Supplemental Information

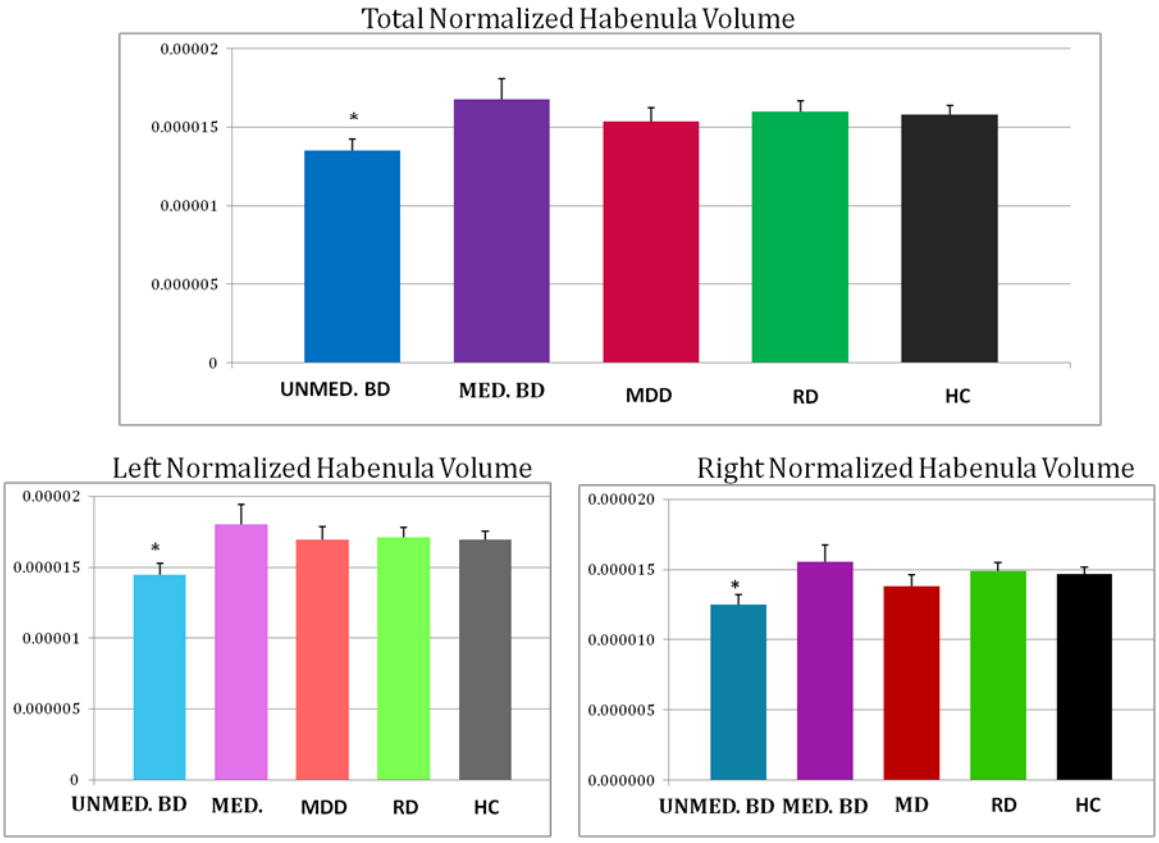

Figure S1. Bar chart showing a comparison of normalized total, left and right habenula volume across the diagnostic groups. Normalized total habenula volumes (y-axis: scale = 0-0.0002) are shown in the top panel, and normalized left and right habenula volumes (y-axis: scale = 0-0.0002) are shown in the bottom panel. Normalized volumes were calculated by dividing absolute habenula volumes by whole brain volume. Since the normalized volume is a ratio, it is unitless. Normalized volumes were used in order to eliminate non-specific effects. Unmed.BD refers to the unmedicated BD sample, and Med.BD refers to the medicated BD sample. The standard error of the mean (SEM) is displayed on the top of each bar. The symbol * is indicative of a statistically significant difference ($p < 0.05$) in habenula volume compared with the healthy control group.

