Supporting Information

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SI Methods and Materials

Image Acquisition. One hundred and seventy-six high-resolution T1-weighted anatomical images were first acquired using Siemens' magnetization-prepared rapid-acquired gradient echo pulse sequence with the following specifications: echo time (TE), 2.53 ms; repetition time (TR), 1,900 ms; flip angle (FA), 9°; field-of-view (FOV), 250 mm; image matrix, 256 mm × 256 mm; slice thickness, 1 mm. Whole-brain functional images were then acquired using a T2*-weighted echo planar imaging sequence sensitive to BOLD contrast with the following specifications: TE, 40 ms; TR, 2,000 ms; FA, 90°; FOV, 192 mm; image matrix, 64 mm × 64 mm; slice thickness, 3.5 mm; slice gap, 22%—using 125 (n = 27) or 130 (n = 71) successive brain volumes of 28 slices coplanar with the anterior and posterior commissures. Stimuli were presented with Psychophysics Toolbox for MATLAB using an LCD AVOTEC projector onto a screen located behind the subject's head and viewed through an integrated head-coil mirror.

Preprocessing. Data preprocessing was carried out using FEAT (FMRI Expert Analysis Tool) Version 6.00, part of FSL (FMRIB's Software Library) (1). Motion was assessed by center of mass measurements (BXH/XCEDE Tools, version 1.8.16, Bioinformatics Information Research Network) to ensure that no participants had greater than a 3-mm deviation in the x, y, or z dimensions. The following prestatistics processing was applied: motion correction using MCFLIRT (2), nonbrain removal using BET (3), spatial smoothing using a Gaussian kernel of 5.0 mm full width at half maximum to reduce noise, grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor, and high-pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma equal to 50.0 s). Additionally, each functional volume was registered to the participant's high-resolution anatomical image and then to FSL's standard Montreal Neurologic Institute (MNI 152, T1 2 mm) template brain using FSL's linear registration tool (2, 4).

1. Smith SM, et al. (2004) Advances in functional and structural MR image analysis and implementation as FSL. *Neuroimage* 23(Suppl 1):S208–S219.
2. Jenkinson M, Bannister P, Brady M, Smith S (2002) Improved optimization for the robust and accurate linear registration and motion correction of brain images. *Neuroimage* 17(2):825–841.
3. Smith SM (2002) Fast robust automated brain extraction. *Hum Brain Mapp* 17(3):143–155.
4. Jenkinson M, Smith S (2001) A global optimisation method for robust affine registration of brain images. *Med Image Anal* 5(2):143–156.

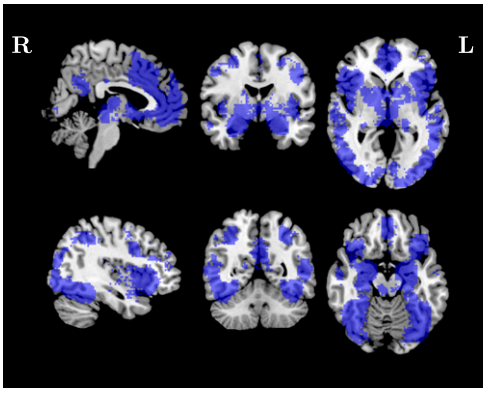

Fig. S1. Functional ROI search space created using Neurosynth.org meta-analysis feature set keywords "face" and "emotion." Image is depicted in MNI space (*Top*, x = 3, y = −2, z = 0; *Bottom*, x = 38, y = −54, z = −16).

