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Functional activation during a cognitive control task in healthy youth specific to externalizing or internalizing behaviors

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Abstract

Background—Externalizing behaviors are negative behaviors expressed outwardly, including rule-breaking, aggression and risk taking; internalizing behaviors are expressed inwardly, including depression, withdrawal and anxiety. Such behavior can cause problems in early life and predict difficulties across the lifespan. There is evidence for a relationship between executive function and both externalizing and internalizing. However, although these behaviors occur along a spectrum, there is little neuroimaging research on this relationship in typically developing youth.

Methods—We assessed 41 youth (10–19 years) using the Multi-Source Interference Task (MSIT), during functional magnetic resonance imaging (fMRI) and related the findings to self-reported externalizing and internalizing scores as measured by the Youth Self Report. We performed a GLM using FSL; externalizing, internalizing, age and sex, were included in the model.

Results—Compared to the control condition, the more difficult MSIT interference condition was associated with greater engagement of the fronto-parietal cognitive control system, and decreased engagement of regions in the default mode network (DMN), based on a cluster threshold of $Z>3.1$, $p=0.01$. When we examined regions uniquely associated with either internalizing or externalizing, we found that within the same group of subjects, higher externalizing behavior was associated

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with hyperactivity in the parietal lobe; alternately, higher internalizing behavior was associated with increased activation in the medial prefrontal cortex.

Conclusions—These findings suggest that both externalizing and internalizing may be associated with altered, but different, patterns of activation during cognitive control. This has implications for our understanding of the relationship between cognitive control and behavioral problems in youth.

Keywords

externalizing; internalizing; functional MRI; fMRI; development; cognitive control; executive function

1. Introduction

Early signs of many behavioral disorders begin to surface during childhood and adolescence. Externalizing behavior is described as a combination of aggression and rule breaking behavior and is a common cause of child referrals to mental health services (1, 2). While such behaviors fall along a broad continuum of severity and are relatively common in even in healthy youth (3), they can be a prelude to more severe behavioral problems in adulthood (4–7). In particular, externalizing behavior in childhood or adolescence can be conceptualized as being on a lifetime spectrum of maladaptive behavioral patterns that include antisocial personality disorder, conduct disorder (CD), attentional disorders, oppositional defiant disorder (ODD), and substance use disorder (8). Internalizing behaviors are a combination of anxiety, depression, and withdrawal, all of which are directed inwards (3). These behaviors may also be on a lifetime spectrum with mood problems, eating disorders and somatization disorders (9). Importantly, even when not a precursor to later disorders, and even when manifested subclinically, such behavior may result in difficulties in school, home, and social environments and can have long term effects on quality of life.

Given the ramifications of early exhibition of problem behaviors, it is of interest what the neural underpinnings might be. Neural and cognitive development continue throughout adolescence and into early adulthood (10). During this time, cognitive control and the broader executive functions generally make improvements with age (11, 12). This change is supported by development in the function (13) and structure (14) of the cognitive control system in the brain as well as its interactions with other systems. The cognitive control or executive system is a set of regions consistently activated by cognitive control/executive tasks, including the dorsolateral prefrontal cortex (PFC), frontal eye field, anterior cingulate (ACC), and parietal cortex (15). In addition to the positively activated regions, there is a frequently described pattern of task induced ‘deactivation’. This decrease in activation during task performance occurs in regions such as the medial PFC and posterior cingulate cortex that overlap with the regions that are included in the default mode network (DMN). Due, in part, to the protracted development of the cognitive control network in relation to other large scale brain networks, such as the reward network, behavior during adolescence is characterized by poor self-regulation, impulsivity, susceptibility to social influences, and risk-taking (16–19). Correspondingly, there is evidence that increases in self-regulation may predict the natural developmental decrease in externalizing behavior patterns seen across

childhood (20) and that children who continue to show externalizing behavior have particular difficulty with inhibitory control (21–25). However, internalizing is also related to the executive functions (26, 27). One theory is that the disruptions in internalizing behavior related to executive function may result in part from the association between decreased executive function and development of social competence (28, 29) and academic readiness (28). This combination of deficits can contribute to social isolation or withdrawal and anxiety that may serve as a prelude to other later problems (30). Individuals with internalizing problems seem to have difficulty with shifting, inhibition and working memory (22, 31). In sum, the patterns observed across development highlight the impact of lower executive function in childhood and adolescence on a wide range of behaviors. Further, even after adolescence, lower executive function across the lifespan may contribute to a pattern of ongoing problematic behavior.