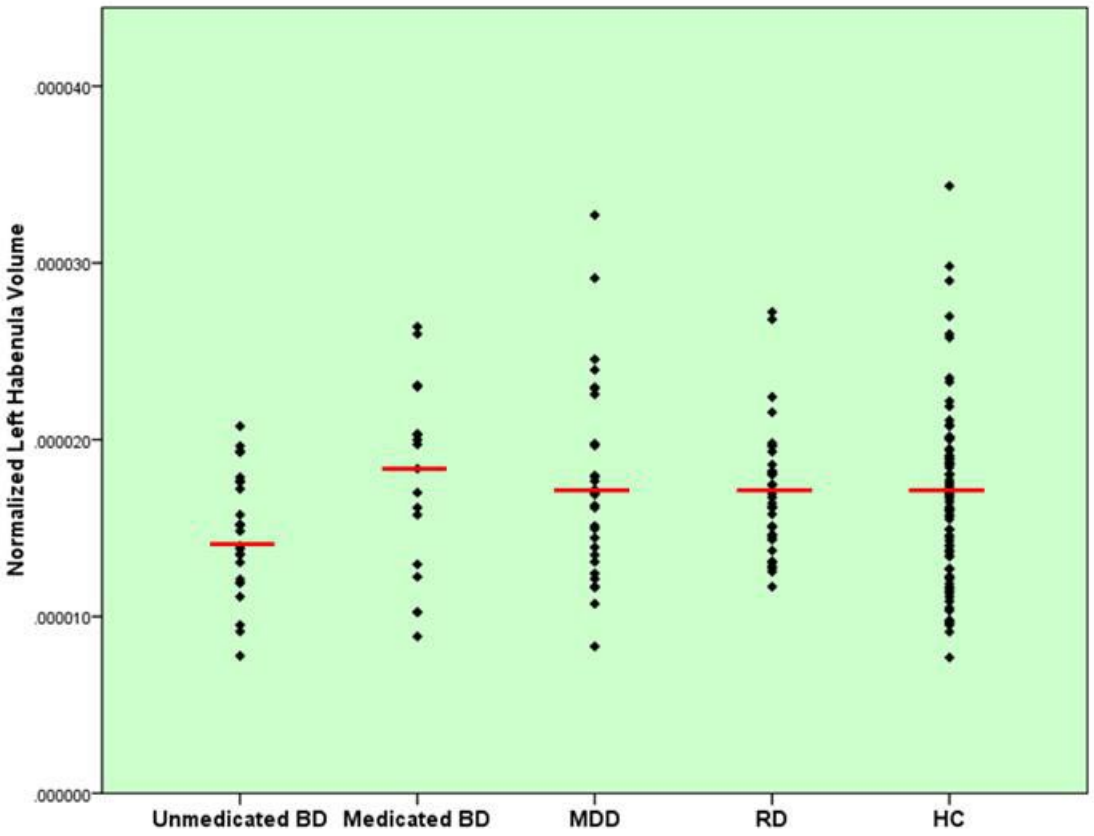

Figure S2. Scatterplot of normalized left habenula volumes (y-axis) for the medicated BD, unmedicated BD, and HC samples, respectively. Normalized volumes were calculated by dividing absolute habenula volumes by whole brain volume. Since the normalized volume is a ratio, it is unitless. The red horizontal bar shows the mean volume of each group.

