

Supplementary material

Supplemental Figures

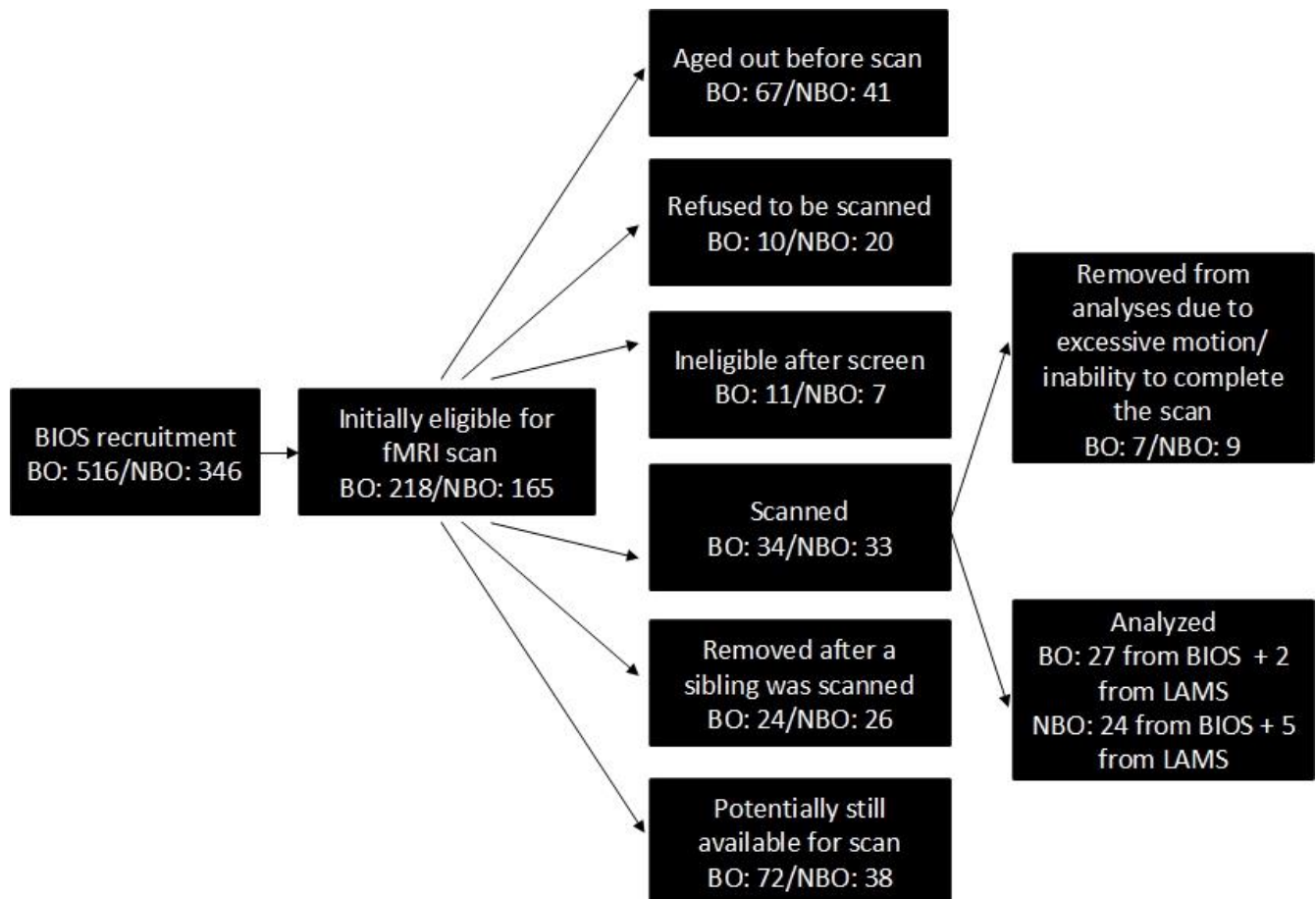


Figure S1. A graphic representation of selection of BIOS participants for the present fMRI study.