Although both externalizing and internalizing behaviors have been associated with executive dysfunction, it remains unclear whether this is due to separate or overlapping neural factors. While previous cognitive and behavioral research has supported a relationship between executive function with externalizing behaviors in youth (24, 25), there is relatively little research using functional neuroimaging to probe the basis of this relationship. In adults, antisocial traits were associated with alterations in activation in regions associated with cognitive control and emotion processing during a Stroop task (32). In children and adolescents, one study did find that functional activation positively predicted working memory performance, and separately that low working memory performance predicted higher externalizing behavior (33). In terms of internalizing, youth with depression have been found to have alterations in functional activation during a wide range of tasks including executive function tasks (34). However, these studies have primarily assessed groups with a specific diagnosis, such as depression; imaging studies of the executive system have rarely been done as related to the broader internalizing construct. Furthermore, while work has been done using task-based functional magnetic resonance imaging (fMRI) studies, no work in developmental samples has examined the direct relationship between cognitive control network activation and naturally occurring variability in externalizing or internalizing behavior in otherwise healthy youth, or specifically compared the effects of internalizing and externalizing behavior in the same analysis.

Here, we have investigated differences in functional activation during a cognitive control task, the Multisource Interference Task (MSIT), in a sample of healthy children and adolescents age 10–19 during fMRI, as related to real life externalizing and internalizing behaviors. Performance on the MSIT is particularly reliant on inhibitory processes, which have been shown to be impaired in youth with both internalizing and externalizing (22). Given that internalizing and externalizing consist of different sets of behavioral patterns and yet both have been associated with executive behavioral deficits, our goal was to understand whether there were unique differences in activation associated with each of these constructs. Understanding how engagement of the cognitive control system impacts behavior is important not just for understanding individual differences in healthy populations, but also in patient populations associated with cognitive control deficits such as substance use disorders, attentional disorders, CD, and depression.

2. Materials and Methods

2.1 Participants

Fifty-three healthy individuals between the ages of 10 and 19 years were recruited from the community through local advertisements and word of mouth. They participated as part of a longitudinal study (Comprehensive Assessment of Neurodevelopment in Youth; CANDY) at Zucker Hillside Hospital and the Feinstein Institute for Medical Research. This sample has been published on previously on its own and as subsets of other samples, but neither this functional task, nor the internalizing and externalizing data have been previously published (14, 35–37). Four participants were excluded for poor performance (below chance), three were excluded for excessive motion, and five were excluded for other technical reasons (not completing both runs of the task, most commonly), resulting in a final sample of 41.

Written informed consent was obtained from participants; if the participant was a minor, consent was obtained from a parent or guardian and all minors provided assent. Participants had no current or past history of a *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*, axis I psychiatric disorder. The Structured Clinical Interview for DSM-IV (SCID) (38) was administered to all participants, with those under the age of 15 additionally completing a supplementary Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) for childhood specific disorders such as autism and ADHD. Corroborative interviews were performed with parents or guardians for participants who were minors. Ratings were performed by trained Masters level raters, and diagnoses were confirmed in a department wide consensus meeting supervised by licensed clinicians and trained psychometricians. Other exclusion criteria included: (1) intellectual disability, (2) learning disability, (3) medications with known adverse cognitive effects, (4) MRI contraindications, (5) pregnancy, (6) significant medical illness that could affect brain structure or function. This study was approved by the Institutional Review Board of the Northwell Health System.

2.2 Behavior

To assess behavior, the Youth Self-Report (YSR), the self-report version of the Child Behavior Checklist (CBCL) was administered as a self-report measure (39). The YSR consists of eight sub-scales: anxious/depressed (13 items), withdrawn/depressed (8 items), somatic complaints (10 items), social problems (11 items), thought problems (12 items), attention problems (9 items), rule-breaking behavior (15 items), and aggressive behavior (17 items). Each item can be answered as 0 (not true), 1 (sometimes or somewhat true) or 2 (very true or often true), and the subscales are the sums of ratings on the individual items. Internalizing and externalizing behaviors are then calculated from these subscales: internalizing consists of the sum of anxiety/depression and depression/withdrawal, while externalizing consists of the sum of aggressive behavior and rule-breaking. This method resulted in both an externalizing and an internalizing score for each of the 41 participants.

