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Neural correlates of *p*-factor in adolescence: Cognitive control with and without enhanced positive affective demands

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Abstract

Background.—Recent research has aimed to characterize processes underlying general liability toward psychopathology, termed *p*-factor. Given previous research linking *p*-factor with difficulties in both executive functioning and affective regulation, the present study investigated non-affective and positive affective inhibition in the context of a sustained attention/inhibition paradigm in adolescents exhibiting mild-to-severe psychopathology.

Method.—Functional magnetic imaging data were collected during an integrated reward conditioning and Go/No-Go task in 138 adolescents assigned female at birth. We modeled *p*-factor using hierarchical confirmatory factor analysis. Positive affective inhibition was measured by

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examining responses to No-Go stimuli with a history of reward conditioning. We examined associations between *p*-factor scores and neural function and behavioral performance.

Results.—Consistent with non-affective executive function as a primary risk factor, *p*-factor scores were associated with worse behavioral performance and hypoactivation in the left superior frontal gyrus and middle frontal gyrus during response initiation (Go trials). *P*-factor scores were additionally associated with increased error-related signaling in the temporal cortex during incorrect No-Go trials.

Conclusions.—During adolescence, a period characterized by heightened risk for emergent psychopathology, we observed unique associations between *p*-factor scores and neural and behavioral indexes of response initiation, which relies primarily on sustained attention. These findings suggest that shared variation in mental disorder categories is characterized in part by sustained attention deficits. While we did not find evidence that *p*-factor was associated with inhibition in this study, this observation is consistent with our hypothesis that *p*-factor would be related to non-affective control processes.

Keywords

Adolescence; psychopathology; *p*-factor; inhibition; sustained attention; Go/NoGo Task

Introduction

A relatively recent development in the field of psychiatry has been modeling of a general dimension of psychopathology, termed the *p*-factor (1,2), to account for high comorbidity between different psychiatric syndromes (3,4). The *p*-factor is proposed to reflect the experience of symptoms as persistent, comorbid, and severe and has been found to be more strongly related to functional impairment across the lifespan than specific disorders dimensions (1,2). More so than simply summarizing the co-occurrence of symptoms, *p*-factor is theorized to reflect one's liability to develop psychopathology across the lifespan (2,5–7), and has been modeled in children (7,8), adolescents (9–14), and adults (15–21). In light of these findings, increasingly there have been calls to understand what risk processes underlie *p*-factor.

Adolescence is a crucial period for studying *p*-factor, as risk for psychopathology sharply increases from childhood to adolescence (22–24). This risk for psychopathology in general, and internalizing psychopathology, in particular, is especially heightened for adolescent girls (25–29) and occurs within the context of normative pubertal-onset changes in emotional reactivity and cognitive maturation (30–33). The impact of adolescent-onset psychopathology is not limited to adolescence, as it is associated with multiple negative health and life outcomes in adulthood, including psychopathology (34,35), impaired academic functioning (36–39), suicide attempts and psychiatric hospitalizations (37–38,40), and health risk behaviors (41). Therefore, adolescence represents an important period to study emergent psychopathology that may have implications for future development.

A natural question that follows is: what are the core components underlying shared variation among mental disorder categories? Substantial work links greater *p*-factor scores and shared

variation across DSM disorder categories to impaired cognitive control, including deficits in working memory, sustained attention, visual-motor planning, task switching, and inhibition (1,11,16,19,42). During these tasks, higher *p*-factor scores are associated with greater disruption in the multiple demand network, a network responsible for diverse cognitive functions, which encompasses frontal-parietal regions as well as the insula and dorsal anterior cingulate (10,20,43). Higher *p*-factor scores are additionally associated with neural structure, specifically decreased gray matter volume in the dorsal anterior cingulate and insula, indicating that these functional deficits do not reflect only transient differences in cognitive processing. In addition to its associations with cognitive control processes, higher *p*-factor scores and shared variation across DSM disorder categories are associated with disruptions in various affective processes, including heightened emotional reactivity and disrupted emotion regulation (44,45) and impulsive responding to both positive and negative emotions (46–48).

Disentangling non-affective cognitive control from affective cognitive control is critical to understanding how general psychopathology emerges in adolescence, particularly given normative increases in emotional reactivity (49–50) and emotion regulation difficulties (51–53) during this time period. However, the unique contributions of affective and non-affective regulation to the development of *p*-factor are not yet clear. Some theorize that affective dysregulation underlies *p*-factor above and beyond non-affective executive function, and that affective dysregulation leads to observed deficits in non-affective cognitive control (16,46). Others have proposed that cognitive dysfunction underlies *p*-factor in part because it is involved in a variety of outcomes, including the kind of affective dysregulation associated with *p*-factor (1,17,19).

The purpose of the present study was to better characterize the unique contributions of non-affective and positive affective inhibition on *p*-factor in adolescence by examining both processes during the same paradigm. Examining these two processes within the same task yields a high degree of experimental control because we can manipulate the affective valence of the cue while holding inhibitory control processes constant. Further, this approach increases the likelihood that task differences correlated with non-affective and positive affective inhibition do not contribute to differential associations with *p*-factor. For example, affective inhibition is often assessed using complex stimuli such as emotional faces (44), whereas non-affective inhibition is generally assessed using simple stimuli within well-controlled and commonly used experimental paradigms (19,20).

Using the Conditioned Appetitive Response Inhibition Task (CARIT; 54–57), a Go/No-Go task with both positive affective and non-affective cues, we examined associations between both types of inhibition and *p*-factor scores in 138 adolescents assigned female at birth with mild-to-severe psychopathology. Prior studies have found associations between externalizing symptoms in a community sample of adolescents and neural activity during positive affective inhibition in the CARIT (56). Given the large body of work linking *p*-factor to cognitive function, we hypothesized that higher *p*-factor scores would be associated with impaired non-affective inhibition, consistent with the possibility that disruption in non-affective cognitive function is a primary component of psychopathology risk. Alternatively, given the transdiagnostic role of affective dysregulation in adolescent psychopathology, we

may observe that *p*-factor is related to impaired positive affective inhibition *above and beyond* its association with non-affective inhibition. If supported, this hypothesis would suggest that positive affective disruption of executive function is a primary transdiagnostic risk factor for psychopathology.

