Oxytocin Facilitates Learning with Social Feedback and Activity in Emotion and Reward Regions

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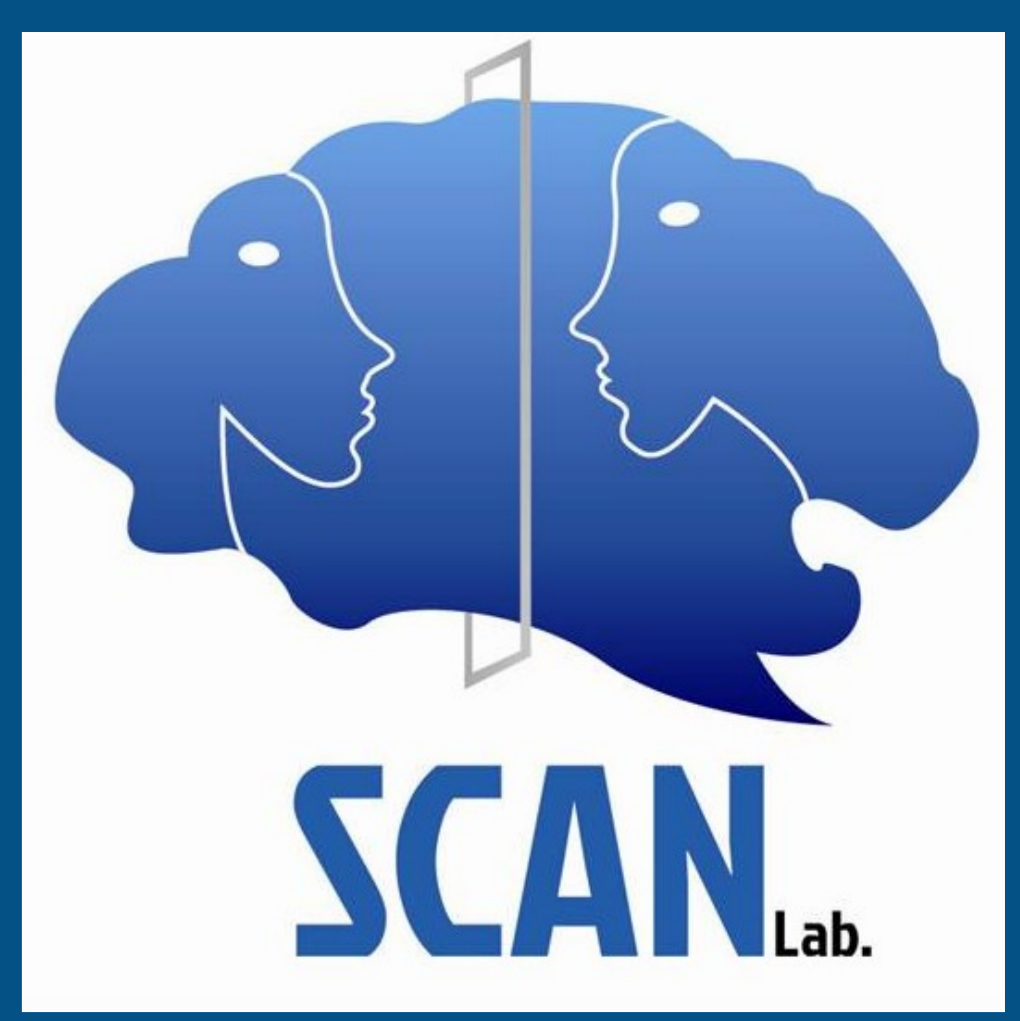
Introduction

■ Oxytocin (OXT) is a hypothalamic neuropeptide that influences many human social and emotional behaviors. OXT has been shown to facilitate socially-reinforced learning[1] and the present study investigated how it acts on the brain to produce this effect.