2.3 Image Acquisition

Imaging data were collected in North Shore University Hospital in Manhasset, NY using a 3T GE MRI scanner. Functional T2-weighted echo planar images (EPIs) were collected with

the following parameters: slice thickness = 4mm, 30 slices, TR = 1500 ms, TE = 30ms, 64×64 matrix. Each run contained 268 EPIs. Additionally, a T2 high-resolution fast spin echo (FSE) anatomical scan and 3D coronal SPGR were collected. The parameters for the T2 are as follows: TR = 7100 ms, TE = 98.9 ms, 256×256 matrix, axial plane, slice thickness = 2.5 mm, 51 slices. The parameters for the SPGR are as follows: TR = 7.8 ms, TE = 3.02 ms, 256×256 matrix, coronal plane, slice thickness = 1mm, 216 slices.

2.4 Task Design

The MSIT is a cognitive control task, specifically focused on inhibition; it was designed to probe the dorsal anterior cingulate (dACC) but also engages a larger fronto-cingulo-parietal cognitive control system (40). The task includes two conditions, the easier “control” condition, in which the finger used to respond congruently maps onto the spatial location of the stimuli, and the harder “interference” condition, in which the participant must override the impulse to use the congruent finger and instead use a different one (see Supplementary Figure S1).

Subjects complete two runs of the MSIT during the MRI exam, with each scan lasting 6 minutes and 42 seconds. Each condition was presented in alternating blocks with fixations in the first and last 30 seconds of the run. The first run began with the control condition (F=fixation, C=control, I=interference; FCICICICIF) while the second run began with the interference condition (FICICICICF.) Each block lasted 42 seconds and contained a randomized 24 trials that were presented continuously with no delay or jitter between trials, totaling in 96 trials per condition and 192 trials per run.

2.5 Image processing

Functional analysis was performed using FSL (FMRIB’s Software Library v5.0.2; {Smith, 2004}). The first 4 volumes of each scan were discarded. Data for each scan were first realigned to account for small head movements (41, 42). Individual subject analyses employed FEAT (FMRI Expert Analysis Tool) using a 5mm (FWHM) Gaussian smoothing kernel and 100s high-pass filter. A three-step registration process was performed; first, EPI images were registered to the T2 scan, then to the SPGR, and finally into standard (MNI) space using non-linear transformation (43, 44). We took several steps to account for motion effects. First, subjects with average translational motion greater than 3mm were excluded. Second, individual volumes with uncorrectable motion artifacts (i.e. pronounced striping) were modeled separately and thus censored from the analysis. If there were more than 10 volumes with uncorrectable motion induced artifacts, the subject was excluded. Third, the six regular motion parameters along with the 24 extended parameters (derivative of motion parameters, and squares of motion parameters and derivatives) were included in the model. Time-series statistical analysis was carried out using FILM (FMRIB’s Improved Linear Model) with local autocorrelation correction (45). Correct trials for control and interference conditions were each modeled separately; all incorrect trials were modeled together. Temporal derivatives for all regressors were included as covariates of no interest to improve statistical sensitivity. The two runs for each subject were combined in a second level analysis using fixed effects.

As is customary for cognitive control tasks, our group analyses focused on the Interference – Control condition, to isolate the neural changes associated with the more demanding interference effects. Analyses were carried out using FLAME stage 1 (FMRIB's Local Analysis of Mixed Effects) (46, 47) which has been shown to be less vulnerable than other methodologies to inflation of familywise Type-1 error rates (48).

A single higher level model was run, which included both externalizing and internalizing scores as continuous values for every subject; scores were demeaned across the group and entered into the model. In addition, the model included age, sex, and average performance, all demeaned. To correct for multiple comparisons, resulting Z-statistic images were thresholded using clusters determined by Z>3.1 and a (corrected) cluster significance threshold of P=0.01 (49–51). Cluster p-values were determined using a spatial smoothness estimation implemented in FEAT (41). All figures were created using FSLview, peaks were defined using local maxima as defined in FEAT.