Methods and Materials

Participants and Procedures

The sample included 229 adolescents assigned female at birth (ages 9–15; M_{age} = 11.8, SD_{age} = 1.8) who were recruited for a larger longitudinal study examining responses to stress and psychopathology risk in adolescent girls. Participants were recruited from community and clinical placements, including inpatient psychiatric units, outpatient mental health agencies, high schools, and the local community using flyers and mass-email advertisements. All study procedures were conducted at the University of North Carolina at Chapel Hill. Exclusion criteria were active psychosis and any developmental disorder. As part of the larger study, families completed a baseline lab visit where they completed self- and parent-report questionnaires, clinical interviews, and other behavioral tasks not reported here (58). All participants provided written informed consent and all procedures were pre-approved by the Institutional Review Board. This larger sample was used to model *p*-factor.

After completing the baseline visit, interested families were enrolled in the imaging component of the study. Exclusion criteria included MRI contraindications, active substance dependence or substance use on the day of scan, and the presence of an acute suicidal crisis. Participants were asked to refrain from taking stimulant and allergy medications 24 hours before their scan session[1]. 138 adolescents (M_{age} = 11.6, SD_{age} = 1.8) completed both the baseline and fMRI visits. On average, initial scans were completed 4.5 months (*SD* = 6.8 months) following baseline visits. Sample demographics are reported in Table 1. The scanned (*N* = 138) and unscanned sample (*N* = 91) were compared on age, gender, race/ethnicity, and SES. The scanned sample reported lower SES ($t = 2.61(142.5)$, $p = 0.017$) relative to the unscanned sample. No other demographic differences were observed (all *p*'s > .05).

We excluded participants who lost at least two out of three runs due to task performance and/or imaging data quality concerns. Runs were excluded for task performance if average accuracy was below 50% on Go trials and/or below 25% on No-Go trials. Runs were excluded for imaging data quality concerns if 40% of timepoints exceeded 0.9mm relative translational motion or if runs contained a single relative movement greater than 5mm (*N* = 1 run excluded for motion). Twelve participants were excluded due to behavioral performance, six participants were excluded due to ending the task early or excluding the task for time constraints, one participant was excluded due to behavioral performance and motion, one participant was excluded due to the incidental observation of a neuroanatomical abnormality, and one participant was excluded due to technical difficulties. The final sample size for imaging analysis was 117 adolescents (M_{age} = 11.8, SD_{age} = 1.8).

[1]16 participants reported taking a stimulant medication on the day of the scan (11.6% of the sample)

Psychopathology and *P*-factor Modeling

We used questionnaire assessments of psychopathology symptoms in the following categories to estimate *p*-factor: aggressive behavior (Youth Self-Report; 3), ADHD (Conners-3 Parent Assessment; 59), depressed mood (parent and self-report on Mood and Feelings Questionnaire; 60), and anxiety (parent and self-report on the Screen for Child Anxiety Related Disorder; 61). All subscales had acceptable alpha levels ($\alpha > 0.60$). In addition, symptom counts obtained via a semi-structured clinical interview administered to parent and youth separately (MINI-KID; 62) were included in *p*-factor estimation for the following syndromes: Conduct Disorder, Oppositional Defiant Disorder, most symptomatic Major Depressive Episode, Generalized Anxiety Disorder, and Post-Traumatic Stress Disorder (see Figure S1 for a correlation matrix of these measures). For measures with both parent and self-report, the average score of the two were used (See Supplementary Methods for details).

P-factor was modeled in R (63) using the Lavaan package (64). Within the larger sample ($N = 229$), we conducted a confirmatory factor analysis using two analytical models. For the primary analyses, we used a higher-order model with internalizing and externalizing as first-order factors (65–66). Second, as a sensitivity analysis, we used a bifactor model, with *p*-factor, internalizing, and externalizing as orthogonal factors (Figure 1). The models were estimated using a maximum likelihood estimation with robust (Huber-White) standard errors (67) and full information maximum likelihood estimation for missing data. Factor scores were extracted as manifest variables and used in subsequent analyses (see 'Data Analytic Plan').

Pubertal Status

Pubertal status was evaluated as an additional covariate to age (see 'Covariates'). Pubertal status was measured using the Pubertal Developmental Scale, which consists of five items about physical development with good psychometric properties (68).

Inhibitory Control Task (CARIT)

The Conditioned Appetitive Response Inhibition Task (CARIT; 54–57) assessed non-affective and positive affective inhibition using two phases: (1) a reward conditioning phase and (2) an inhibitory control phase. The first CARIT phase used a modified version of the Monetary Incentive Delay task (MID; 69; Figure 2.A.). The second CARIT phase used cues conditioned during the MID as No-Go cues in a Go/No-Go paradigm: the unrewarded cue (Previous Unrewarded target; PU) and the high reward cue (Previously Rewarded target; PR; Figure 2.B.). Task methods were previously described (55–57), and the supplement includes additional details about task stimuli.

fMRI Scanning, Acquisition, and Processing

Scanning was performed on a 3.0-T Siemens Prisma Scanner, using a 32-channel head coil. We followed standard pediatric scanning acquisition parameters and used a standard processing pipeline in FSL v5.0.9 (70; See Supplementary Methods for extensive details about data acquisition and processing).

Data Analytic Plan

Covariates—Age, the quadratic of age, and puberty onset were evaluated as age-related covariates. The main contrasts of interest (i.e., non-affective and positive affective inhibition) were regressed onto these measures. No associations were found between these contrasts and the quadratic of age or puberty onset. Age was associated with increased activation in the left occipital cortex during successful non-affective inhibition (Figure S2). Thus, age was used as a covariate for all analyses.

Due to significant correlation between medication use (i.e., psychotropic, allergy, or asthma medication) and *p*-factor scores, $t(136) = 0.33$, $p < 0.001$, we included medication use in sensitivity analyses as an additional covariate.

Behavioral Analysis Plan—For the MID phase of the CARIT, reaction times (RT) below 50ms were excluded. Motor response bias was calculated (unrewarded > high reward RT). Higher values indicated more speeding to reward (i.e., greater motor response bias to reward).

