing and clinical and diagnostic evaluation and were eligible for structural equation models to test experimental hypotheses (primary hypothesis-testing analyses were performed on the clinical evaluation sample and reported in the main text).

Table S2. Behavioral Task Performance Means and Quality Assurance

	Raw Performance					**QA Pass Performance**					
	n	Min, Max	M (SD)	Skw	Kurt	*n*	Min, Max	M (SD)	Skw	Kurt	Rel
BAN-LRN	624	0.01, 0.99	0.36 (0.31)	0.64	-0.58	514	0.01, 0.95	0.24 (0.27)	097	-0.22	0.77
PRT-DIS	615	-0.11, 1.63	0.62 (0.28)	<0.01	0.21	557	0.05, 1.63	0.66 (0.25)	0.30	0.48	0.91
ILT-ACC	623	0.61, 0.93	0.82 (0.06)	-0.92	0.62	623	0.61, 0.93	0.82 (0.06)	-0.92	0.62	0.88
ANT-ACC	623	0.11, 0.99	0.64 (0.18)	-0.53	-0.33	609	0.21, 0.99	0.65 (0.17)	-0.38	-0.65	0.95
S2B-ACC	622	0.21, 1.00	0.80 (0.10)	-1.03	4.57	607	0.60, 1.00	0.81 (0.08)	-0.11	-0.49	0.83
CSS-SWC	624	-282.91, 995.79	227.91 (180.26)	0.65	0.93	622	-282.91, 995.79	228.38 (180.36)	0.64	0.92	0.93

Note: ANT-ACC = antisaccade task accuracy, BAN-LRN = bandit task learning rate CSS-SWC = color shape switch task reaction time switch cost (note that this variable was reversed for structural equation models, but unreversed/raw scores are reported here), ILT-ACC = instrumental learning task accuracy, Kurt = kurtosis of the distribution, PRT-DIS = probabilistic reward task discriminability, Rel = reliability computed with the Spearman Brown prophecy formula for split-half (odd/even for bandit task, probabilistic reward task, antisaccade task, color-shape switching task; comparing parallel trials blocks for instrumental learning task, spatial n-back task), S2B-ACC = spatial 2-back accuracy, Skw = skewness of the distribution. These descriptive statistics are reported on all available data in a pooled sample of adolescents who completed behavioral testing and were eligible for confirmatory factor analyses.

Table S3. Simple Associations Among Performance Parameters and Development or Mood

	Bandit Learning Rate	**Probabilistic Reward Discrimin.**	**Instrumental Learning Accuracy**	**Anti-saccade Accuracy**	**Spatial 2-back Accuracy**	**Color-Shape Switch Cost**
	r (p)	*r (p)*	*r (p)*	*r (p)*	*r (p)*	*r (p)*
BAN-LRN	1	**0.10 (0.03)**	**0.11 (0.03)**	0.05 (0.30)	**0.11 (0.03)**	0.08 (0.07)
PRT-DIS		1	**0.20 (<0.01)**	**0.25 (<0.01)**	**0.22 (<0.01)**	-0.07 (0.11)
ILT-ACC			1	**0.22 (<0.01)**	**0.31 (<0.01)**	**-0.10 (0.01)**
ANT-ACC				1	**0.32 (<0.01)**	**-0.14 (<0.01)**
S2B-ACC					1	**-0.10 (0.01)**
CSS-SWC						1
	b *(p)*	b *(p)*	b *(p)*	b *(p)*	b *(p)*	b *(p)*
PDS	0.33 (0.83)	2.01 (0.11)	1.44 (0.18)	1.48 (0.20)	-0.20 (0.86)	-0.37 (0.75)
PDS2	-0.03 (0.90)	-0.26 (0.18)	-0.21 0.21)	-0.19 (0.27)	0.09 (0.62)	0.00 (0.97)
Age	0.07 (0.63)	0.27 (0.06)	-0.06 (0.63)	**0.46 (<0.01)**	**0.52 (<0.01)**	-0.14 (0.29)
Age2	-0.00 (0.54)	-0.01 (0.07)	0.00 (0.59)	**-0.01 (<0.01)**	**-0.01 (<0.01)**	0.00 (0.45)
	t *(p)*	t *(p)*	t *(p)*	t *(p)*	t *(p)*	t *(p)*
Gender	0.29 (0.77)	**-3.04 (<0.01)**	1.03 (0.30)	**4.64 (<0.01)**	1.14 (0.26)	1.20 (0.23)
	r (p)	*r (p)*	*r (p)*	*r (p)*	*r (p)*	*r (p)*
GBI-MH	0.02 (0.68)	-0.09 (0.06)	**-0.12 (<0.01)**	**-0.13 (<0.01)**	**-0.12 (<0.01)**	0.03 (0.44)
MASQ-AD	0.09 (0.05)	-0.08 (0.07)	**-0.11 (<0.01)**	**-0.10 (0.01)**	-0.06 (0.13)	0.05 (0.18)