3. Results

In the final sample of 41 participants, mean full scale IQ was 108.87 ± 11.85, as estimated from the Wide Range Achievement Test (WRAT-3). Handedness was determined using the Edinburgh Handedness Inventory, and the median laterality quotient was .75 ± .38 (range −1 to 1). YSR Externalizing scores ranged from 0–27 and Internalizing scale scores ranged from 0–30. These corresponded to T-scores of 27–69 for Externalizing, and 27–72 for Internalizing. Clinically, scores above 64 (dotted line) and below 70 (solid line) are considered borderline clinical, and 70 and above considered to be in the clinical range (see Figure 1). With the exception of one participant, all were below the clinical range, and this sample can be considered representative of variability expected in healthy subjects. When controlled for age there was no significant sex difference in externalizing ($F(2,163)=2.9$, $p=.0629$) however there was a difference for internalizing ($F(2,163)=3.783$, $p=.0256$) such that males had a lower mean (7.72) than females (10.30). Therefore, sex was controlled for in all subsequent analyses. There was no relationship between externalizing and overall percent correct ($F(3,37)=.33$,$p=.641$) (corrected for age and sex) or for internalizing ($F(3,37)=.95$), $p=.241$. There was also no relationship between either externalizing and response time (RT) during interference ($F(3,37)=.4$),$p=.981$) or control conditions ($F(3,37)=.38$),$p=.961$) or between internalizing and RT during interference ($F(3,37)=.44$),$p=.888$) or control conditions ($F(3,37)=.51$),$p=.607$).

Performance on this task is typically quite high, and in this sample, the average percent correct was 88.1 ± .04. To test whether there was an interference effect present, we calculated the difference in RT for the interference and control conditions. Mean RT for control trials was 215.16 ± 28.74ms, for interference was 339.02 ± 35.63ms, with a significant difference of 123.87 ± 25.64ms ($F[1,38]=34.975$, $p<.001$); all participants showed RT interference effects. A robust regression controlled for sex revealed no significant relationship of percent correct with age ($F[2,38]=1.15$, $p=.33$) but did show a trend towards a relationship of the interference effect with age such that the interference effect decreased as age increased ($F[2,38)=2.89$, $p=.068$). Further, internalizing and externalizing scores were highly positively related ($F[3,37]=7.87$, $p=.0003$).

We first examined the positive overall activation pattern elicited from the MSIT, based on the mean activation on correct trials only for the Interference – Control (I-C) contrast across all subjects, to establish the normative activation pattern. This specific contrast is frequently used in this style of cognitive task as it most effectively isolates the interference aspect of the task. In the Interference – Control contrast, the MSIT robustly engaged the fronto-parietal-cingulo cognitive control system, activating the superior parietal cortex, lateral frontal cortex, occipital lobe, and cerebellum (Figure 2; Table 1). In the reverse Control – Interference (C-I) contrast there were significant effects in regions consistent with the default mode network (DMN), including the medial prefrontal cortex, posterior cingulate, and lateral parietal regions (Figure 2; Table 1), consistent with a greater decrease in those regions during the more difficult interference condition.

Then, we tested the primary model in which levels of externalizing and internalizing scores were assessed in relationship to functional activation in the Interference-Control contrast, with age, performance, and sex as covariates. Our primary contrasts of interest were Externalizing – Internalizing, to see the regions unique to externalizing, and the converse, Internalizing – Externalizing. Higher externalizing behavior scores, relative to internalizing, were associated with increased activation in the parietal lobe, which was included in the I-C positive activation pattern. (Figure 3, Table 2). Higher internalizing behavior scores, relative to externalizing, were associated with increased activation in medial prefrontal cortex (mPFC), this region was included in the ‘negative’ regions from the C-I contrast, indicating that this alteration in activation may be best described as a failure to show the typical suppression of this region during difficult task performance (Figure 4, Table 2).

In supplementary analyses, we analyzed the effects of the secondary variables, age, sex, and performance. A significant relationship was seen with age such that there was a decrease in medial prefrontal cortex activation as age increased (Supplementary Figure S2, Supplementary Table S1). There was a significant effect of sex in which males showed greater activation than females in superior parietal lobe, fusiform gyrus, supramarginal gyrus, and paracingulate (Supplementary Figure S3, Supplementary Table S1). There was a significant effect of performance such that individuals with higher performance showed higher activation in the supramarginal gyrus (Supplementary Figure S4, Supplementary Table S1). Notably, while there was also a significant relationship in the parietal lobe with externalizing, this performance effect is centered in the regions that showed decreased activation during interference relative to control; the externalizing effect although adjacent, was centered in the regions showing the opposite effect. This would imply that these effects are reflecting different types of neural changes.