For the inhibitory control phase of the CARIT, accuracy scores (i.e., proportion of successful response withholding) on PU No-Go stimuli were subtracted from accuracy scores on PR No-Go stimuli (PR > PU accuracy). Lower values indicated poorer positive affective inhibition. Non-affective inhibition was defined as the accuracy of withholding responses to PU No-Go stimuli while controlling for the accuracy of pressing to Go targets.

Average accuracy to PR, PU, and Go targets and reaction time to Go targets were checked for outliers (> 3 standard deviation (SD) from the mean). Accuracy data had no outliers, but 1 participant had an average reaction time on Go trials that was an outlier; this value was removed from all relevant behavioral analysis.

To examine associations between behavioral measures and psychopathology, we used a multiple linear regression model in R.

fMRI Analysis Plan—A general linear model (GLM) was constructed to estimate effects of task. The GLM design for task events was comprised of equally weighted event onsets and durations for the six possible task events: correct and incorrect responses to PR No-Go targets, PU No-Go targets, and Go targets (55–57). All task regressors were convolved with the canonical hemodynamic response function using FSL FEAT. Successful positive affective inhibition was modeled by contrasting correct trials of PR No-Go cues with correct trials of PU No-Go cues while regressing out the effect of non-interest cues (i.e., the four other possible task events). Successful nonaffective inhibition was modeled by contrasting correct trials of PU No-Go cues with correct trials of Go cues while regressing out the effect of non-interest cues. Following typical FSL procedures, statistical analysis of functional images was conducted for each participant and each run. Then, the runs were combined in a fixed-effect analysis for each participant using the linear registration of functional images to MNI-template space.

Group level-mixed effect statistical analyses were performed in FSL FEAT with FLAME1. Successful positive affective inhibition (correct PR > correct PU) and successful non-affective inhibition (correct PU > correct Go) were regressed onto *p*-factor scores to test for the association between general psychopathology symptoms and neural activation while inhibiting responses to cues with and without a history of reward (i.e., affective and non-affective cues). All group-level results were thresholded in FSL using a voxel-wise Z-statistic of Z = 3.1 and a cluster threshold of $p = 0.05$ for a family-wise error correction of FWE $p < 0.01$, consistent with recommendations (71).

We ran sensitivity analyses for the main contrasts of interest using the following control variables in separate analyses: (1) having a dental crown, retainer, or spacer ($N = 5$) (2) having issues with the head coil ($N = 5$). Since these variables did not interfere with imaging (Figure S3), we did not exclude these subjects from the imaging analysis.

Secondary analyses.

Due to finding a significant association between *p*-factor scores and Go performance (see Results), we conducted a secondary analysis regressing successful response initiation (correct Go > baseline) on *p*-factor scores. Given work suggesting that psychopathology may be related to error-related neural signaling (72–73), we conducted an exploratory analysis examining associations between *p*-factor scores and a whole-brain analysis of (a) incorrect No-Go trials > correct Go trials (b) incorrect PU No-Go trials > correct Go trials (c) incorrect PR No-Go trials > correct Go trials.

Results

Estimation of *P*-factor

In the bifactor model, the indicators did not load significantly on the internalizing factor, despite the internalizing factor being well-established (3; Table S1). Thus, the higher-order model was chosen for primary analyses (sensitivity analyses using the bifactor model are reported in the supplement). *P*-factor scores calculated using the higher-Sorder and bifactor models were highly correlated, $r(224) = 0.95$, $p < 0.001$. The model statistics indicated adequate fit (Chi-sq = 55.3, $p = 0.001$, CFI = 0.95, TLI = 0.93, RMSEA (90%CI) = 0.05–0.10, SRMR = 0.05). Standardized factor loadings for the internalizing factor ranged from 0.45 to 0.79. Standardized factor loadings for the externalizing factor ranged from 0.57 to 0.93. The factor structure accounted for 20% to 87% of the variance in the indicators (see Table 2.A. for model statistics). Psychopathology data from the MINI are reported to show the characteristics of the sample in terms of DSM-IV diagnosis (Table 2.B.).

Behavioral Findings

Main Effects—During the MID, participants responded more quickly to high reward cues ($M = 229.5$ms, SD = 31.8ms) relative to unrewarded cues ($M = 236.6$ms, SD = 32.9ms), although this difference was not significant, $t(267) = 1.81$, $p = 0.07$. During the inhibitory control phase, typical of Go/No-Go task performance, participants had significantly lower accuracy on PU No-Go targets ($M = 62.1\%$, SD = 14.6%) than on Go targets ($M = 84.6\%$, SD = 11.9%), $t(227) = 13.0$, $p < 0.001$. There were no significant differences between

accuracy on PR targets (M = 60.1%, SD = 16.0%) and accuracy on PU targets (M = 62.1%, SD = 14.6%), $t(234) = 1.01$, $p = 0.31$.

Associations with P-Factor—During the MID, *p*-factor scores were not associated with motor response bias to reward (β = −0.0005, $p = 0.91$). During the inhibitory control phase, higher *p*-factor scores were associated with better positive affective inhibition (i.e., a smaller difference in false alarms to PR relative to PU targets; β = 1.4, $p = 0.03$), which was robust to medication use controls (β = 1.2, $p = 0.04$). There were no significant associations between *p*-factor scores and non-affective inhibition (β = −0.18, $p = 0.69$). Higher *p*-factor scores were associated with less accurate response initiation to Go targets (β = −2.5, $p < 0.001$), which was robust to medication use controls (β = −2.6, $p < 0.001$). *P*-factor scores were not associated with reaction time to Go targets (β = 0.001, $p = 0.44$).

fMRI results

Main Effects—There were no main effects of successful positive affective inhibition. In contrast, successful non-affective inhibition was associated with increased activation in the bilateral insular cortex extending into the inferior frontal gyrus, the paracingulate gyrus extending into the supplementary motor area, and occipital regions (Table 3, Figure 3).

Associations With P-Factor—*P*-factor scores were not associated with activation during successful positive affective inhibition or successful non-affective inhibition. During successful response initiation, *p*-factor scores were associated with hypoactivation in the left superior frontal gyrus/MFG and right supplementary motor cortex; hypoactivation in the left superior frontal gyrus/MFG was robust to medication controls (Table 3, Figure 4). During incorrect trials of No-Go stimuli (compared to correct Go responding), *p*-factor scores were associated with increased activation in the right inferior temporal gyrus; increased activation in the right inferior temporal gyrus, right temporoparietal junction, and left lateral occipital cortex were robust to medication controls (Table 3, Figure 5). No specific associations were found between *p*-factor scores and activation during incorrect trials of PU No-Go or PR No-Go.