Methods

■ In two double-blind, between-subject placebo (PLC) controlled designed studies we investigated the effect of intranasal OXT (24IU) on learning in a reinforcement associative learning task (RALT). Subjects learn which of a set of 3-digit numbers are associated with two arbitrary categories (A or B) guided by social or non-social feedback (**figure 1**). 52 male subjects participated in experiment 1 (behavioral) and 54 in experiment 2 (behavioral & fMRI combined).

■ Learning performance was recorded during 6 presentation cycles (numbers presented in a random order). The response and feedback phases were analyzed sepa-
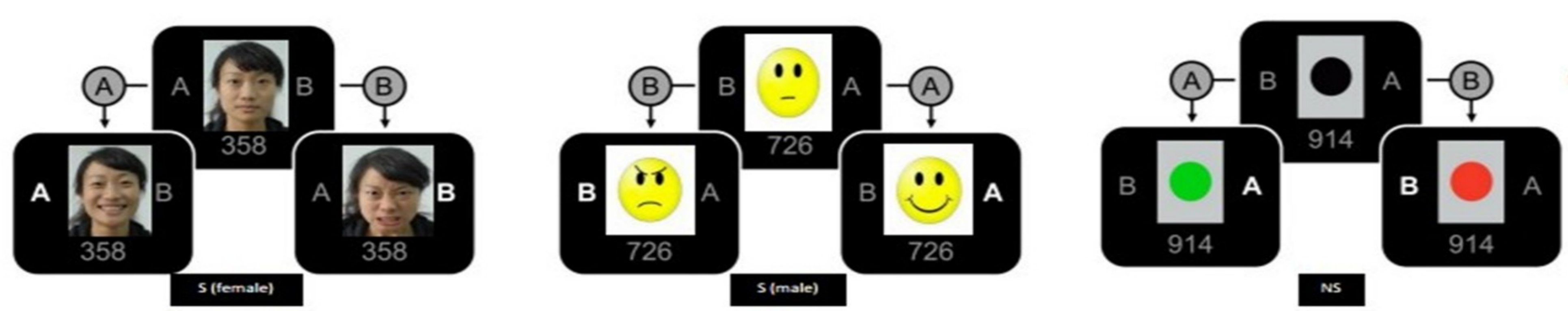

Figure 1. RALT Paradigm : Different social (emotional faces) and non-social feedback are given when subjects make category assignments in the RALT task (Exp 2).