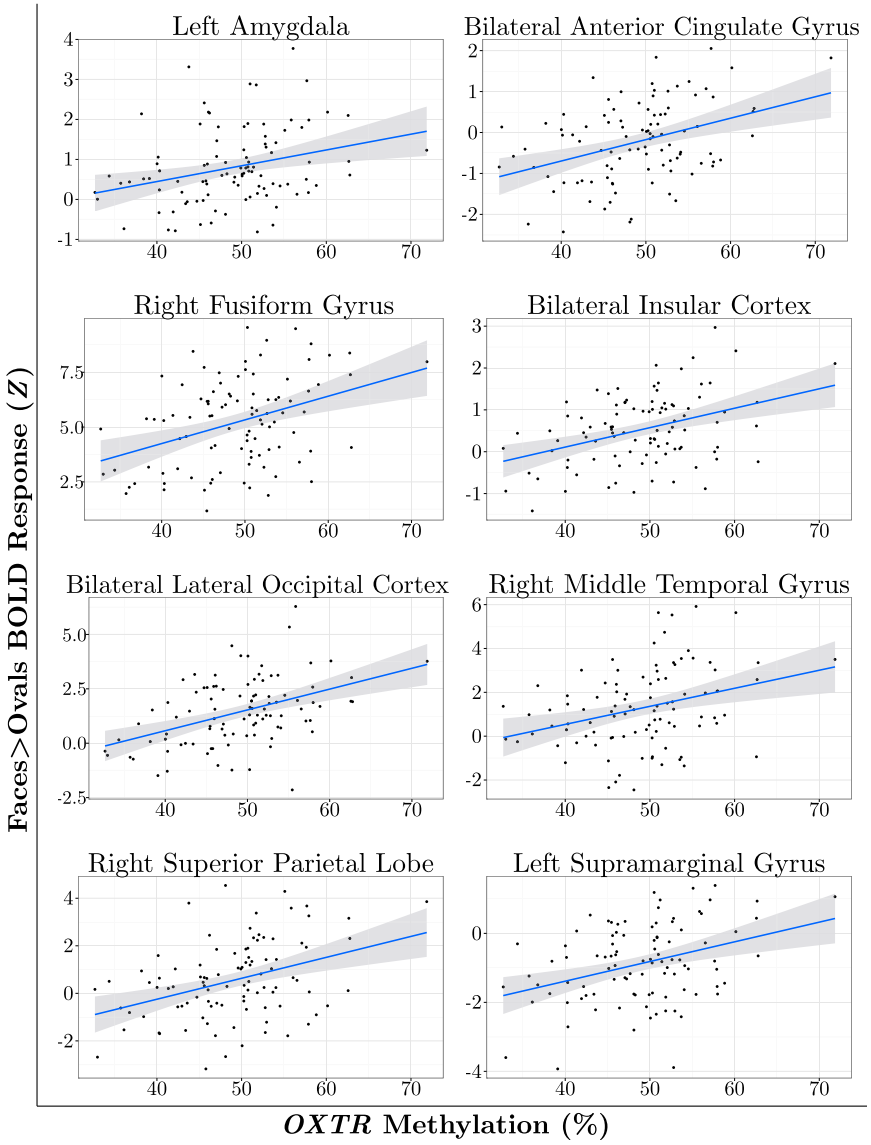

Fig. S2. Methylation of *OXTR* is associated with increases in brain response to angry and fearful faces. Mean *Z* statistic values from clusters of voxels within ROI show a significant positive main effect of methylation on BOLD response (extent threshold $k \geq 10$ voxels) are plotted against percent *OXTR* methylation for each participant ($n = 98$). Gray shading indicates 95% confidence interval around the best-fit line.

