Study Title: Social Safety Learning in the Brain Oxytocin System

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Statistical Analysis Plan

Two-tailed independent-sample t-tests compared demographics and self-report symptoms between SAD and HC groups and between oxytocin and placebo groups. To test effects of vicarious extinction, linear mixed-effects models with main effects of patient group, gender, and stimulus type tested mean SCR differences across all phases; for vicarious extinction and reinstatement, analyses included placebo participants only. Effects of oxytocin and interactions with gender were tested using mixed-effects models that added drug condition and hypothesized interactions (group*drug, gender*drug, stimulus type*drug*gender). We used t-tests for post-hoc comparisons for all phases. We also examined changes from the end of vicarious extinction to the start of reinstatement to assess generalized versus CS-specific reinstatement; these models added main effects of time and stimulus type*time interactions.

Task-based fMRI ROI analyses were conducted using Nilearn. Vicarious extinction and reinstatement were modeled separately. First-level models included event onsets for CS+R, CS+S, and CS- (6-second boxcar functions). During vicarious extinction, the demonstrator's shock (CS+R) and the omission of shock (CS+S) were modeled as stick functions at stimulus offset; in reinstatement, the reminder shocks were modeled as stick functions at task onset. As the first CS- trial during reinstatement typically elicits an orienting response, it was regressed out. The design matrix included CS regressors, patient group, gender, drug, and their interaction terms (drug*patient group, drug*gender). The matrix was convolved with an HRF and images were smoothed at 6mm FWHM; 32 motion-related nuisance regressors were included (six rigid-body parameters, white-matter and CSF signals, and their derivatives and quadratic terms). Contrast images between CS types (i.e., CS+R > CS+S) were generated at the first level. Second-level GLMs compared these contrasts across groups (SAD vs. HC, oxytocin vs. placebo, male vs. female) and tested drug*gender and drug*patient group interactions. To parallel the SCR analyses, a time effect was included to examine changes from the end of vicarious extinction to the start of reinstatement. Whole-brain exploratory analyses used the same design matrix and are detailed in the Supplementary Materials.