Supplementary Information

Methods and Materials

Control for nonspecific effects of oxytocin

To control for nonspecific effects of oxytocin, all subjects completed a multidimensional mood questionnaire (MBDF; [1]) after arriving at the laboratory (prior to substance administration) and directly before the MRI scanning (40min after substance administration). These data were analyzed in a series of 2x2x2 ANOVAs using group (borderline, control) and substance (oxytocin, placebo) as between-subject factors and time point as a within-subject factor.

Stimulus Material

Male and female faces unambiguously depicting angry, fearful, and happy expressions were selected from four established data sets: NimStim Face Stimulus Set (http://www.macbrain.org/), Pictures of Facial Affect [2], Karolinska Directed Emotional Faces (KDEF, http://www.facialstimuli.com/index_files/Page369.htm), and FACES database [3]. These faces were slightly rotated to ensure that, when displayed, both eyes were at the same vertical height in each image. Additionally, an elliptical mask was fitted to solely reveal the face itself while hiding hair and ears. Colored images were converted to grayscale and the cumulative brightness was normalized across images.

A different set of six faces was used to familiarize subjects with the task and the button assignment before scanning

Analysis of Eye Movements

To examine whether borderline diagnosis and/or oxytocin have an effect on gazing behavior, we analyzed the fixation changes that were triggered by the stimulus and occurred

in a period of 1,000ms following stimulus offset. Trials with fixation changes during the prestimulus period (-500ms to 0ms) or during stimulus presentation (0-150ms) were excluded. Blinks were interpolated as long as the blink period did not exceed more than 30% of the trial. In this latter case, the whole trial was excluded from statistical analyses. Overall, the average percentage of valid trials was 56% (*SD*=23%), and did not differ as a function of emotion or initial fixation ($p>.05$). Subjects in the placebo condition, however, had slightly fewer trials with valid eye-tracking data for happy faces (*M*=51%; *SD*=23%) as compared to fearful (*M*=57%, *SD*=24%) and angry faces (*M*=57%, *SD*=23%) and compared to subjects in the oxytocin condition (*M*=56%, *SD*=23%); interaction of substance and emotion: $F(2,124)=4.50$, $\varepsilon=.93$, $p=.015$, $\eta^2=.07$.

For all valid trials, we determined the latency and proportion of fixation changes (>0.5°) after stimulus offset that were directed toward the other major facial feature. That is, when the eyes were presented at the position of the fixation cross, we determined the proportion of downward fixation changes toward the mouth, and when the mouth followed the fixation cross, we calculated the corresponding proportion of upward fixation changes toward the eyes.

Preprocessing of fMRI data

In a first step, each participant's data were slice-time corrected for each session. Afterwards, realignment with unwarping was performed for each session. The high-resolution T1 image was then coregistered with the mean EPI image and subsequently segmented. The resulting transformation parameters of the segmentation were applied to all functional images to normalize them to the standard anatomical MNI space. Images were saved with a spatial resolution of $1x1x1mm^3$, and smoothing was accomplished using a narrow 4-mm full-width at half maximum (FWHM) isotropic Gaussian kernel to optimize the detection of small

activation foci within the amygdala. Finally, images were high-pass filtered at 128s, and an autoregressive AR model was used to account for serial correlations in fMRI time series [4].

Results

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We found generally reduced mood, wakefulness, and arousal in borderline patients compared to healthy women (main effects of group: Fs(1,75)≥5.24, ps≤.=.025) and an overall reduction of mood, wakefulness, and arousal as a function of time (main effects of time: Fs(1,75)≥7.89, ps≤.006). Significant interactions of group and time point, however, revealed that mood and arousal only dropped in healthy women as a function of time (Fs(1,75)≥37.14, ps≤.001) and that patients and participants did not differ in mood and arousal at the second time point, and thus directly before the experiment started (p>.05). Finally, only participants of the placebo group reported enhanced arousal compared to borderline patients (interaction of substance and group: F(1,75)=7.34, p=.008). Importantly, we did not find any significant interaction between substance and time or substance, group, and time, indicating that effects were stable across substance administration.

References

1. Steyer R, Schwenkmezger P, Notz P, Eid M. *Der Mehrdimensionale Befindlichkeitsfragebogen MDBF [Multidimentional mood questionnaire]*. 1997. Göttingen: Hogrefe.
2. Ekman P, Friesen WV. Constants across cultures in the face and emotion. *J Pers Soc Psychol*. 1971; 17:124–129.
3. Ebner N, Riediger M, Lindenberger U. FACES–A database of facial expressions in young, middle-aged, and older women and men: Development and validation. *Behav Res Methods.* 2010; 42:351–62.
4. Ashburner J. A fast diffeomorphic image registration algorithm. *Neuroimage.* 2007;38(1):95-113.

Supplementary Table 1. Proportion of correct emotion classification (in % ± SEM) of patients with borderline personality disorder and healthy controls in the placebo and oxytocin condition as a function of the depicted facial expression (angry, fearful, happy) and the initial fixation (eyes, mouth).

			Placebo		Oxytocin	
Measure	Group	Emotion	Eyes	Mouth	Eyes	Mouth
	borderline patients	Angry	88.9 ± 1.9	92.2 ± 2.1	92.1 ± 1.8	91.4 ± 1.9
		Fearful	92.9 ± 2.3	88.4 ± 2.6	90.5 ± 2.1	89.2 ± 2.4
		Happy	97.6 ± 1.5	99.0 ± 1.2	96.2 ± 1.4	95.6 ± 1.1
	healthy controls	Angry	87.9 ± 2.1	87.9 ± 2.3	91.9 ± 2.1	90.1 ± 2.3
		Fearful	89.3 ± 2.5	85.3 ± 2.7	93.1 ± 2.5	89.9 ± 2.7
		Happy	98.8 ± 1.6	98.4 ± 1.3	98.8 ± 1.6	98.2 ± 1.3

Data supplement for Bertsch et al. (doi: 10.1176/appi.ajp.2013.13020263)