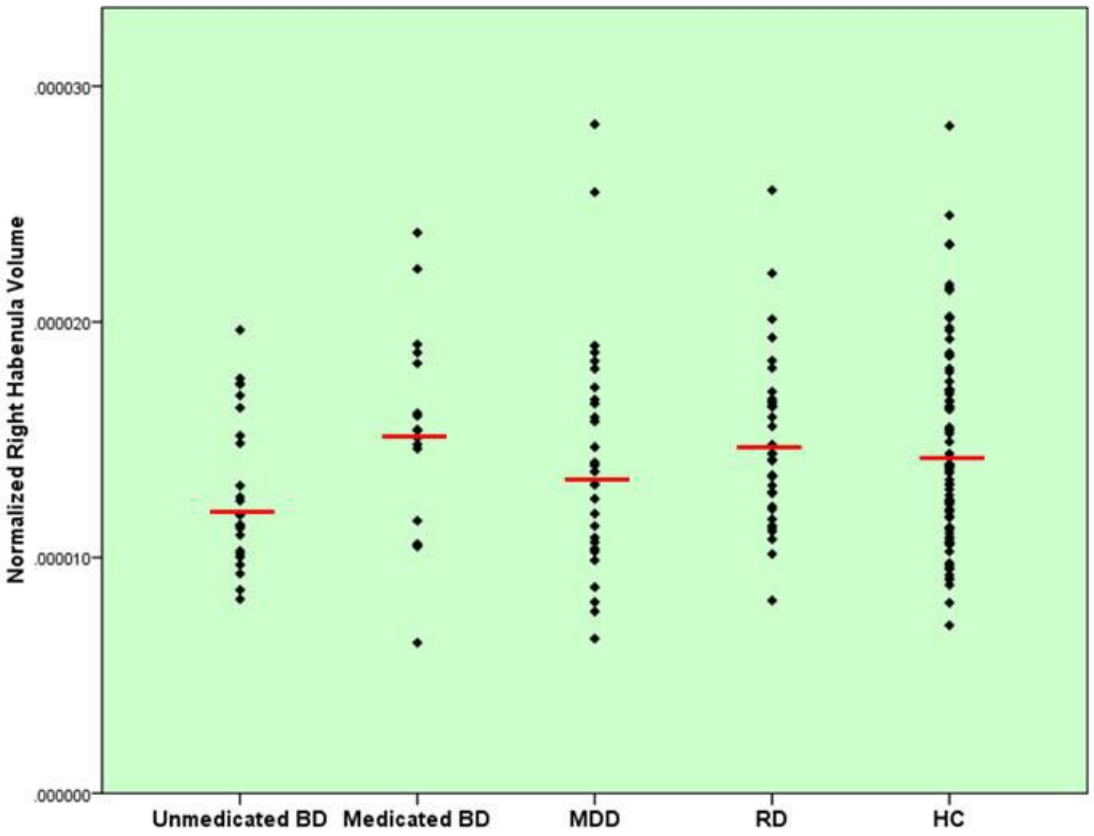

Figure S3. Scatterplot of normalized right habenula volumes (y-axis) for the medicated BD, unmedicated BD, and HC samples, respectively. Normalized volumes were calculated by dividing absolute habenula volumes by whole brain volume. Since the normalized volume is a ratio, it is unitless. The red horizontal bar shows the mean volume of each group.

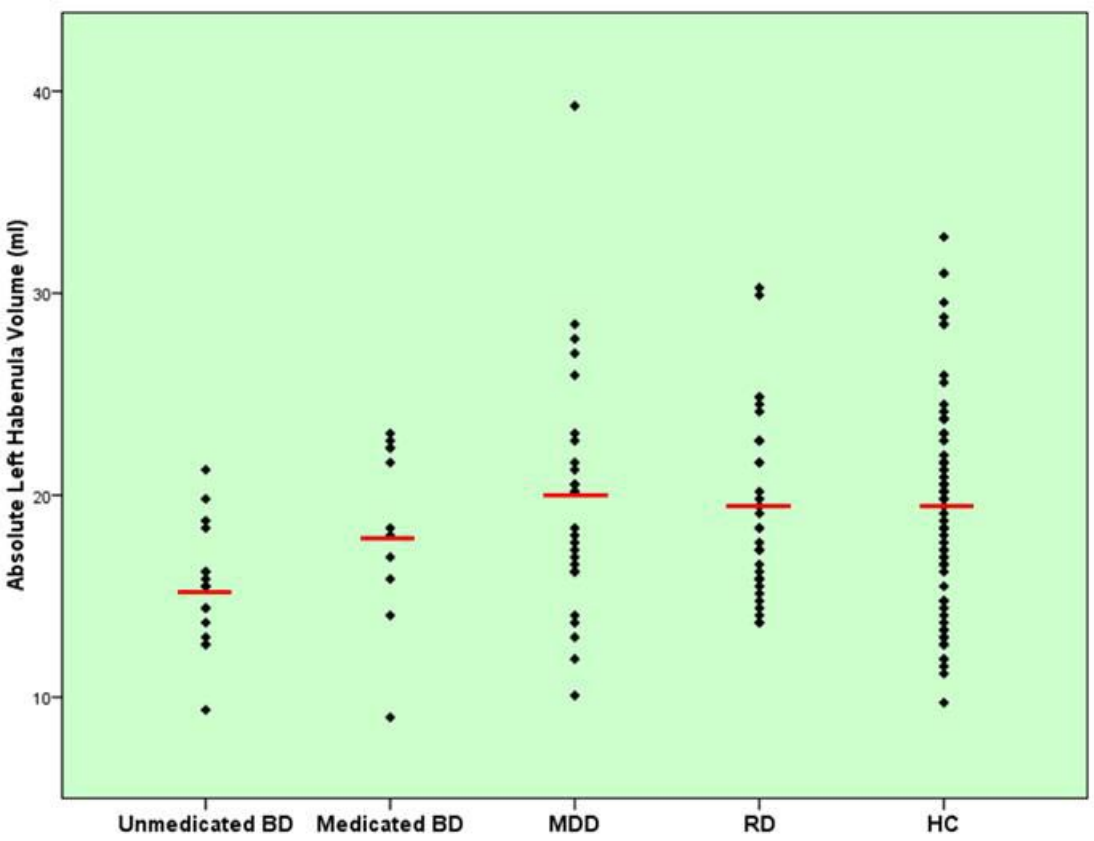

Figure S4. Scatterplot of absolute left habenula volumes (y-axis) for the *right-handed* medicated BD, unmedicated BD, MDD, HC, and RD samples, respectively. The red horizontal bar shows the mean volume of each group.