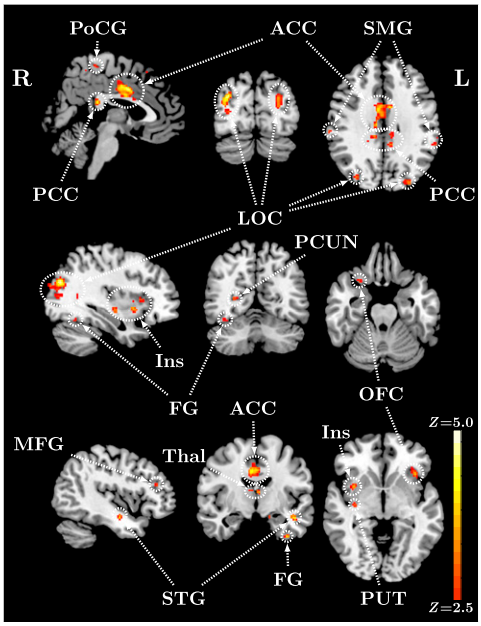

Fig. S3. Positive main effect of *OXTR* methylation on BOLD activity within whole-brain analysis. *Z* statistic map of voxels shows a significant positive main effect of *OXTR* methylation on BOLD activity for faces > ovals contrast within the whole-brain analysis, FDR corrected at $q < 0.05$. Images are depicted in MNI space (*Top*, $x = 2$, $y = -80$, $z = 32$; *Middle*, $x = 34$, $y = -62$, $z = -24$; *Bottom*, $x = -44$, $y = -8$, $z = -4$). ACC, anterior cingulate cortex; FG, fusiform gyrus; Ins, insular cortex; LOC, lateral occipital cortex; MFG, medial frontal gyrus; OFC, orbitofrontal cortex; PCC, posterior cingulate cortex; PCUN, precuneus; PoCG, postcentral gyrus; PUT, putamen; SMG, supramarginal gyrus; STG, superior temporal gyrus; Thal, thalamus.

