Supplementary Online Content


**eText.** Potential Impact of Age, Sex, Pubertal Status, and Child Depression Rating Scale Scores

This supplementary material has been provided by the authors to give readers additional information about their work.
In post hoc analyses, age was added as a covariate in the L amygdala ROI analysis and there remained a main effect of group ($F_{2,53} = 3.78, P < .03$), but no main effect of age ($F_{1,53} = 1.84, P = .18$). Similarly, we included age as a covariate in the analysis of the 1 whole brain cluster for N→A and the 4 clusters for N→H that showed significant between-group differences. Again, all the main effects of group remained significant ($F_{3,9}, P < .001$ for all comparisons), with no effects of age ($F_{1,12}, P > .30$ for all comparisons).

To investigate the effect of sex, it was included as a between-groups variable in the amygdala ROI and whole-brain clusters. In the left amygdala ROI for N→A there was a significant main effect of sex ($F_{1,56} = 6.83, P = .03$, with males having a lower average $\beta$ weights (–0.01) than females (0.05). There was also a trend for a main effect of sex in the left middle/superior frontal gyrus for N→H, ($F_{1,56} = 3.78, P = .06$, with females having lower average $\beta$ weights (–0.03) than males (0.02). However, in neither the amygdala ROI nor any of the whole-brain clusters was there a significant group x sex effect.

Possible group differences in pubertal status were evaluated by analyzing Tanner stage data. Unfortunately, Tanner stage data were available for some, but not all, of the participants (number of participants in each group: BD =18, SMD =13, HV = 7). Unfortunately, the majority of HVs did not have Tanner Breast/Testes (TannerBT) or Tanner Pubic Hair (TannerPH) data. Using the available data, we assessed possible group differences for both TannerBT and TannerPH and found no group differences in either measure (TannerBT, $F_{2,37} = 2.28; P = .12$; TannerPH, $F_{2,37} = 2.11, P = .14$).

Since BD and SMD differed significantly on CDRS score, CDRS score was used as a covariate in post hoc analyses in the four whole brain N→H clusters where these two patient groups differed from each other. (HV, by definition, were not depressed and CDRS ratings were not obtained, so they were not included in these analyses.) With CDRS scores covaried, BD and SMD still differed significantly from each other in all four clusters ($F_{2,10}, P < .001$ for all comparisons), and there was no effect of CDRS ($F_{1,12}, P > .80$ for all comparisons).

In regions where BD and SMD differed in their BOLD response patterns, an analysis of the effect of ADHD in BD was conducted in order to aid in the interpretation of the N→H results. For the left amygdala ROI, an ANOVA was conducted including only BD patients, with the between-groups factor being with or without ADHD. There were 10 BD patients with ADHD and 9 BD patients without ADHD. There was no significant difference in the N→A slope for BD patients with vs without ADHD, $F_{1,17} = .26, P = .62$. A similar ANOVA was conducted on the 1 whole brain cluster identified in the whole-brain analysis for N→A (ie, in the posterior cingulate). Again, we found no significant difference in BD with vs without ADHD ($F_{1,17} = .83, P = .34$). The 4 whole brain clusters that were significant for N→H also showed no ADHD effects, all, $F_{1,30}, P > .38$ for all comparisons.

An additional analysis examined correlations between behavioral and neural measures in the amygdala ROI and in the clusters from the whole-brain analysis that showed significant between-group differences. Specifically, we examined correlations between the slope of the behavioral ratings (ie, hostile and nose ratings) and the slope of the $\beta$ weights in each of these rating conditions. The only significant finding was in the amygdala for the BD youth, where there was a positive correlation between the slope
of neural activation during nose width ratings of angry faces and the slope of the nose width ratings themselves ($r = 0.53$, $P = .02$). Of note, this finding would not remain significant after correction for multiple comparisons. All other correlations between neural activation and behavioral ratings (hostile ratings of angry faces, hostile ratings of happy faces, nose width ratings of angry faces, and nose width ratings of happy faces) were not significant.

Since the samples of medicated vs unmedicated patients were very small and thus prone to type II error, we covaried medication status (with/without medication) within BD vs SMD (since HVs were not medicated) in the 4 whole brain N→H clusters where the 2 patient groups differed from each other. With medication status scores covaried, BD and SMD still differed significantly in all 4 clusters ($>13$, $F_{>13}$; $P < .001$ for all comparisons), and there was no effect of medication status ($F_{<1.5}$; $P > .20$ for all comparisons).

A group × attention ANOVA for N→A in the whole-brain cluster of the posterior cingulate, conducted in euthymic patients only, showed a main effect of group, driven by BD vs HVs ($P < .005$), with a trend for SMD vs HVs ($P = .06$). For N→H in the R inferior parietal lobule (BA40/7), SMD continued to differ from both BD and HVs. In the L middle occipital/fusiform gyrus (BA37), the main effect of group remained, and the post hoc analyses were not significant. In the right middle occipital gyrus/cuneus (BA18/19) and the left middle/superior frontal gyrus (BA6/8), the results of the main effect of group and post hoc analyses were unchanged from the primary analysis.