Behavioral Results

■ In both experiments 3-way ANOVA revealed significant main effects of treatment (p<0.05) and cycle (p<0.001) with social feedback being less effective than non-social (including emoticons) in PLC (contrary to findings in Caucasian subjects[1]). There was a significant feedback x treatment interaction (p<0.05) and T-tests showed OXT improved learning performance with social female feedback in cycles 3-5 (**figure 2**).
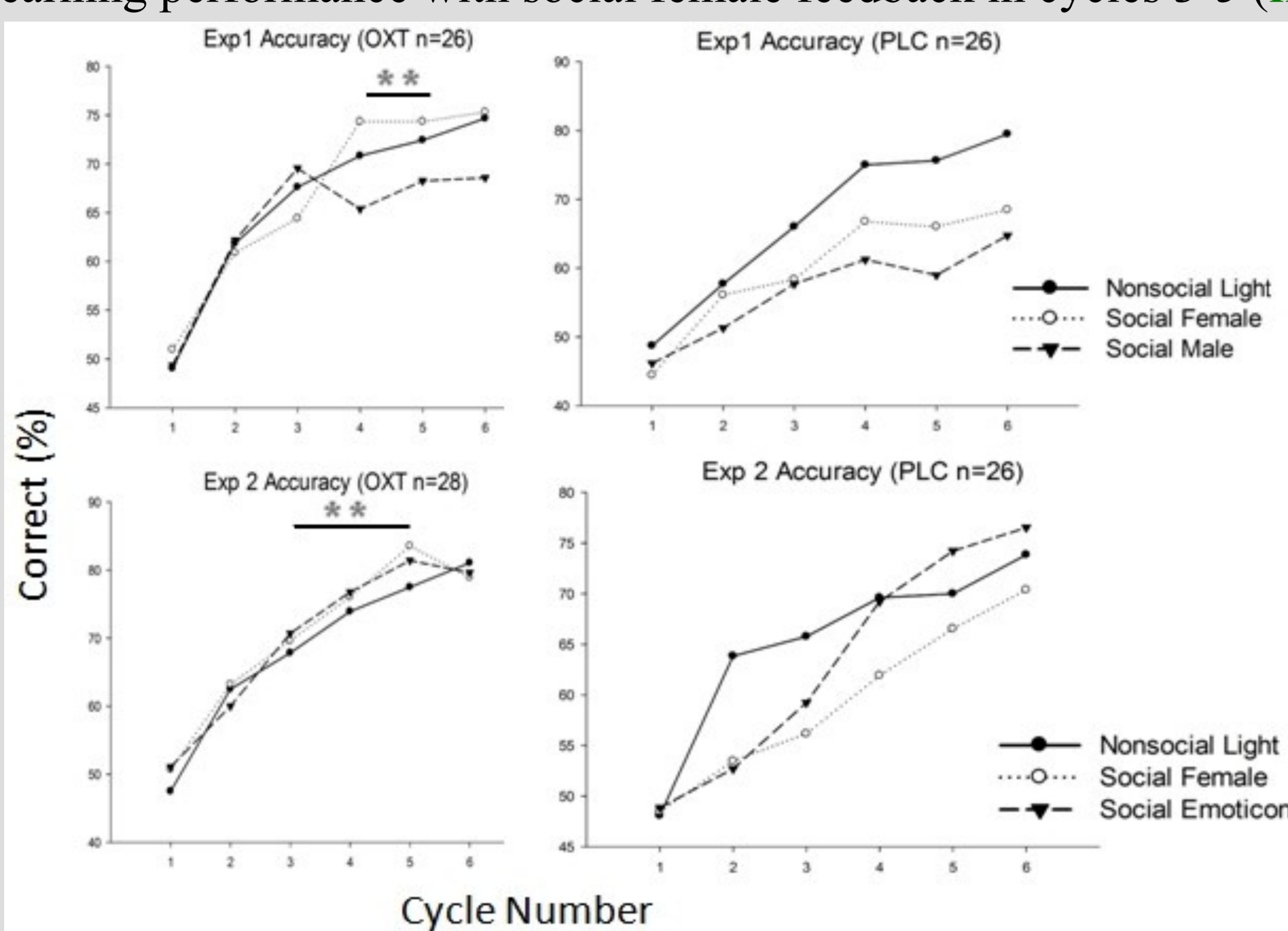

Figure 2. RALT behavioral results for OXT and PLC groups in Exps. 1& 2 **p<0.01 for OXT vs. PLC with female face. In both experiments the light feedback is significantly more effective than the social (but not emoticon) in the PLC (p<0.05) but not OXT group.