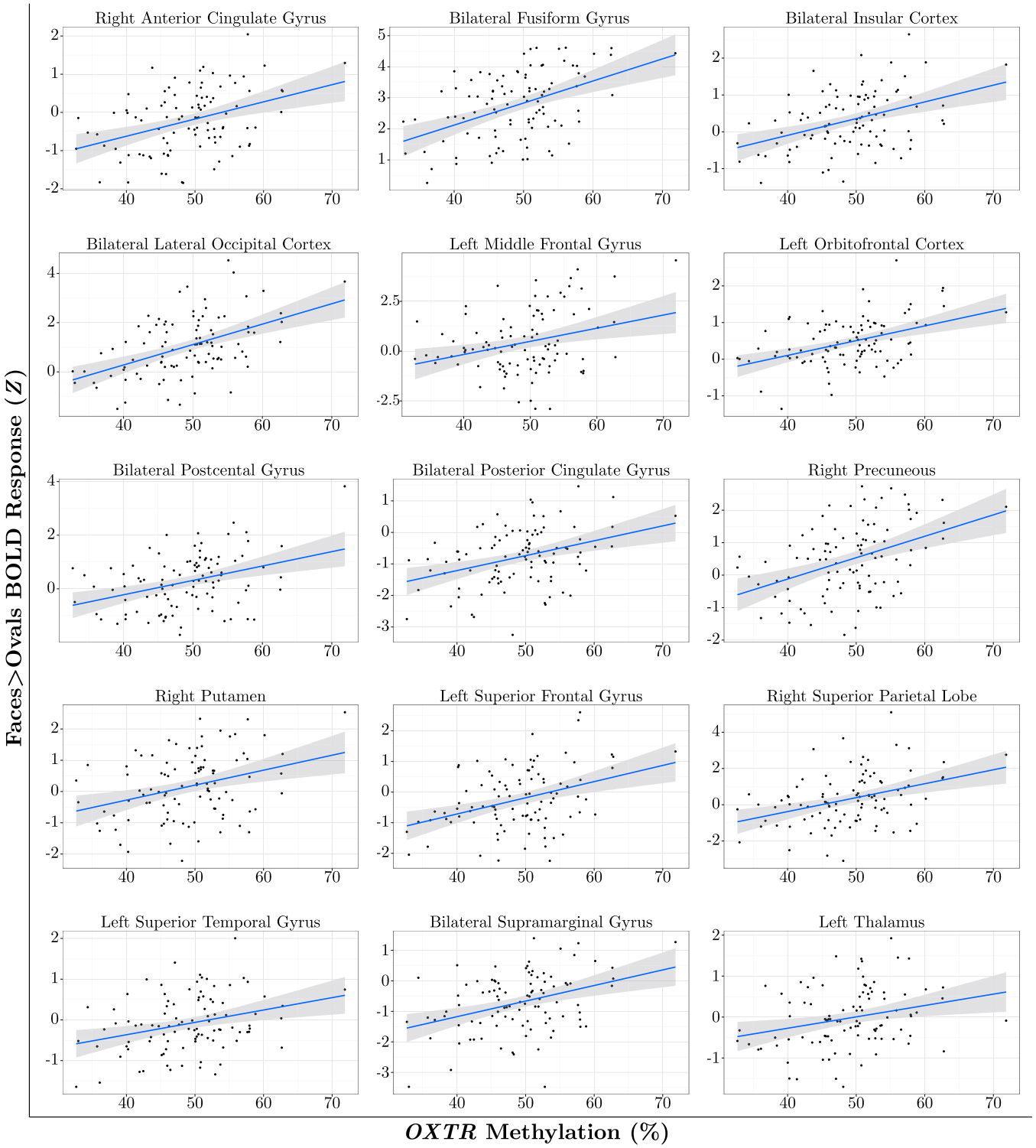

Fig. S4. Relationship between *OXTR* methylation and BOLD activity within areas identified in whole-brain analysis. Mean *Z* statistic values from clusters of voxels within whole-brain analysis showing a significant positive main effect of methylation on BOLD response (extent threshold $k \geq 10$ voxels) are plotted against percent *OXTR* methylation for each participant ($n = 98$). Gray shading indicates 95% confidence interval around the best-fit line.