Discussion

Better characterizing underlying processes associated with shared variation among mental disorder categories requires disentangling basic non-affective from affective control processes. As such, the current study examined associations between *p*-factor scores and both non-affective and positive affective inhibition within the same paradigm in a sample of adolescents with mild-to-severe psychopathology.

Behaviorally, higher *p*-factor scores were related to worse performance on Go trials but not non-affective No-Go trials. Similarly, we did not observe associations between *p*-factor scores and activation during successful non-affective inhibition. Instead, we observed hypoactivation in the left superior frontal gyrus and middle frontal gyrus associated with *p*-factor during successful response initiation. Given our observations of impaired Go performance related to *p*-factor scores, we interpret this hypoactivation as impaired recruitment of regions that would facilitate task performance (74). Go/No-Go tasks are

conceptualized as probes of sustained attention, with performance on Go trials reflecting the ability to engage in on-task behavior (75–77). Previous work suggests that the superior frontal gyrus and MFG plays a central role in executive attention (78–83) and that disruptions of circuits involving the ventral and dorsal attention networks may underlie psychopathology risk in adolescence (44). The current findings further add to a body of work associating left MFG function during executive function tasks with adolescent psychopathology symptoms (56; 84–85). Most relevant to the current findings, previous work has found that after isolating sustained attention from response inhibition during a Go/No-Go task, higher ADHD symptom severity was associated with blunted superior frontal cortex activation during sustained attention (86). Our observation of alterations in performance and neural activation to Go but not No-Go trials suggests that *p*-factor may be characterized by underlying impairment in sustained attention, which is a building block to diverse executive functions, including but not limited to inhibition (54; 87–89). Given that we did not hypothesize associations between *p*-factor scores and sustained attention a priori and further given accuracy trade-offs between Go and No-Go stimuli within the Go/No-Go task, future research should further examine the relationship between *p*-factor and sustained attention isolated from inhibition or affective control in a diverse range of experimental paradigms to better characterize psychopathology risk in adolescence.

We observed that higher *p*-factor scores were associated with increased error-related signaling during No-Go trials in temporal regions, including the inferior temporal gyrus and temporoparietal junction. As nodes in the ventral attention network, these regions have been found to be associated with attentional reorienting to unexpected or infrequent stimuli across a range of fMRI tasks (78–79; 91–92). Given that No-Go stimuli appear infrequently compared to Go stimuli, these findings lend support to our interpretation that *p*-factor may be associated with disruptions to attentional processes that can impact a broad array of cognitive sequalae.

Regarding positive affective inhibition, *p*-factor scores were associated with *improved* inhibition to affective No-Go cues. However, no associations were found between *p*-factor and neural activation during positive affective inhibition.

Of note, recent work suggests that executive functioning may be better characterized as unidimensional, particularly during childhood and adolescence, and that individual dimensions of executive functioning (i.e., inhibition) may not have much predictive validity (93–94). While we term responding to No-Go cues as “inhibition” for consistency with the broader Go/No-Go literature, Go and No-Go cues likely share overlapping general executive function processes. Nonetheless, it is notable that we observe both behavioral and neural disruptions associated with *p*-factor scores exclusively during Go trials, the task condition with the most cues and the least novelty. This finding suggests that our interpretation that *p*-factor is associated with general attentional processes would apply regardless of whether No-Go cues are defined as inhibition or general executive functioning.

Several strengths of this study should be noted. We disentangled positive affective inhibition from non-affective inhibition, which is important to isolate the basic components of cognition driving general psychopathology. In the context of this task, we limited potential

learning confounds by controlling for previous history (i.e., controlling exposure to positive affective and non-affective cues). In addition, we examined positive affective and non-affective cognitive processes in a sample with a wide range of psychopathology. Previous studies have sometimes relied on samples with low rates of diagnosable disorders. Even if psychopathology symptoms are distributed normally in the population, individuals at the tails of the distribution may evidence specific types of cognitive and affective risk factors which will not be observed if only the middle of the distribution is sampled. Indeed, previous work by our group using this task in a sample with low rates of psychological disorders found different associations between psychopathology symptoms, neural activation, and task performance, suggesting exactly this kind of non-linear relationship (56).

Several limitations should also be noted. First, in defining our constructs as “affective” and “non-affective,” we made assumptions that these constructs measure trait-like domains of functioning. Although these constructs show discriminative validity within this experimental task (54–57), we have not established whether they differentially predict affective vs. non-affective measures outside of the task. In addition, our “affective” construct only indexes inhibition to positively-valenced cue. Thus, we cannot make conclusions about the relationship between *p*-factor and inhibition to negatively-valenced cues. Future research should investigate the criterion validity of these constructs. Second, although we obtained variability in individuals meeting DSM-IV criteria for both internalizing and externalizing disorders, the majority of participants with externalizing disorders had comorbid internalizing disorders (81.6%). Therefore, it is possible that internalizing symptoms were overrepresented in our *p*-factor estimates due to missing purely externalizing presentations. Future research should examine these processes with a more diverse range of symptom presentations and using a mixed-sex sample to improve generalizability. Third, work on reproducibility in fMRI studies indicates that our sample size limits statistical power (95). Finally, given its cross-sectional nature, this study is limited in its ability to make inferences about whether observed impairments in task performance are a cause or consequence of psychopathology.