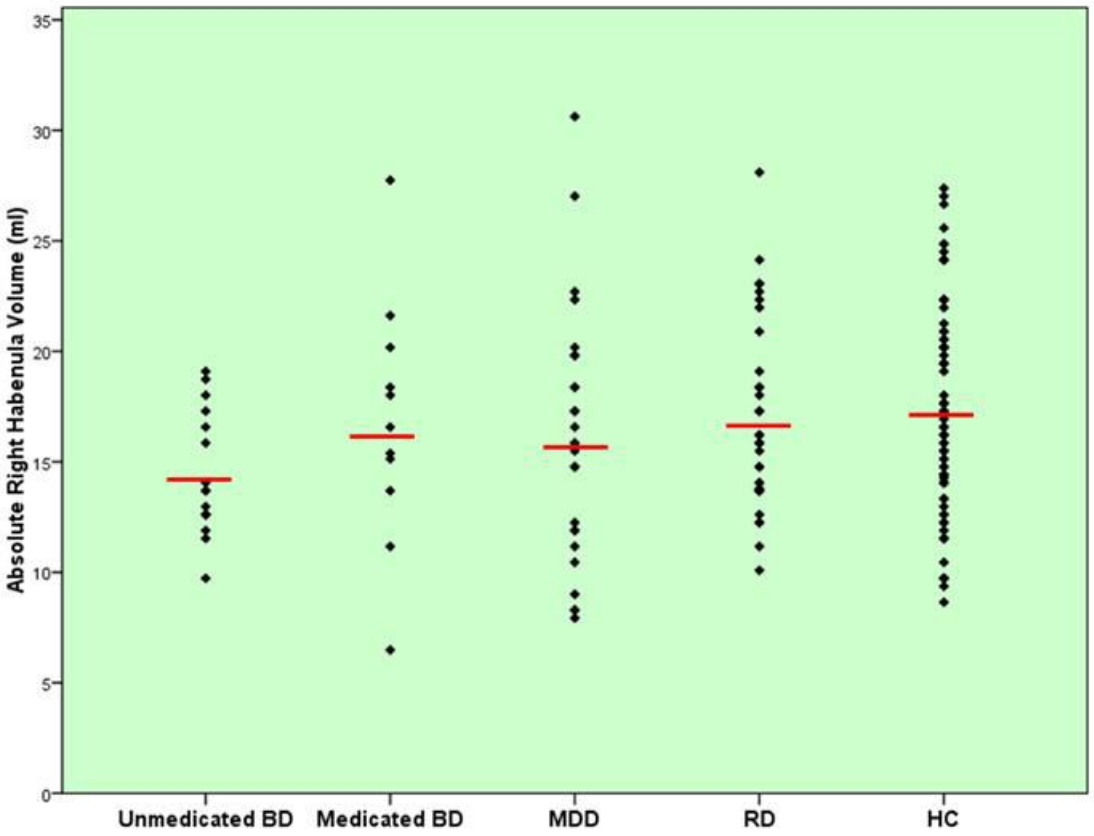

Figure S5. Scatterplot of absolute right habenula volumes (y-axis) for the *right-handed* medicated BD, unmedicated BD, MDD, HC, and RD samples, respectively. The red horizontal bar shows the mean volume of each group.

Table S1. Demographic, Clinical and Habenula Volume Data of the Unmedicated, Medicated BD and HC Groups: Right-Handed Participants Only.