Note: Reported are bivariate correlation coefficients (*r*s) among task performance parameters, or between task performance parameters and either anhedonic or manic symptom severity; or standardized estimates (bs) from regressions in which each task performance parameter is regressed on (linear and quadratic) effects of pubertal or age variables; or independent samples t-tests (ts) comparing task performance between cis-gender females and cis-gender males (negative t statistic indicates higher scores in females). ANT-ACC = antisaccade task accuracy, BAN-LRN = bandit task learning rate, CSS-SWC = color shape switch task reaction time switch cost (note that this variable was reversed for structural equation models, but unreversed scores are reported here), ILT-ACC = instrumental learning task accuracy, PRT-DIS = probabilistic reward task discriminability, S2B-ACC = spatial 2-back accuracy, Discrimin. = Discriminability, GBI-MH = General Behavior Inventory, Mania/Hypomania subscale, MASQ-AD = Mood and Anxiety Symptom Questionnaire, Anhedonic Loss of Interest subscale, PDS = Pubertal Development Scale.

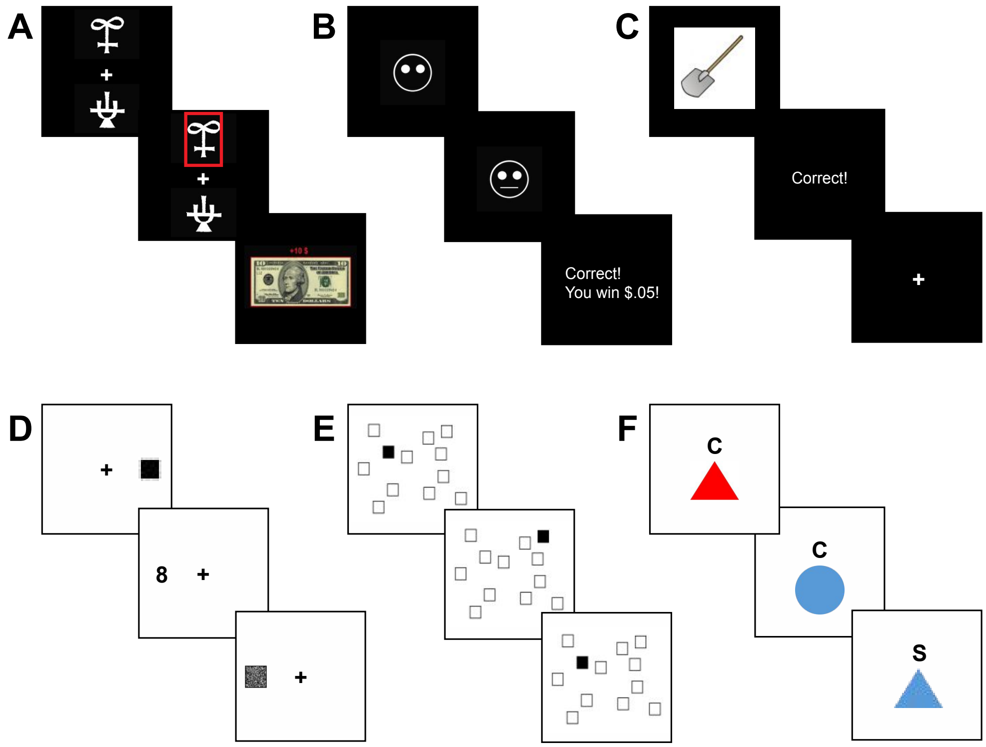

Figure S1. ***Behavioral tasks***. Six tasks were administered to each participant over the course of approximately one hour of testing (stimuli are not to scale). (**A**) *Two-armed bandit task*. In each trial the participant was presented with a pair of symbols and instructed to make a choice that elicited a desired outcome, using a button to select either the top or the bottom stimulus. For one stimulus pair (the reward condition, of interest for this study), the desired outcome was to gain monetary reward (shown). Unbeknownst to the participant, one stimulus within the pair had an 80% probability of eliciting monetary reward, and the other stimulus had a 20% probability of eliciting monetary reward. (**B**) *Probabilistic reward task*. For each trial, the participant was presented with a cartoon face, and either a short or long mouth stimulus appeared on the face. The participant was asked to respond as quickly as possible to indicate which stimulus was displayed. Correct responses either resulted in reward feedback (shown) or null feedback. The reward reinforcement schedule was asymmetrical: one "rich" stimulus was rewarded for correct responses at a rate that was three times higher than the reward rate for the "lean" stimulus. (**C**) *Instrumental learning task*. Participants