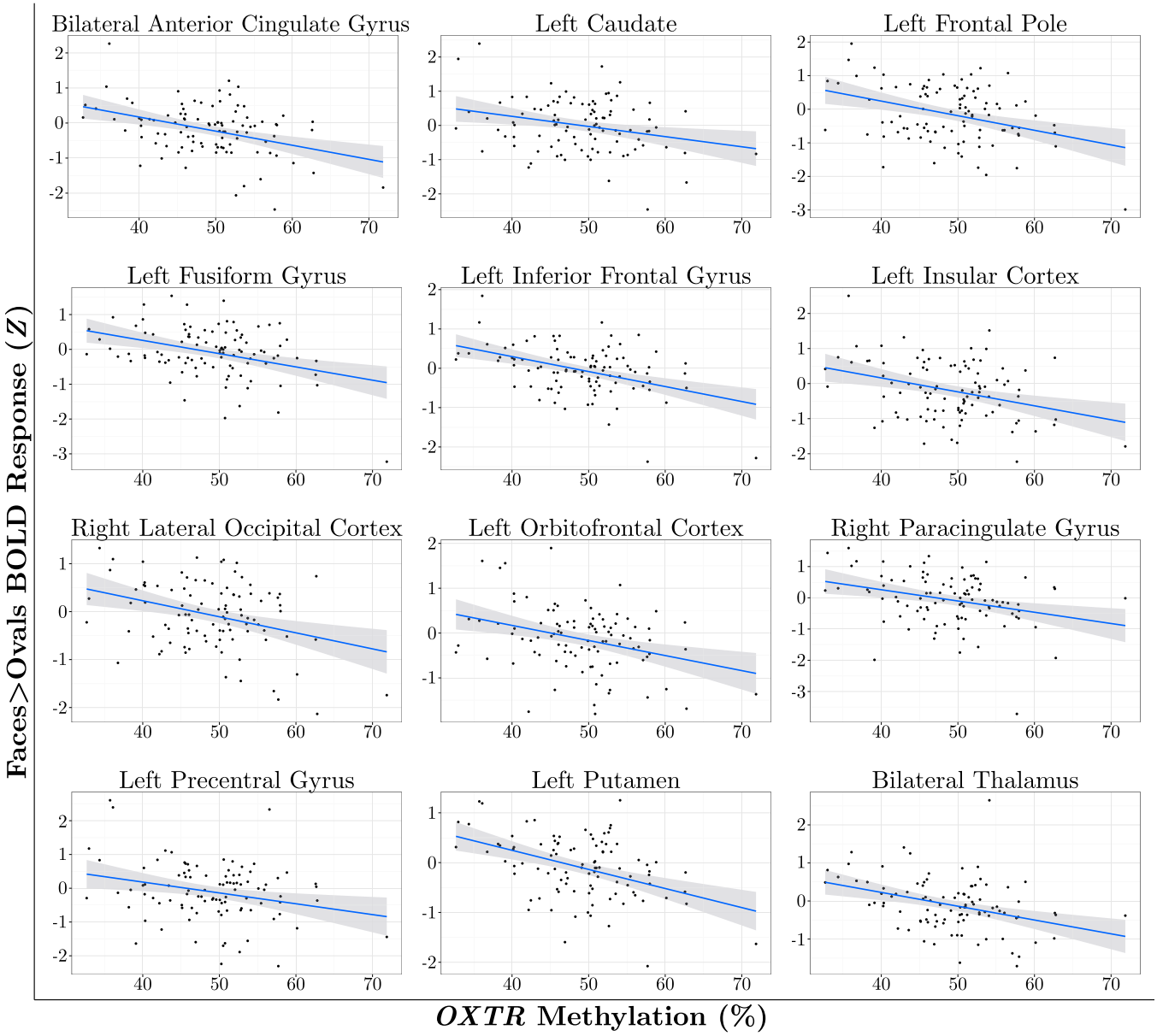

Fig. S5. Increased *OXTR* methylation attenuates amygdala connectivity with brain regions important for emotion regulation and face perception. Mean *Z* statistic values from clusters of voxels within ROI showing a significant negative main effect of methylation on right amygdala functional connectivity (extent threshold $k \geq 10$ voxels) are plotted against percent *OXTR* methylation for each participant ($n = 98$). Gray shading indicates 95% confidence interval around the best-fit line.

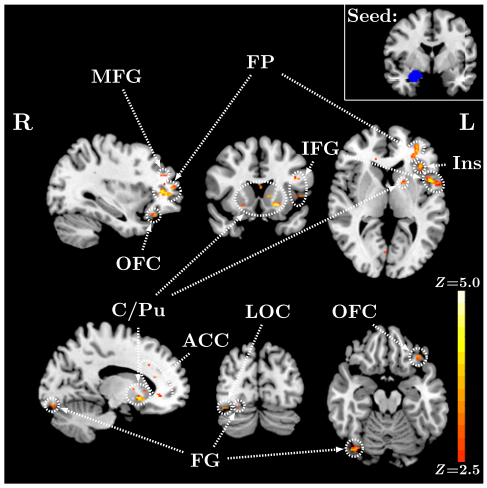

Fig. S6. Negative main effect of *OXTR* methylation on right amygdala functional connectivity within whole-brain analysis. *Z* statistic map of voxels showing a significant negative main effect of *OXTR* methylation on right amygdala functional connectivity for faces > ovals contrast within whole-brain analysis, FDR corrected at $q < 0.05$. Images are depicted in MNI space (*Top*, $x = -36$, $y = 16$, $z = 4$; *Bottom*, $x = -16$, $y = -78$, $z = -18$). (*Inset*) Right amygdala seed region ($y = -4$). ACC, anterior cingulate cortex; C/Pu, caudate/putamen; FG, fusiform gyrus; FP, frontal pole; IFG, inferior frontal gyrus; Ins, insular cortex; LOC, lateral occipital cortex; MFG, medial frontal gyrus; OFC, orbitofrontal cortex.