4. Discussion

Our study uses fMRI to provide the first evidence that altered activation during cognitive control is related to variability in both externalizing and internalizing behaviors in typically developing youth. Further, while we found effects associated with both internalizing and externalizing constructs during the task, the significant regions were located in different systems, implying different etiologies of the alterations in cognitive control and inhibitory processes. It is notable that we were able to dissociate these differences between

internalizing and externalizing associated activation within the same model even though those two constructs were highly correlated.

There is a great deal of behavioral evidence showing that decreased cognitive control or executive function is associated with increased externalizing behavior (24, 25, 52, 53). However, there is substantially less neuroimaging data focused on the contribution of the cognitive control system to these behaviors. Here we demonstrate that increased activation in a region of the cognitive control system was specifically associated with higher levels of externalizing and not internalizing behavior in children and adolescents. One interpretation is that this pattern may be consistent with an 'inefficient' activation pattern, however it is also possible that this represents improved or adaptive increases in the recruitment of neural circuitry to support task performance (19). In contrast, internalizing behavior was specifically associated with reduced deactivation within the mPFC, a region of the DMN system that typically shows deactivation during difficult task performance. This DMN disruption is similar to patterns observed in individuals with depressive disorders (54), but was not similar to the cognitive control system effects seen in the externalizing contrast.

There are limited data on the neural basis of variability in externalizing behavior in individuals without diagnosed disorders. Unlike many studies using community samples, our participants were formally screened for, and thus free of, Axis-1 disorders. In a study of youth with CD and attention deficit hyperactivity disorder (ADHD) there were alterations in activation during an interference task such that those with CD showed alterations in superior temporal lobe and precuneus, and those with ADHD, in the medial parietal cortex (55), with similar patterns observed during a study of inhibition in the same populations (56). In addition, Castellanos-Ryan et al showed decreased frontal lobe activation during failed inhibition during a stop signal reaction time task in a large sample of youth with ADHD/CD cluster symptoms (57). Consistent with the executive nature of these findings, Ziermans et al found executive system activity during working memory positively predicted working memory capacity, which in turn negatively predicted externalizing behavior (33). Such functional activation findings are also broadly consistent with executive system structural (36) and functional (1, 58) connectivity findings related to externalizing. Interestingly, in these analyses, activation was decreased in the patient groups, where our sample showed increased activation with increased externalizing. This may be due to the difference between healthy individuals showing varying levels of typical behavior vs. those with a more severe condition. It also may be because we focused specifically on the activation differences within the context of the I-C contrast, because this otherwise healthy sample may have exhibited compensatory activation patterns, or because we specifically sought to assess regions unique from those associated with internalizing.

There is also little work exploring neuroimaging as related to the broadly defined internalizing construct in general, and even less in individuals who are otherwise typically developing. In contrast, several studies have examined adolescents with depressive and anxiety disorders, representing a more severe manifestation of internalizing problems (59). For instance, a recent review showed that among youth with depression, elevated activity in medial regions, including ventromedial prefrontal, orbitofrontal, ACC and amygdala were most common (60) which is consistent with our finding in the mPFC. However, while

investigations in youth with disorders are undeniably important, they cannot necessarily inform the question of whether there is neural variability associated with the subclinical range of behavior. Children exhibiting such behavior may be experiencing challenges at home, school, or socially, which may impact quality of life, in addition to the risk that is imparted for developing ongoing problem behaviors later in life. Our work demonstrates that even in otherwise healthy children without symptoms at the level of a diagnosable disorder, there are still differences in neural functioning associated with internalizing and externalizing behaviors

4.1 Limitations

Our study had a number of limitations. First, the measures of externalizing and internalizing behavior as measured by the YSR are fairly broad indices of problematic behavior, and further exploration of more specific behavioral measures as related to cognitive control may be of interest. In addition, there can be concerns about self-report in young children. However, we assessed the relationship of the scores to the parental reports on the CBCL. CBCL (parent) and YSR (child) scores were highly related in the younger children, indicating that we would not gain new information from using the parental report, and were less correlated in older children who we would expect to have more independent experiences that parents might be unaware of, so we used the YSR data. However, it is also possible that there are age differences in self-report procedures, such that the parents were providing more support for the younger than older children when answering questions, which may impact results. Secondly, while rates of drug and alcohol use were relatively low in this sample, precluding any specific analyses, future studies in samples with a higher frequency of use might explore ways in which substance use contributes to imaging or behavior differences. Third, motion effects are always a concern, however we took extensive steps to edit motion, by including extended motion parameters as covariates in all analyses and also by visually inspecting each scan for motion and either excluding individuals with excessive motion effects or censoring affected volumes. Fourth, there was little variability in the performance on our cognitive control task, such that there was a ceiling effect that may have prevented us from detecting performance deficits related to internalizing and externalizing, this would likely be more apparent in a clinical sample. It would also be interesting to be able to model the task in a way that allowed comparison of correct and incorrect trials to fully understand performance effects. Next, in future analyses, it will be important to include assessments of puberty in addition to age, to better estimate physiological development. Additionally, we cannot test whether the activation differences observed are a consequence or a cause of externalizing or internalizing behavior. Finally, a larger sample, and longitudinal analyses, might allow more in depth understanding of potential changes across development.