were instructed to learn which of three response buttons corresponded with each stimulus in a set of sequentially-presented neutral images. After responding, feedback on accuracy was displayed ("Correct", shown, or "Incorrect"). Participants were instructed that monetary bonus would be calculated on the basis of accuracy. Stimuli were blocked, and in each block the participant had to learn stimulus-response mappings for two, three, four, or five images. (**D**) *Antisaccade task*. For each trial, the participant viewed a fixation point at the center of the monitor. After a variable amount of time a visual distractor (small black square) was shown on one side of the screen, after which a target stimulus (number symbol between 1 and 9) appeared on the opposite side of the screen. The participant was instructed to keep their eyes on the fixation point and not saccade to the visual distractor, instead saccading to the target stimulus in time to see it before it was masked, and then report the numeric value out loud to the research assistant. (**E**) *Spatial n-back task*. In each block of this task, the participant viewed a display of twelve open squares distributed across the screen. For each trial, one square in the display turned black ("flashed"). The participant was instructed to respond by pressing a button to indicate whether the square that flashed for that trial was the same spatial location as the square that flashed two trials earlier. (**F**) *Color-shape task*. For each trial, a shape stimulus (red or blue, circle or triangle) appeared in the center of the screen accompanied by a cue letter (C or S) to indicate whether the participant should respond to categorize the shape based on color or shape. The task consisted of a mixed sequence in which a trial of one cue type could be preceded by the same ("repeat" trials) or the other ("switch" trials) cue type.

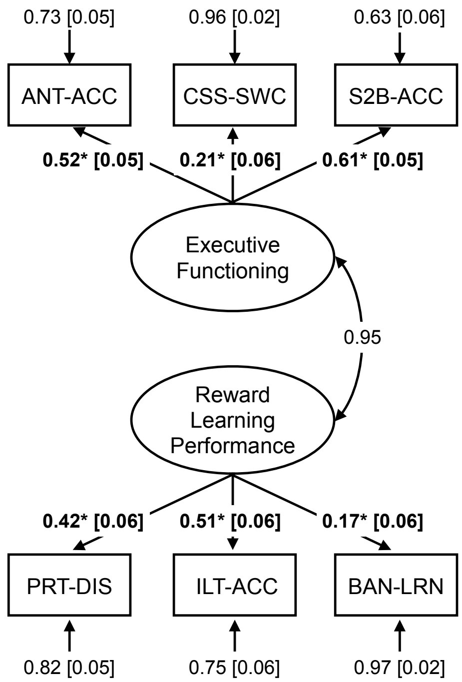

Figure S2. ***Confirmatory Factor Analysis***. In confirmatory factor analysis, a reward learning performance factor was estimated across probabilistic reward task discriminability (PRT-DIS), instrumental learning task accuracy (ILT-ACC), and bandit task learning rate (BAN-LRN); and an executive functioning factor was estimated across antisaccade accuracy (ANT-ACC), color-shape task reaction time switch cost (reversed for models and display, CSS-SWC), and spatial 2-back accuracy (S2B-ACC). *p<0.05 loadings.