In conclusion, parsing affective and non-affective contributions to *p*-factor and their neural correlates is essential for advancing our understanding of how to intervene on emerging psychopathology during adolescence. Using a well-controlled Go/No-Go task, we observed that *p*-factor scores were associated with deficits in response initiation, rather than deficits in inhibition *per se*. Our findings thus suggest that sustained attention deficits, rather than inhibition deficits specifically, may play a central role in the development of multiple psychiatric conditions captured by *p*-factor and may be an important point of clinical intervention and assessment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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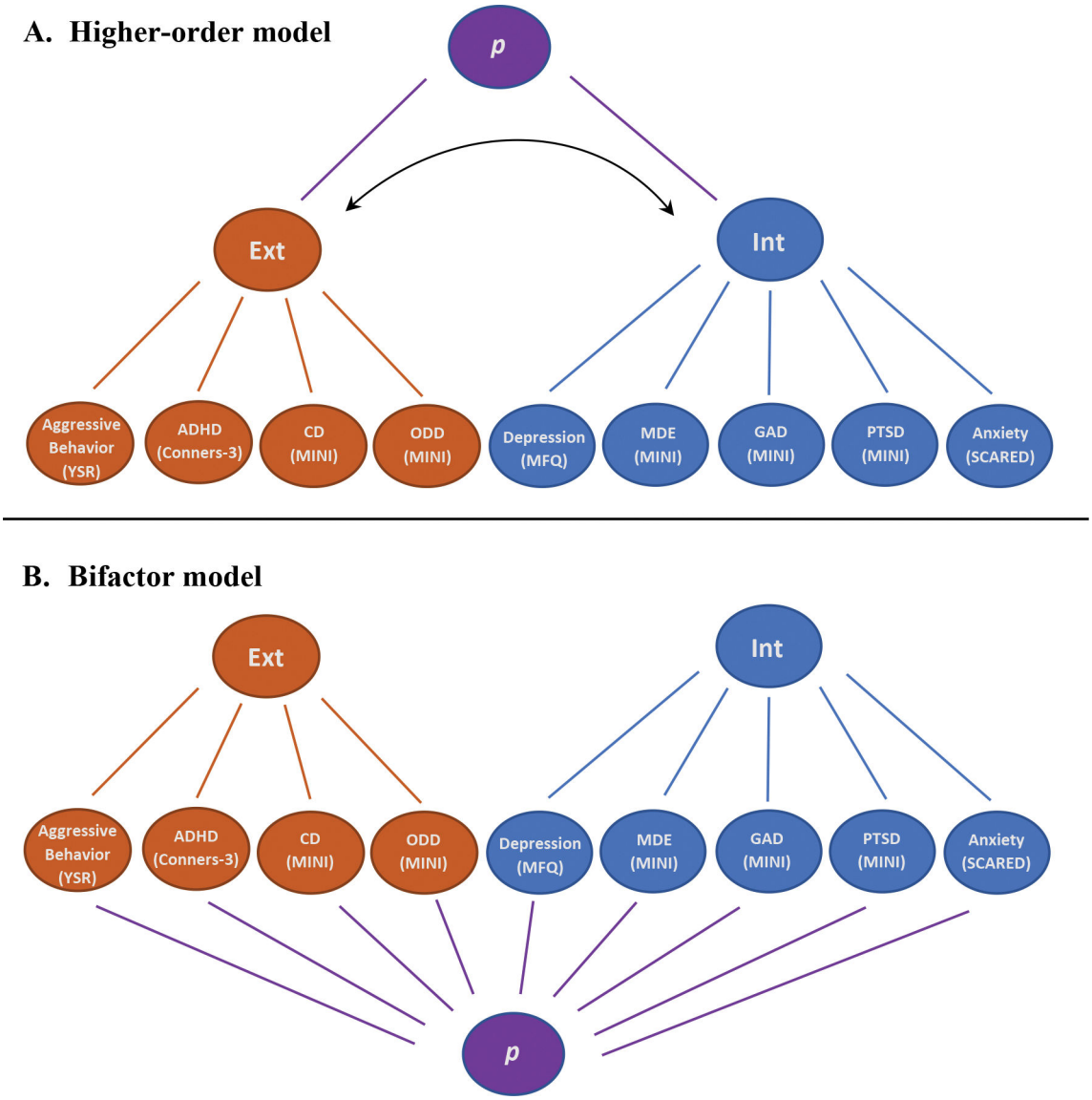

Figure 1. P-Factor Modeling.

Modeling of p-factor using a confirmatory factor analysis: **A.** hierarchical modeling of p-factor used as the main analysis. **B.** Bifactor modeling of p-factor used as a sensitivity analysis. Ext = externalizing, Int = internalizing. ADHD = Attention-Deficit Hyperactivity Disorder, CD = Conduct Disorder, ODD = Oppositional Defiant Disorder, MDE = most symptomatic Major Depressive Episode, GAD = Generalized Anxiety Disorder, PTSD = Post-Traumatic Stress Disorder. Psychopathology questionnaires: Youth Self-Report (YSR), Conners-3 Parent Report, Mini Neuropsychiatric Interview for children and adolescents (MINI-KID), Mood and Feelings Questionnaires (MFQ), Screen for Child Anxiety Related Disorders (SCARED).