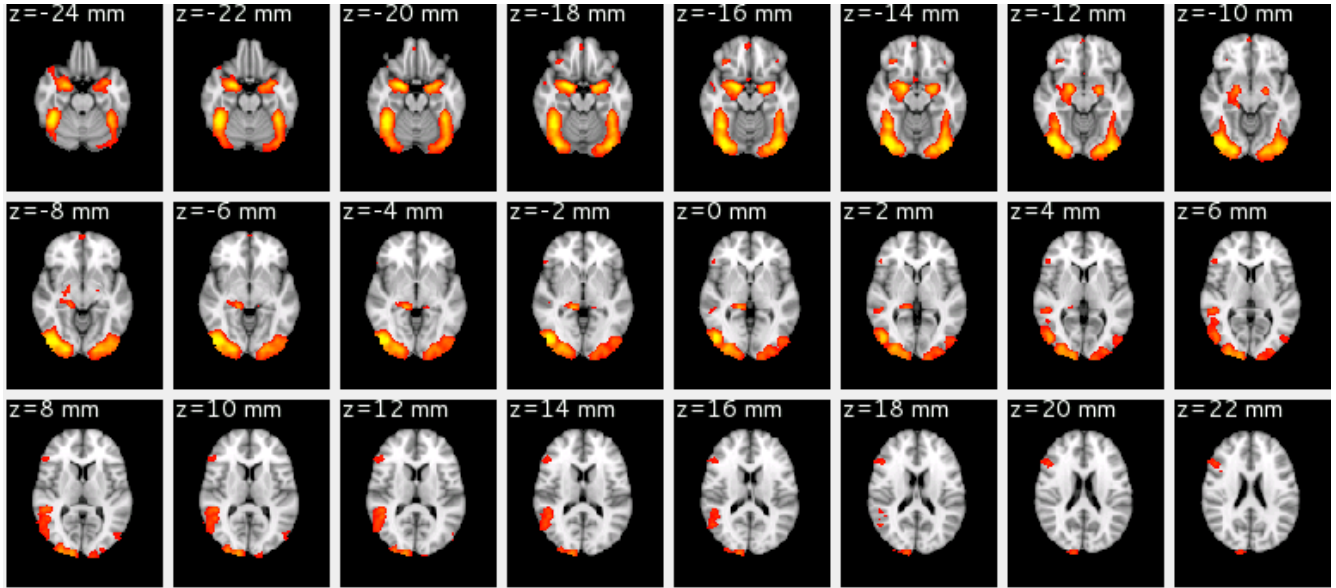


Figure S2. Neural regions showing greater mean activation across subjects for all faces vs. shapes.

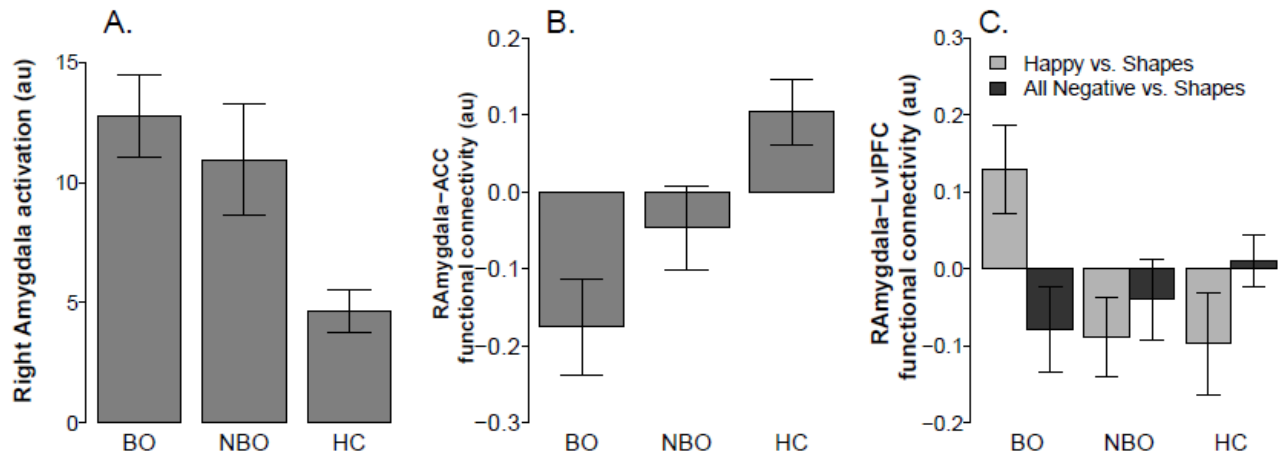


Figure S3. RAmygdala activation, and RAmygdala-ACC and RAmygdala-LvIPFC functional connectivity in participants without current psychopathology. RAmygdala – right amygdala, ACC – anterior cingulate cortex, LvIPFC - left ventrolateral prefrontal cortex. The emotional face processing ROI mask is shown in green. “au” stands for arbitrary units. BO – offspring of parents with bipolar disorder, NBO – offspring of parents with psychiatric disorders other than bipolar disorder, HC – healthy offspring of psychiatrically healthy parents.