	Unmed.BD (n=17)	Med.BD (n=10)	HC (n=71)	Med.BD VS Unmed.BD	Unmed.BD VS HC	Med.BD VS HC
Age at Scan	**33.6±6.6**	**43.5±7.6**	**36.7±12.0**	**Med>Unmed t=3.5 df=25 p=0.002**	**NS**	**NS**
Sex (M/F)	**4/13**	**3/7**	**27/44**	**NS**	**NS**	**NS**
Right/Left Hand	**17/0**	**10/0**	**71/0**	**NS**	**NS**	**NS**
BDI/BDII	**4/13**	**2/8**	**NA**	**NS**	**NA**	**NA**
Family History (yes/no/adopted)	**17/0/0**	**10/0/0**	**NA**	**NS**	**NA**	**NA**
Age at Illness Onset (years)	**18.2±6.9**	**18.8±10.1**	**NA**	**NS**	**NA**	**NA**
Duration of illness (years)	**14.3±8.3**	**24.7±12.3**	**NA**	**Med>Unmed t=2.5 df=23 p=0.019**	**NA**	**NA**
Weeks Unmedicated	**67.8±91.0**	**NA**	**NA**	**NA**	**NA**	**NA**
MADRS	**24.4±11.1**	**22.6±11.3**	**0.2±0.8**	**NS**	**Unmed>HC t=14.5 df=55 p<0.001**	**Med>HC t=13.3 df=50 p<0.001**
YMRS	**5.4±4.4**	**5.1±3.9**	**0.4±1.0**	**NS**	**Unmed>HC t=5.3 df=55 p<0.001**	**Med>HC t=5.7 df=50 p<0.001**
Past Medication Use (N)				**NA**	**NA**	**NA**
Naïve	**5**	**NA**	**71**	**NA**	**-**	**-**
AD	**8**	**1**	**0**	**NA**	**-**	**-**
Mood Stabilizers	**3**	**2**	**0**	**NA**	**-**	**-**
Antipsychotic	**1**	**1**	**0**	**NA**	**-**	**-**
Other	**1**	**1**	**0**	**NA**	**-**	**-**
Past History of Substance Abuse (N)				**NS**	**NA**	**NA**
Present	**7**	**3**	**0**	**-**	**-**	**-**
Absent	**10**	**7**	**71**	**-**	**-**	**-**
Common Comorbid Disorders in Sample (N)				**NS**	**NA**	**NA**
Panic Disorder	**2**	**2**	**0**	**-**	**-**	**-**
Other Anxiety Disorder	**5**	**4**	**0**	**-**	**-**	**-**

Eating Disorder	**1**	**1**	**0**	**-**	**-**	**-**
Absolute Left Habenula Volume (mm^3)	**15.5±2.9**	**18.2±4.5**	**19.4±5.3**	**α NS**	**β Unmed<HC t=3.0 df=86 p=0.004**	**β NS**
Normalized Left Habenula Volume	**$1.39x10^{-5}$ ± $3.53x10^{-6}$**	**$1.69x10^{-5}$± $4.72 x10^{-6}$**	**$1.68 x10^{-5}$± $5.24x10^{-6}$**	**α NS**	**β Unmed<HC t=2.2 df=86 p=0.033**	**β NS**
Absolute Right Habenula Volume (mm^3)	**14.3±2.8**	**16.8±5.9**	**17.1±4.7**	**α NS**	**β Unmed<HC t=2.3 df=86 p=0.023**	**β NS**
Normalized Right Habenula Volume	**$1.28x10^{-5}$± $3.14x10^{-6}$**	**$1.55x10^{-5}$± $5.38 x10^{-6}$**	**$1.47 x10^{-5}$± $4.42x10^{-6}$**	**α NS**	**β Unmed=HC t=1.7 df=86 p=0.097**	**β NS**
Total Absolute Habenula Volume (mm^3)	**29.8±4.4**	**34.9±8.7**	**36.5±8.86**	**α NS**	**β Unmed<HC t=3.0 df=86 p=0.003**	**β NS**
Total Normalized Habenula Volume	**$2.68x10^{-5}$± $5.88x10^{-6}$**	**$3.25x10^{-5}$± $8.66x10^{-6}$**	**$3.16x10^{-5}$± $8.79x10^{-6}$**	**α NS**	**β Unmed<HC t=2.1 df=86 p=0.035**	**β NS**
WBV (mm^3)	**1168502.4± 117836.8**	**1116796.0± 105411.5**	**1192123.4± 119537.8**	**α NS**	**β NS**	**β NS**

Blue shading = demographic and clinical variables. Light blue shading = volumetric data. Pink shading = demographic and clinical data for each diagnostic group. Green shading = statistical comparisons.

AD, antidepressants; BDI, bipolar disorder type I; BDII, bipolar disorder type II; HC, healthy controls; MADRS, Montgomery-Asberg Rating Scale for Depression; NA, not applicable; NS, not significant; WBV, whole brain volume; YMRS, Young Mania Rating Scale.

α = F-test controlling for age at scan and duration of illness.
B = t-test (no covariates).