fMRI Results

■ For the response phase, whole-brain analysis revealed altered (p<0.001 uncorrected) BOLD signals in the right amygdala [24,-8,-12], hippocampus [32,-8,-16]and superior temporal gyrus [54,-12,-8] with different feedback. Specific contrasts with (p<0.001 uncorrected threshold) showed OXT effects in the left precuneus [-18, 62,36], right post-cingulate gyrus [-12,-46,10] and parahippocampal gyrus [20,-35,-4]. ROI analyses for the two groups of regions are shown in **figures 3 & 4** and shows OXT treatment reduced deactivation in default mode regions independent of feedback type and increased activation only with female face social feedback in other regions.
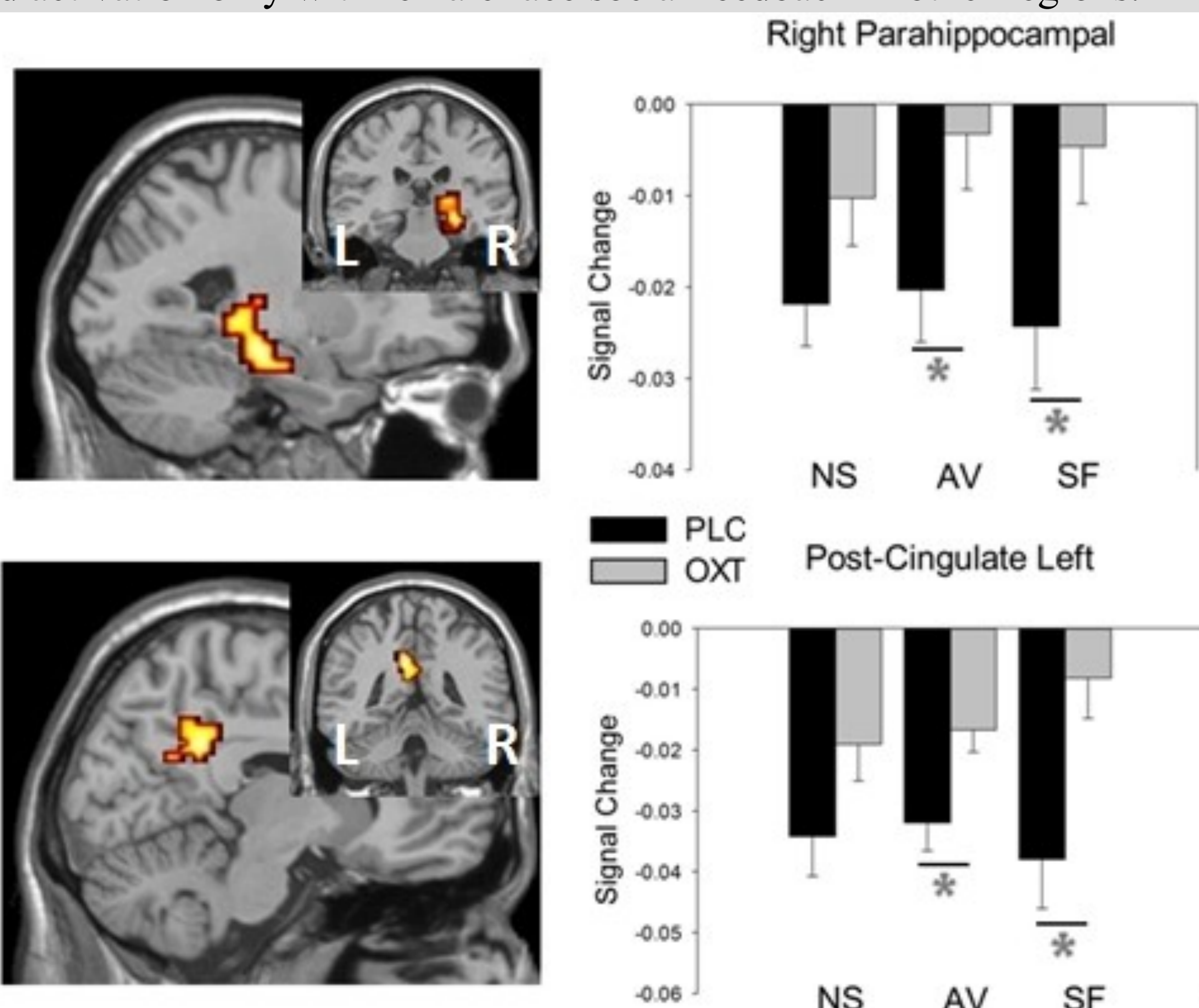