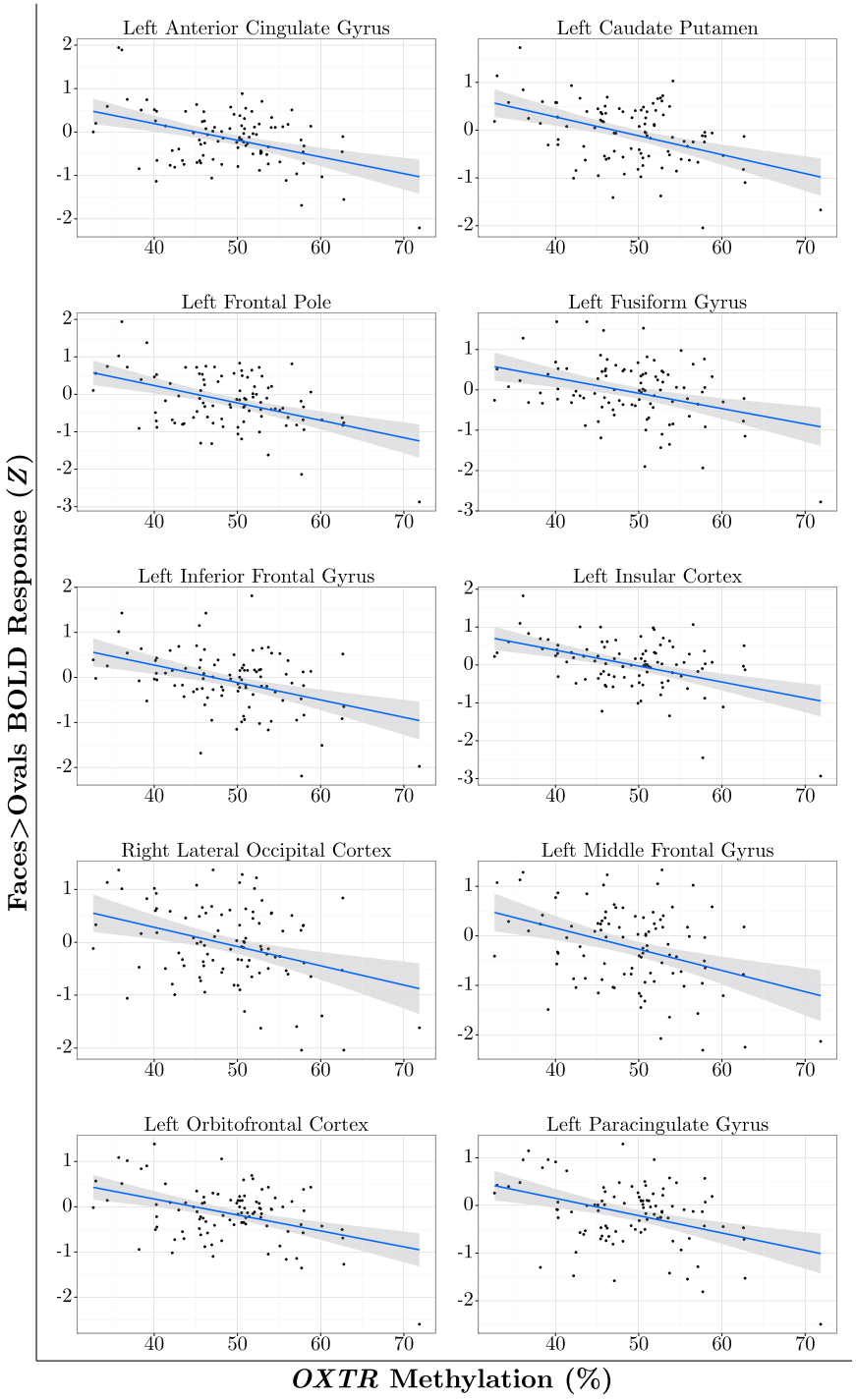

Fig. S7. Relationship between *OXTR* methylation and right amygdala functional connectivity within areas identified in PPI whole-brain analysis. Mean *Z* statistic values from clusters of voxels within whole-brain analysis showing a significant negative main effect of methylation on right amygdala functional connectivity (extent threshold $k \geq 10$ voxels) are plotted against percent *OXTR* methylation for each participant ($n = 98$). Gray shading indicates 95% confidence interval around the best-fit line.