4.2 Conclusions

In summary, our study suggests distinct associations of internalizing and externalizing behavior to neural correlates of cognitive control. By dissecting the neural basis of these early behaviors, even at relatively low levels, we may begin to develop more effective intervention strategies, as well as ways to better predict which children may be at risk for later behavioral issues.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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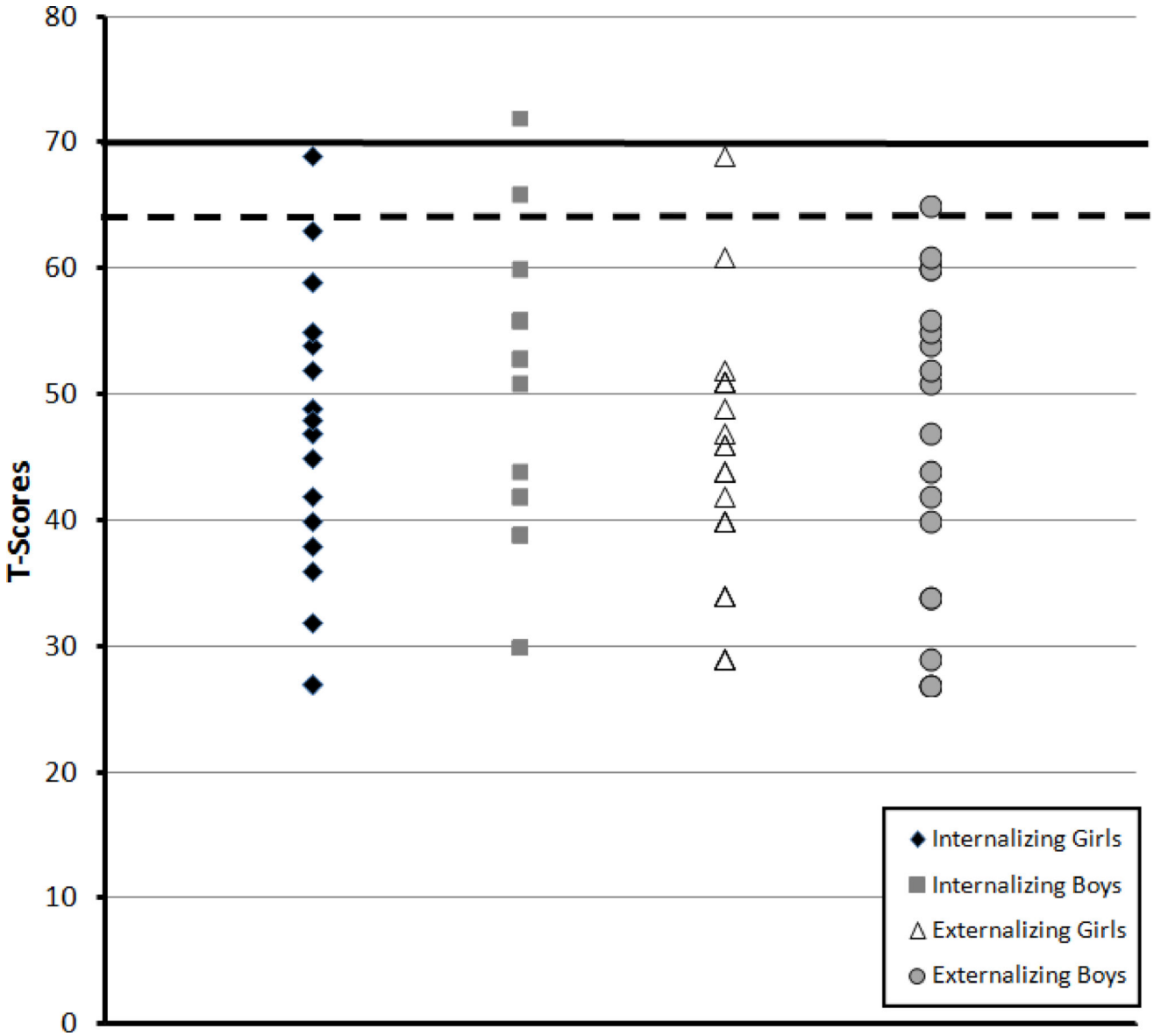

Figure 1.