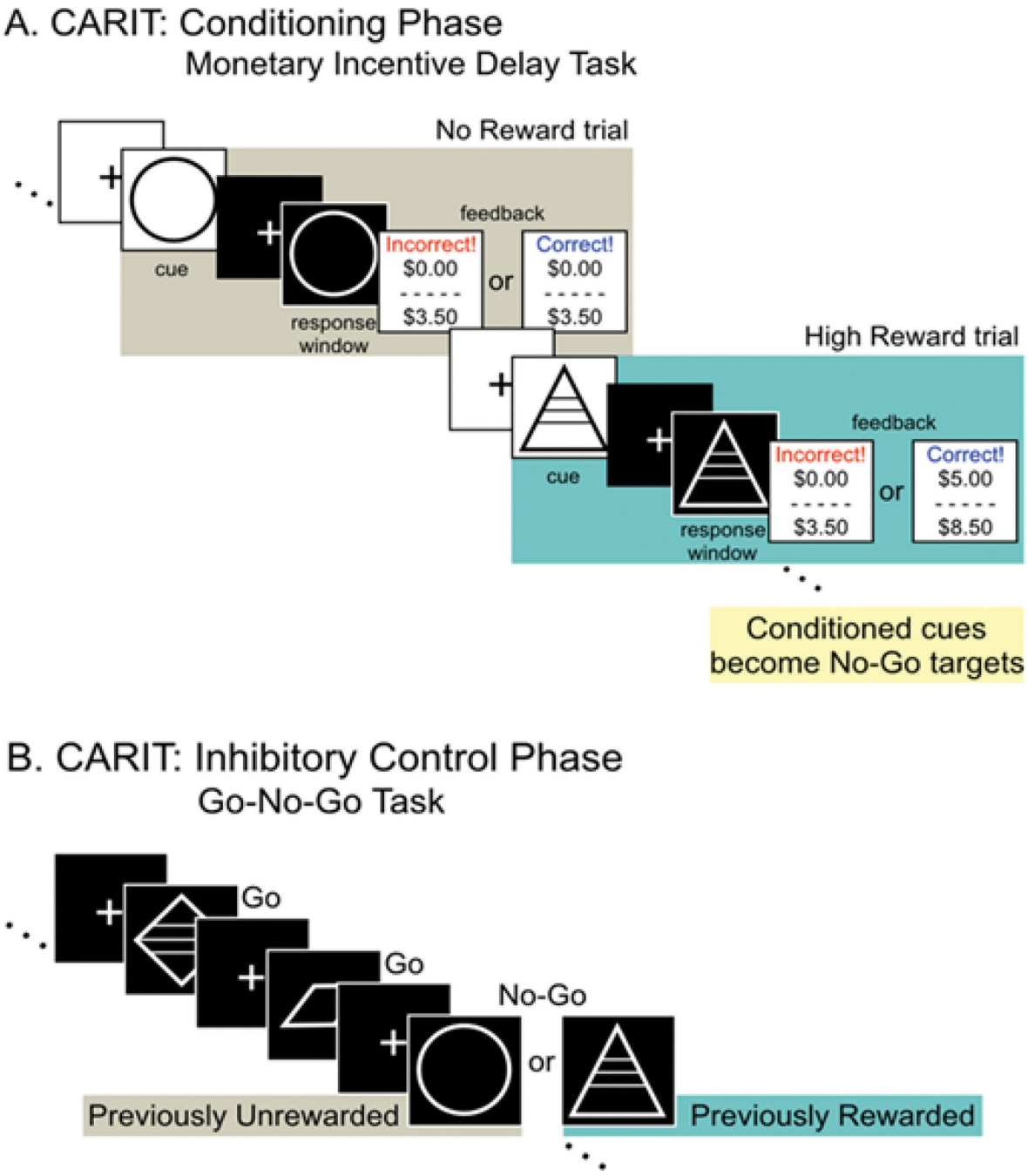

Figure 2. The CARIT Task.

The Conditioned Appetitive Response Inhibition Task (CARIT) assessing non-affective and positive affective inhibition. **A.** The reward conditioning phase (modified MID paradigm) **B.** The inhibitory control phase. Figures reproduced with permission from Davidow et al (2018).

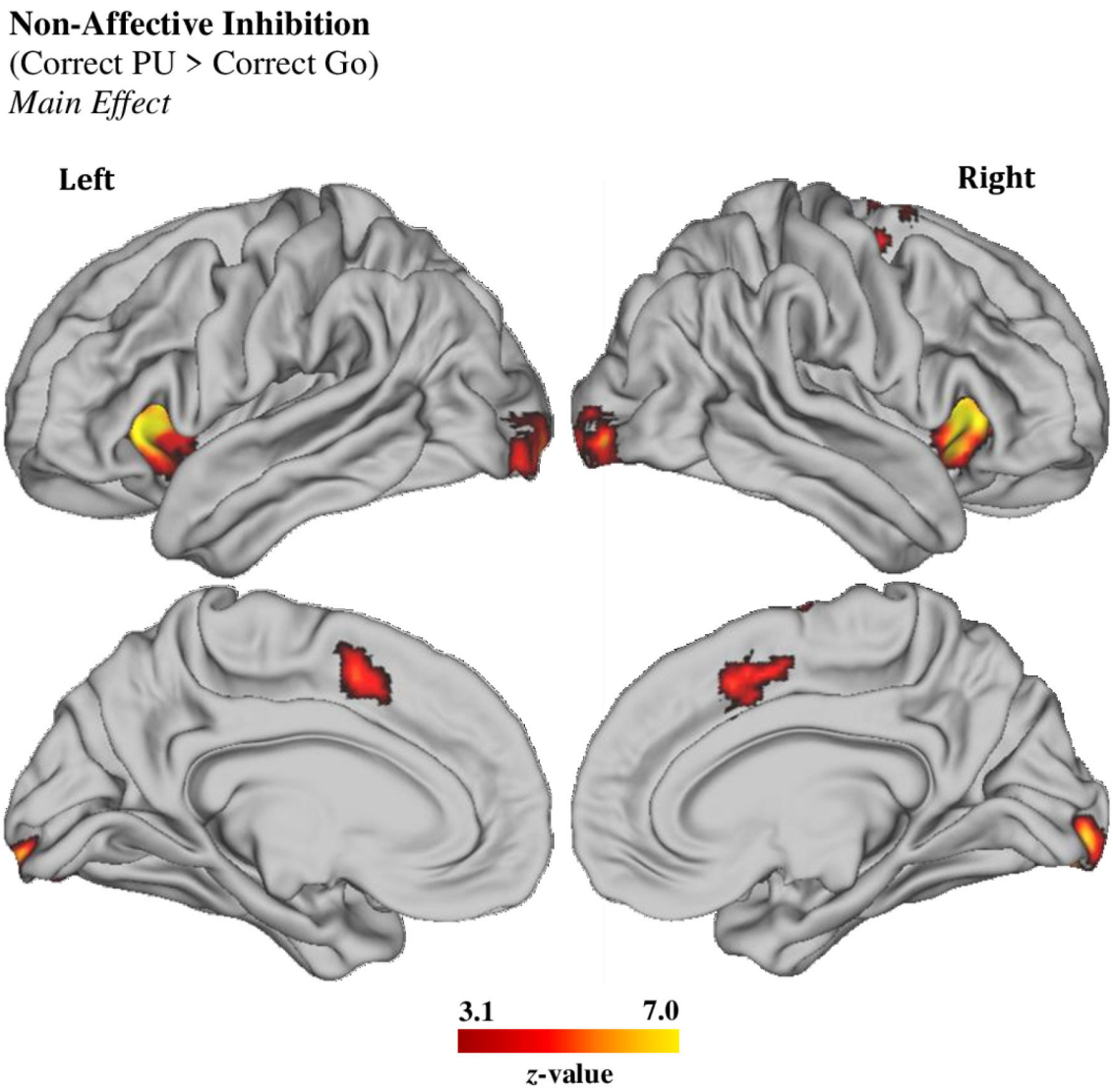

Figure 3. Main Effect of Non-Affective Inhibition.

