Supplemental Materials

Associations with mood state, medication, comorbid illnesses and BD subtype

Post-hoc analyses examined whether clinical differences between pediatric and adult patients might account for the age x diagnosis interaction that we found in the right amygdala activity from the ROI analysis (p=.02). A series of post-hoc univariate ANCOVAs in SPSS were performed to compare right amygdala activity across all expressions among subgroups of patients, as described below (Table s1). Reaction times of fearful, angry, and neutral expressions and IQ scores served as covariates in the model. Because of the small size of the subgroups in these exploratory analyses, results including those at a trend level, p<.10, are reported.

First, because more child than adult BD patients were euthymic when scanned (p=.05), we conducted a univariate ANCOVA comparing amygdala activation in euthymic child (N=15) vs. adult (N=9) patients. Euthymic children tended to show greater amygdala activation (F=3.93, df=1,18, p=.07) than euthymic adults. Because YMRS scores were higher among pediatric than adult patients (p=.001), a univariate ANCOVA with YMRS scores as an additional covariate revealed that children with BD continued to show greater amygdala activation (F=4.50, df=1,28, p=.04) than adult patients.

Second, child patients tended to be more likely than adult patients to be unmedicated (p=.08). When medicated child patients (N=15) were compared with medicated adult patients (N=17), child patients tended to have greater amygdala activity (F=3.62, df=1,26, p=.07). Rates of antiepileptic and stimulant intake also differed between child and adult patients (ps=.02). Stimulant-free child patients (N=13) had greater amygdala activation (F=5.21, df=1,24, p=.03) than stimulant-free adult patients (N=17). However, when child and adult patients receiving

antiepileptic medication were compared, children (N=9) and adults (N=15) did not differ in amygdala activity (F=.78, df=1,18, p=.39).

Third, compared to adult patients, child patients had higher rates of comorbid attention deficit hyperactivity disorder (ADHD; p=.003) and comorbid oppositional defiant disorder (ODD; a trend at p=.08). After excluding patients with comorbid ADHD, child patients (N=6) continued to show greater amygdala activation (F=4.23, df=1,12, p=.06) than adult patients (N=12). When the three child BD patients with lifetime ODD were excluded, child patients (N=15) and adult patients (N=17) did not differ in amygdala activity (F=1.56, df=1,26, p=.22).

Fourth, we restricted the analysis to only patients with BD I, and found that children with BD I (N=14) tended to show greater amygdala activation (F=4.25, df=1,17, p=.06) than adults with BD I (N=9).

The ROI analysis also revealed an emotion x diagnosis interaction indicating amygdala hyperactivity in response to fearful faces in BD patients vs. controls (p=.007). Using a univariate ANCOVA, we found that BD patients (N=20) with no comorbid anxiety showed greater amygdala activity in response to fearful expressions than HV participants (N=39) (F=9.25, df=1,55, p=.004) (Table s1).

Table s1. Post-hoc analysis of effects of mood state, medication, comorbidity and BD types on the age-group X diagnosis and emotion X diagnosis findings from the ROI analysis.

Variables	Compared groups/Analysis	Results	F	df	p
Mood state	euthymic	child BD (N=15) > adult BD (N=9)	3.63	1,18	.07
	YMRS scores as a covariate	child BD (N=18) > adult BD (N=17)	4.50	1,28	.04
Medication	medicated	child BD (N=15) > adult BD (N=17)	3.62	1,26	.07
	stimulant-free	child BD (N=13) > adult BD (N=17)	5.21	1,24	.03
	antiepileptic medication-free	child BD (N=9) > adult BD (N=15)	.78	1,18	.39
Comorbid illnesses	no comorbid ADHD	child BD (N=6) > adult BD (N=12)	4.23	1,12	.06
	no comorbid ODD	child BD (N=15) > adult BD (N=17)	1.56	1,26	.22
BD types	BD I	child BD (N =14) > adult BD (N=9)	4.25	1,17	.06
Comorbid illnesses	no comorbid BD vs. HV	BD (N=20) > HV (N=39)	9.07	1,55	.004