Table S1. Whole-brain analysis local maxima statistics

Anatomical region	Hem	*x*	*y*	*z*	*Z*	*k*
Anterior cingulate gyrus	R	6	−6	38	4.93	413
Fusiform gyrus	L	−36	−10	−40	4.36	17
Fusiform gyrus	R	38	−60	−16	3.63	12
Insular cortex	L	−38	22	−4	4.09	36
Insular cortex	R	40	−18	−8	4.36	46
Insular cortex	R	32	16	6	4.15	32
Insular cortex	R	34	10	−6	4.06	27
Lateral occipital cortex	L	−26	−82	26	4.41	193
Lateral occipital cortex	R	34	−78	26	4.86	265
Lateral occipital cortex	R	36	−58	8	4.05	44
Middle frontal gyrus	L	−42	36	20	3.69	11
Orbitofrontal gyrus	L	−28	14	−28	3.95	20
Postcentral gyrus	B	0	−36	64	4.02	32
Postcentral gyrus	L	−18	−34	62	3.78	12
Posterior cingulate gyrus	B	0	−34	20	4.6	31
Posterior cingulate gyrus	L	−8	−40	30	3.97	41
Posterior cingulate gyrus	R	12	−28	36	4.35	49
Precuneous	R	10	−48	54	3.96	33
Precuneous	R	24	−62	8	3.73	13
Putamen	R	30	−16	6	3.65	10
Superior frontal gyrus	L	−14	12	58	3.82	19
Superior parietal lobe	R	24	−52	56	3.74	47
Superior temporal gyrus	L	−46	−8	−18	4.57	22
Supramarginal gyrus	L	−62	−32	36	4.29	60
Supramarginal gyrus	L	−62	−28	24	3.76	13
Supramarginal gyrus	R	64	−24	30	4.16	26
Thalamus	L	−2	−4	12	4.23	19

Significant cluster threshold: FDR (q) < 0.05, $k \geq 10$ voxels. B, bilateral; Hem, hemisphere; L, left; R, right; *x*, *y*, *z*, coordinates of local maxima in MNI space; *Z*, maximum *Z* statistic.

Table S2. Whole-brain PPI analysis local maxima statistics

Anatomical region	Hem	*x*	*y*	*z*	*Z*	*k*
Anterior cingulate gyrus	L	−20	32	18	4.26	20
Caudate	L	−12	16	2	4.35	11
Frontal pole	L	−30	38	6	4.96	77
Frontal pole	L	−34	52	12	4.16	13
Fusiform gyrus	L	−16	−88	−14	4.37	17
Inferior frontal gyrus	L	−52	8	4	4.56	44
Insular cortex	L	−38	26	4	4.43	22
Lateral occipital cortex	R	42	−78	−18	4.22	17
Middle frontal gyrus	L	−30	32	30	4.62	31
Orbitofrontal cortex	L	−22	26	0	4.27	12
Orbitofrontal cortex	L	−36	32	−20	4.23	16
Paracingulate gyrus	L	−12	38	−4	4.12	14
Putamen	L	−18	14	−8	5.25	45
Putamen	L	−18	6	4	4.15	15

Significant cluster threshold: FDR (q) < 0.05, $k \geq 10$ voxels. Hem, hemisphere; L, left; R, right. *x*, *y*, *z*, coordinates of local maxima in MNI space; *Z*, maximum *Z* statistic.