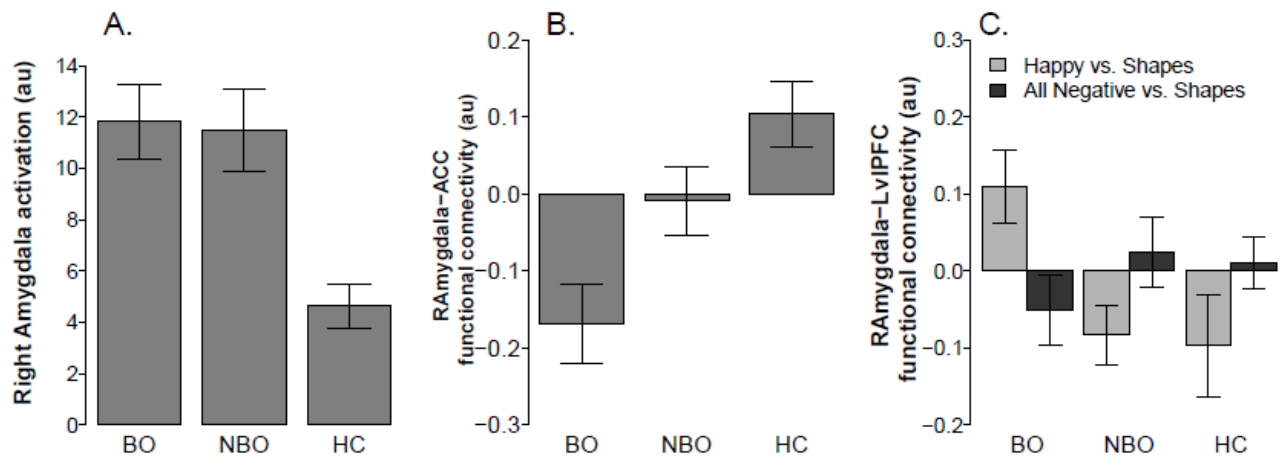


Figure S4. RAmgdala activation, and RAmgdala-ACC and RAmgdala-LvlPFC functional connectivity in unmedicated participants. RAmgdala – right amygdala, ACC – anterior cingulate cortex, LvlPFC - left ventrolateral prefrontal cortex. The emotional face processing ROI mask is shown in green. “au” stands for arbitrary units. BO – offspring of parents with bipolar disorder, NBO – offspring of parents with psychiatric disorders other than bipolar disorder, HC – healthy offspring of psychiatrically healthy parents.

Supplemental tables

Table S1

Demographic and clinical variables for participants without current psychiatric diagnoses and participants untreated with psychotropic medications.

	BO	NBO	HC	Statistics	p-value
<i>Youth without psychiatric diagnoses</i>					
Number of youth without psychiatric diagnoses	18 (62%)	15 (52%)	23 (100%)	BO vs. NBO $\chi^2(2)<1$	ns
Age at scan	13.84(2.60)	13.77(2.14)	13.74(1.80)	F(2,53)<1	ns
Gender (female)	6	7	11	$\chi^2(2)<1$	ns
Handedness (right hand)	16	15	21	Yates' $\chi^2(2)<1$	ns
IQ (WASI)	106.67(13.63)	99.53(12.88)	105.78(13.79)	F(2,53)=1.4	ns
SES based on parental education	5.44(0.92)	5.40(1.06)	5.30(1.02)	F(2,53)<1	ns
SCARED Parent Total	7.56(6.45)	5.00(4.85)	4.17(4.32)	F(2,52)=2.2	ns
SCARED Child Total	8.89(8.56)	6.67(9.27)	9.33(11.42)	F(2,53)<1	ns
MFQ Parent	4.44(5.85)	3.62(3.43)	1.57(2.09)	F(2,51)=2.8	ns
MFQ Child	5.83(8.05)	7.73(9.21)	5.09(10.57)	F(2,53)<1	ns
CALS Parent Total	6.22(8.59)	3.43(5.09)	1.78(2.59)	F(2,52)=3.0	ns
CALS Child Total	6.56(8.51)	6.00(7.91)	5.96(13.39)	F(2,53)<1	ns
<i>Youth untreated with psychotropic medications</i>					
Number of youth untreated with psychotropic medications	24(83%)	24(83%)	23(100%)	BO vs. NBO $\chi^2(2)<1$	ns
Age at scan	14.00(2.43)	13.64(2.39)	13.74(1.80)	F(2,69)<1	ns
Gender (female)	11	11	11	$\chi^2(2)<1$	ns