Distribution of standardized externalizing and internalizing scores. Sixty-four represents the bottom of the subclinical range, seventy represents the bottom of the clinical range.

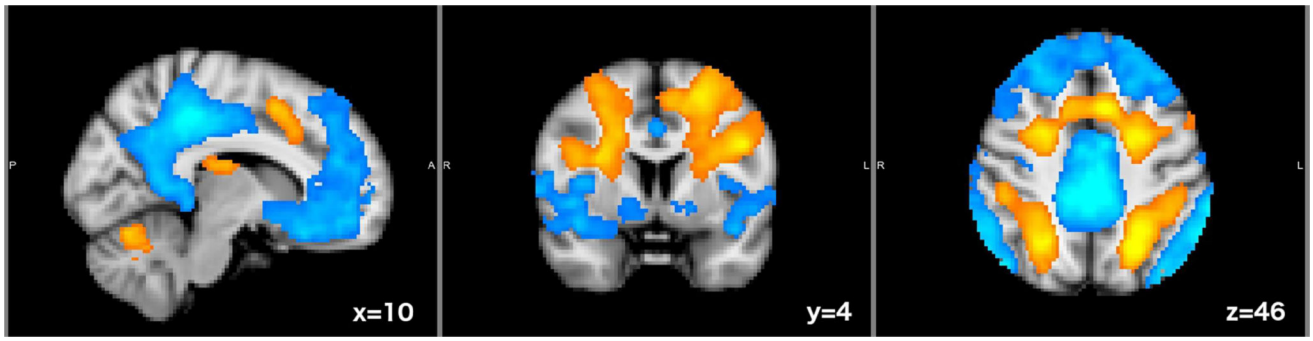

Figure 2.

Activation induced by the Interference -Control (orange) and Control – Interference conditions (blue). The Interference-Control condition revealed activation in regions consistent with the executive system, including superior parietal, superior frontal, and anterior cingulate. The opposite Control-Interference condition demonstrated significant effects in regions consistent with the default mode network, medial prefrontal, posterior cingulate, and angular gyrus. Z-statistic images were thresholded using clusters determined by Z>3.1 and a (corrected) cluster significance threshold of P=0.01.

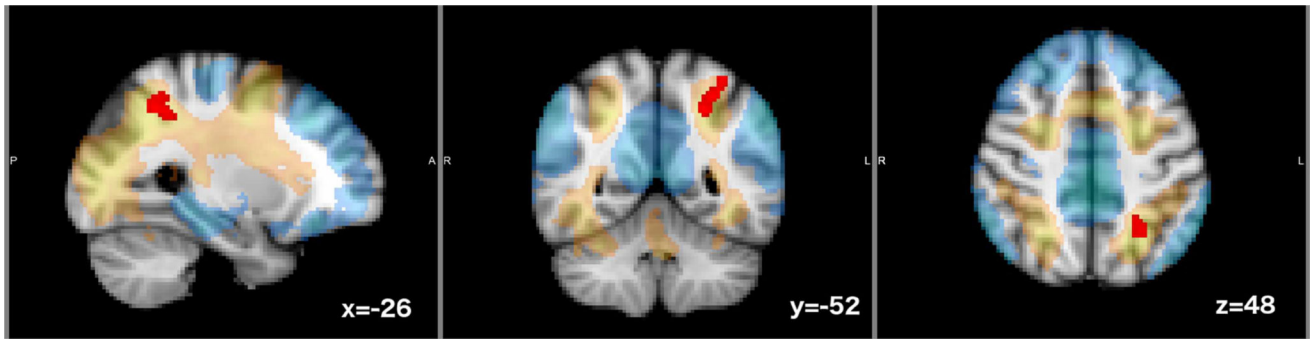

Figure 3.