Main effect of non-affective inhibition to Previously Unrewarded (PU) targets relative to successful responses to Go targets ($N = 117$). These maps demonstrate positive associations with the bilateral insular cortex extending into the inferior frontal gyrus, paracingulate gyrus, supplementary motor area, and occipital regions (voxel-wise corrected $Z = 3.1$, cluster corrected $p < 0.05$).

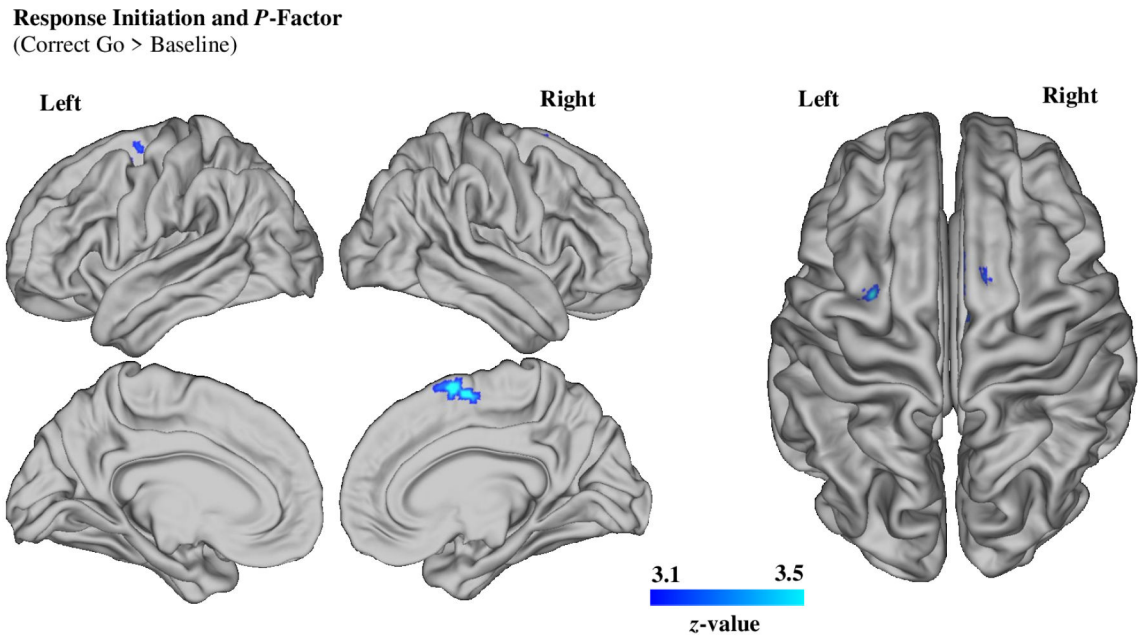

Figure 4. P-Factor Associated with Response Initiation.

Successful response initiation, regressed on *p*-factor scores ($N = 117$). Voxel-wise corrected $Z = 3.1$ and cluster-corrected $p < 0.05$. These maps show a negative association between *p*-factor scores and activation in the left superior frontal gyrus/middle frontal gyrus and right supplementary motor cortex during successful response initiation; activation in the left superior frontal gyrus/middle frontal gyrus was robust to additional controls for medication use.

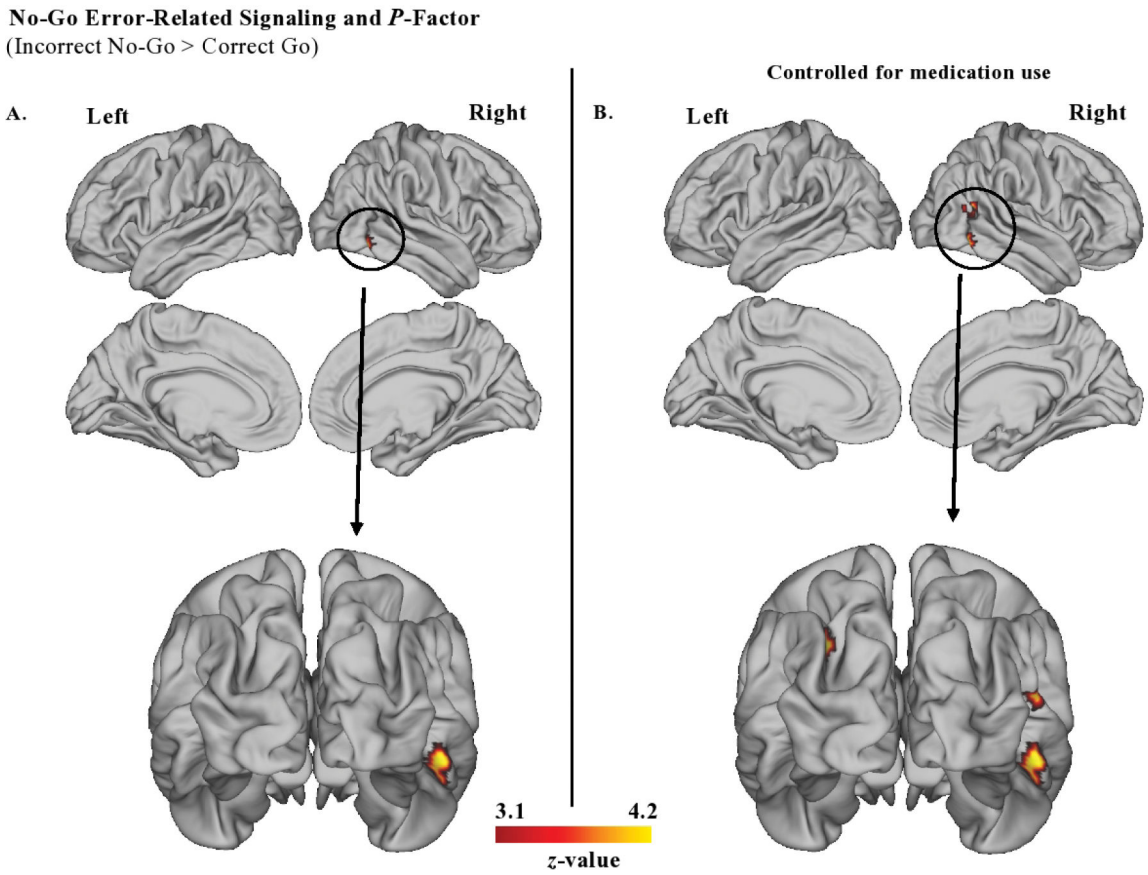

Figure 5. No-Go Error-Related Signaling and *P*-Factor.