Handedness (right hand)	22	24	21	Yates' $\chi^2(2)<1$	ns
IQ (WASI)	104.46(14.39)	101.24(12.82)	105.78(13.79)	F(2,69)<1	ns
SES based on parental education	5.50(0.93)	5.42(0.93)	5.30(1.02)	F(2,68)<1	ns
SCARED Parent Total	9.29(6.30)	8.46(9.30)	4.17(4.32)	F(2,68)=3.6	0.03
SCARED Child Total	11.79(9.13)	9.56(13.95)	9.33(11.42)	F(2,69)<1	ns
MFQ Parent	5.09(6.24)	4.09(3.59)	1.57(2.09)	F(2,66)=4.04	0.02
MFQ Child	8.67(8.90)	8.64(10.76)	5.09(10.57)	F(2,69)<1	ns
CALS Parent Total	6.83(9.40)	4.00(4.83)	1.78(2.59)	F(2,67)=3.7	0.03
CALS Child Total	9.17(8.85)	7.68(11.59)	5.96(13.39)	F(2,69)<1	ns

Note: Standard deviations (SD) are reported in parentheses. BO – youth offspring of parents with bipolar disorder; NBO – youth offspring of parents with non-bipolar psychopathology; HC – healthy offspring of psychiatrically healthy parents; BD – bipolar disorder; MDD – major depressive disorder; PGBI - Parent Version, General Behavior Inventory; SCARED - Self-Report for Childhood Anxiety Related Emotional Disorders; MFQ - Mood and Feelings Questionnaire; CALS - The Children's Affective Liability scale.

Table S2

Greater activation in the occipital pole for Happy than for All Negative faces (i.e., a main effect of emotional condition) across all participants. The statistical maps were thresholded at *voxel-wise-uncorrected* $p<0.005$ ($z>2.57$) and a corrected cluster significance threshold of $p<0.05$ (Worsley, 2001).

Region	nvox	z-score	X	Y	Z
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Activation analysis:
Main effect of face emotional valence (Happy vs. All Negative) in the face processing ROI mask
Happy > All Negative

R	Occipital pole	439	4.99	14	-100	6
L	Occipital pole	228	4.64	-20	-100	2

Note: R – right hemisphere; L – left hemisphere

Supplemental analyses

Activation and functional connectivity in BIOS participants (LAMS participants excluded)

One possible limitation of this study is combining BO and NBO from BIOS with BO and NBO from LAMS (*i.e.*, 2 BO and 5 NBO were added from LAMS). In order to make sure that recruitment source did not impact main findings, we removed LAMS participants from BO and NBO samples and conducted all main analyses on activation and connectivity values extracted from the ROIs identified in the full sample analysis using SPSS. These analyses revealed a significant effect of Group on RAmygdala activation ($F(2,71)=8.5$, $p<0.001$). Based on the Tukey's HSD test, both BO and NBO, compared with HC, had higher RAmygdala activation (BO vs. HC: $p=0.008$, NBO vs. HC: $p=0.001$), but were not different from each other.

There was also a significant effect of Group on RAmygdala-ACC functional connectivity ($F(2,71)=8.3$, $p=0.001$) and a significant Group x Emotion interaction effect on RAmygdala-LvlPFC functional connectivity ($F(2,71)=6.7$, $p=0.002$). The Tukey's HSD posts-hoc test showed that RAmygdala-ACC functional connectivity was significantly less positive in BO vs. HC ($p<0.001$) and marginally significant in BO vs. NBO ($p=0.057$), but was not different for NBO vs. HC. In order to find

out which emotional condition drove the interaction effect, we conducted 2 planned comparison tests using one-way ANOVA on Happy-Shape and Negative-Shape contrasts with Group as a between-subject factor and Bonferroni corrected p-values for 2 comparisons ($0.05/2=0.025$). These tests revealed that the interaction was driven by group-differences for the Happy-Shape condition ($F(2,71)=4.3$, $p=0.017$). Tukey's HSD post-hoc test indicated that RAmygdala-LvlPFC functional connectivity for happy faces vs. shapes was significantly more positive in BO vs. NBO ($p=0.046$) and in BO vs. HC ($p=0.03$), but was not significantly different for NBO vs. HC. Taken together, these results paralleled main findings from *Hypotheses 1-2* suggesting that recruitment source did not impact main findings.