Activation differences associated with level of externalizing score, positive activation in red overlaid on I-C contrast activation in pale red and task-negative system activation in pale blue. A significant difference was found in a superior parietal region that was also part of the Interference-Control regions of activation. Z-statistic images were thresholded using clusters determined by Z>3.1 and a (corrected) cluster significance threshold of P=0.01

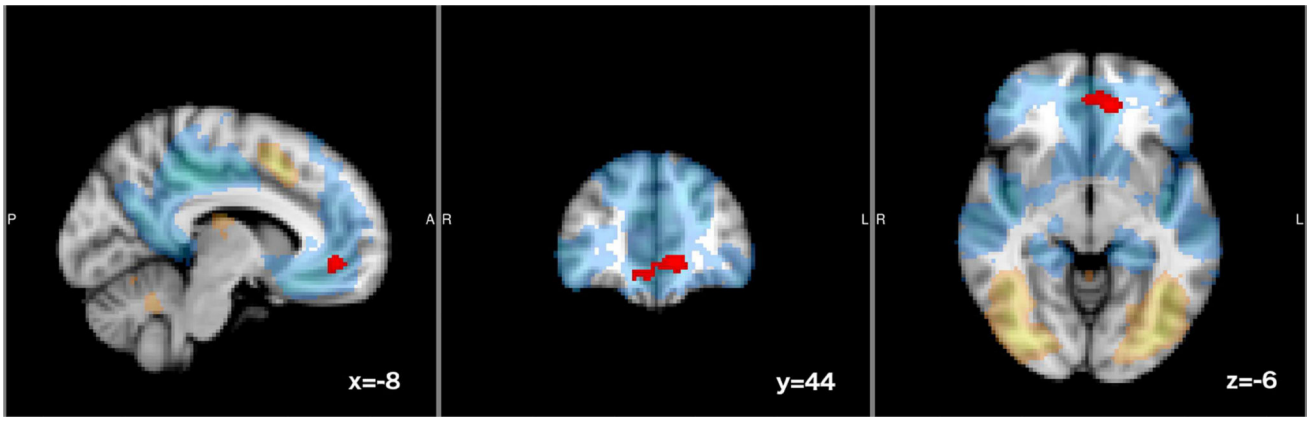

Figure 4.

Activation differences associated with level of internalizing score, positive activation in red overlaid on I-C contrast activation in pale red and task-negative system activation in pale blue. There was a significant effect in the medial prefrontal region that was associated with decreased activation during Interference. Z-statistic images were thresholded using clusters determined by Z>3.1 and a (corrected) cluster significance threshold of P=0.01 (49–51)

Table 1

Regions of activation associated with the overall Interference-Control and Control-Interference contrasts

Regions	MNI Coordinates	Max Z Score
I-C Contrast		
R lateral occipital cortex	38, −82, −6	9.03
L lateral occipital cortex	−36,−80,4	7.46
L superior parietal	−24, −64, 48	7.93
	−28,−64,30	7.71
R superior parietal	28, −64, 30	7.74
L superior frontal gyrus, frontal eye field	−26,0,56	6.88
R superior frontal gyrus, frontal eye field	26,0,48	6.89
L dorsal cingulate	−8,12,46	7.56
R dorsal cingulate	12,10,48	5.48
R anterior insula	−28,16,10	4.46
L anterior insula	−26, 26, 12	4.02
L thalamus	−12,−18,16	5.37
R thalamus	12,−22,18	5.05
R cerebellum	4,−68,−22	6.2
	8,−68,−18	6.13
C-I Contrast		
R medial prefrontal cortex	14,51,−12	6.63
L medial prefrontal cortex	−6,26,−14	6.57
R posterior insula	40,−14,−4	6.52
L posterior insula	−40, −8, −4	6.61
L Posterior cingulate	−8, −32, 42	8.51
	0,−32,44	8.23
R posterior cingulate	12,−36,44	7.55
R middle temporal gyrus	58, −24, −8	5.31
L middle temporal gyrus	−56,−24,−10	5.22
R hippocampus	30, −28,−12	5.87
L hippocampus	−28,−28,16	6.17
L angular gyrus	−62,−46,36	7.83
R angular gyrus	48,−70,42	6.52
R frontal pole	42,38,0	5.68
L frontal pole	−28,50,0	5.57

Table 2

Regions of activation associated with Internalizing and Externalizing behaviors

Region	MNI Coordinates	Max Z-stat
Externalizing – Internalizing Contrast		
L superior parietal	−24, −52, 46	4.23
Internalizing – Externalizing Contrast		
Medial prefrontal cortex	−12, 42, −6	4.65