No-Go error-related signaling (Incorrect No-Go > Correct Go), regressed on p-factor scores ($N = 116$). Voxel-wise corrected $Z = 3.1$ and cluster-corrected $p < 0.05$. A. Uncontrolled for medication use. These maps show a positive association between *p*-factor scores and activation in the right inferior temporal gyrus. B. Controlled for medication use. These maps show a positive association between *p*-factor scores and activation in the right inferior temporal gyrus/temporoparietal junction and left occipital cortex.

Table 1.

Sample characteristics.

Sample demographics ($N = 138$).

Characteristic	Mean (SD) or Count (%)	Min (Max)
Age in years	11.6 (1.8)	9.1 (17.2)
Gender identity		
Female	124 (89.9%)	
Gender non-conforming	7 (5.1%)	
Male	4 (2.9%)	
Unreported	3 (2.2%)	
Race/Ethnicity		
Asian	3 (2.2%)	
American Indian/Alaska Native	2 (1.4%)	
Black/African-American	45 (32.6%)	
Hispanic/Latine	8 (5.8%)	
Multi-racial	4 (6.6%)	
White/Caucasian	59 (42.8%)	

Table 2.

A. Higher-Order Model Statistics. Model statistics for the hierarchical modeling of p (N = 226), including raw estimates of the factor loadings, fully-standardized factor loadings (std. estimate), the standard error of the factor loadings (std. error), the significance of the factor loadings (p-value), and the proportion of the variance explained by the factor structure (R-square). **B. Sample DSM-IV Diagnostic Descriptive Statistics.** The percentage of the sample (N = 138) meeting criteria for diagnosis, as determined by DSM-IV diagnostic criteria.

A.	**Raw Estimate**	**Std. Estimate**	**Std. Error**	***p*-value**	**R-square**
Internalizing					
MFQ	5.6	0.79	0.55	<0.001	0.62
MINI lifetime MDE	1.5	0.72	0.11	<0.001	0.52
MINI GAD	1.3	0.75	0.11	<0.001	0.57
SCARED	0.79	0.66	0.08	<0.001	0.43
MINI PTSD	0.86	0.45	0.18	<0.001	0.20
Externalizing					
Conners ADHD index	3.3	0.57	0.36	<0.001	0.32
MINI CD	0.58	0.78	0.07	<0.001	0.60
MINI ODD	1.5	0.93	0.08	<0.001	0.87
YSR (aggressive behavior)	2.4	0.68	0.28	<0.001	0.46
p-factor					
Externalizing	1.0	0.71			0.50
Internalizing	1.0	0.71			0.50
B.	**Count (%)**				
Lifetime MDE	68 (49.3%)				
Current MDE	17 (12.3%)				
PTSD	25 (18.1%)				
ODD	48 (38.5%)				
CD	20 (14.5%)				
GAD	52 (37.7%)				

MFQ = Mood and Feelings Questionnaire; MDE = Major Depressive Episode, GAD = Generalized Anxiety Disorder, SCARED = Screen for Child Anxiety Related Disorders, PTSD = Post Traumatic Stress Disorder, ADHD = Attention Deficit Hyperactivity Disorder, CD = Conduct Disorder, ODD = Oppositional Defiant Disorder, YSR = Youth Self-Report.

Table 3.

Regions of Peak Activation.

Regions of peak activation associated with the main effects of the inhibitory control phase of the CARIT and associations with *p*-factor scores ($N = 117$). Results thresholded using a voxel-wise threshold of $Z = 3.1$ and a cluster threshold of $p = 0.05$ for a family-wise correction of $p < 0.01$. PU = Previously Unrewarded.

Trial Type	Region of Peak Activation	Cluster Size	x	y	z	z Value	
Non-Affective Inhibition							
(Correct PU > Correct Go)							
Main Effect							
	Anterior insula (R)	781	34	26	2	7.77	*cluster peak*
	Inferior frontal gyrus (R)[a]						
	Anterior insula (L)	624	−30	24	0	8.50	*cluster peak*
	Inferior frontal gyrus (L)[a]						
	Inferior occipital (R)	482	26	−90	−2	6.02	*cluster peak*
	Inferior occipital (L)	463	−20	−94	−2	6.75	*cluster peak*
	Supplementary motor area (R)	279	6	10	48	5.41	*cluster peak*
	Paracingulate gyrus (R)[a]						
	Supplementary motor area (L)	48	16	4	66	5.22	*cluster peak*
	Paracingulate gyrus (L)[a]						
Response Initiation							
(Correct Go > Baseline)							
Associated with P-Factor							
	Supplemental motor cortex (R)	85	10	8	62	4.21	*cluster peak*
	Superior frontal gyrus (L)	66	−26	−2	60		*cluster peak*
	Middle frontal gyrus (L)[a]						
Additional medication control							
	Superior frontal gyrus (L)	68	−26	−2	60	4.28	*cluster peak*
	Middle frontal gyrus (L)[a]						
No-Go Error-signaling							
(Incorrect No-Go > Correct Go)							

Trial Type	Region of Peak Activation	Cluster Size	x	y	z	z Value	
Associated with P-Factor							
	Inferior temporal gyrus (R)	92	54	−58	−10	4.54	*cluster peak*
Additional medication control							
	Temporoparietal junction (R)	108	54	−56	16	3.99	*cluster peak*
	Inferior temporal gyrus (R)	103	54	−58	−10	4.59	*cluster peak*
	Lateral occipital cortex (L)	56	−30	−68	36	4.22	*cluster peak*

[a]Contiguous with the cluster peak