Figure 3. Extracted % signal changes in regions in specific contrasts ([Social Female$_{OXT}$ > Social Female$_{PLC}$], [Social Avatar$_{OXT}$ > Social Avatar$_{PLC}$], etc.). OXT reduces task-related deactivation in these default mode network regions. *p<0.05
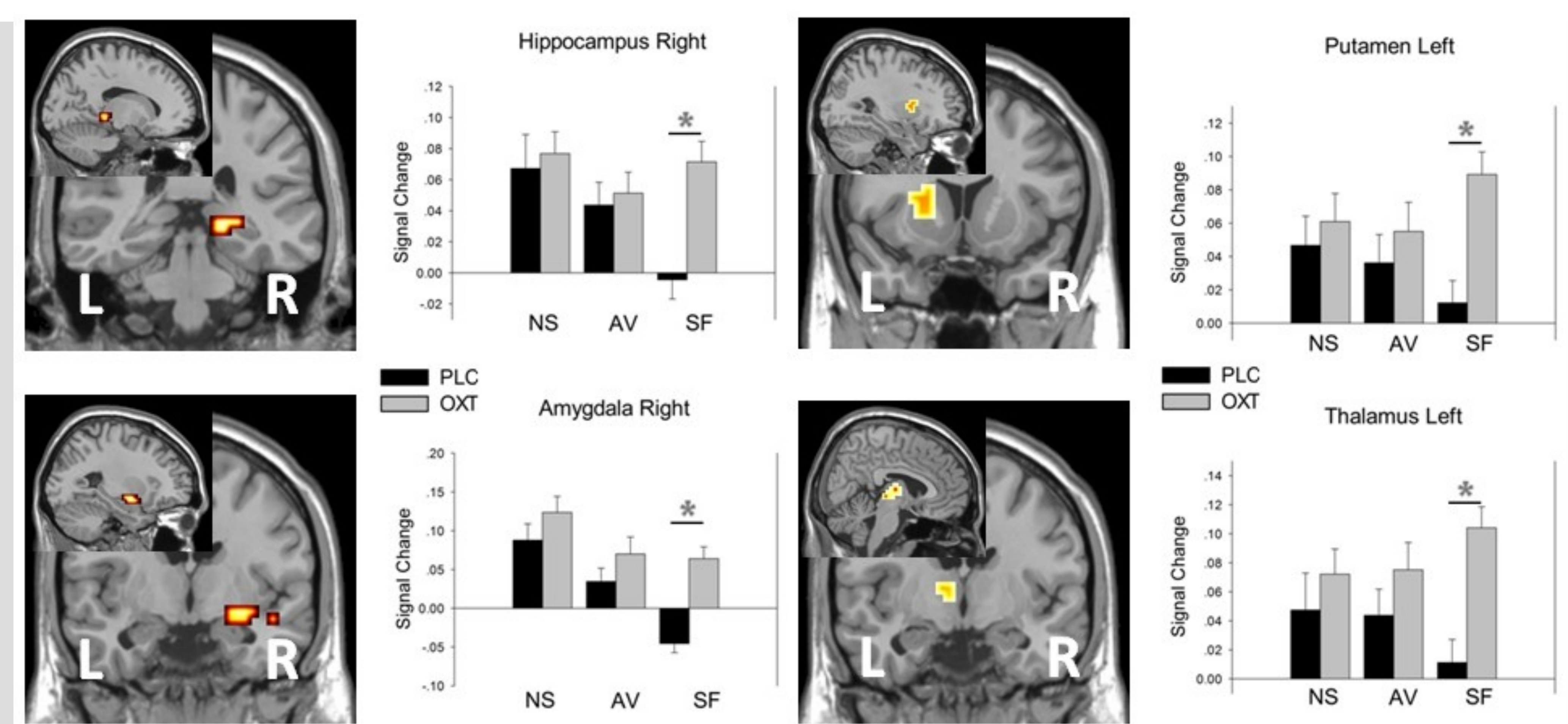

Figure 4. Extracted % signal changes show OXT is selectively facilitates activity with social feedback in hippocampus, amygdala, putamen and thalamus. *p<0.05

■ Correlations (Pearson test) between mean %BOLD signal changes and accuracy and response latency or neuropsychological questionnaires scores across the 6 presentation cycles of the RALT were calculated in PLC and OXT groups in Exp 2 (**figure 5**).
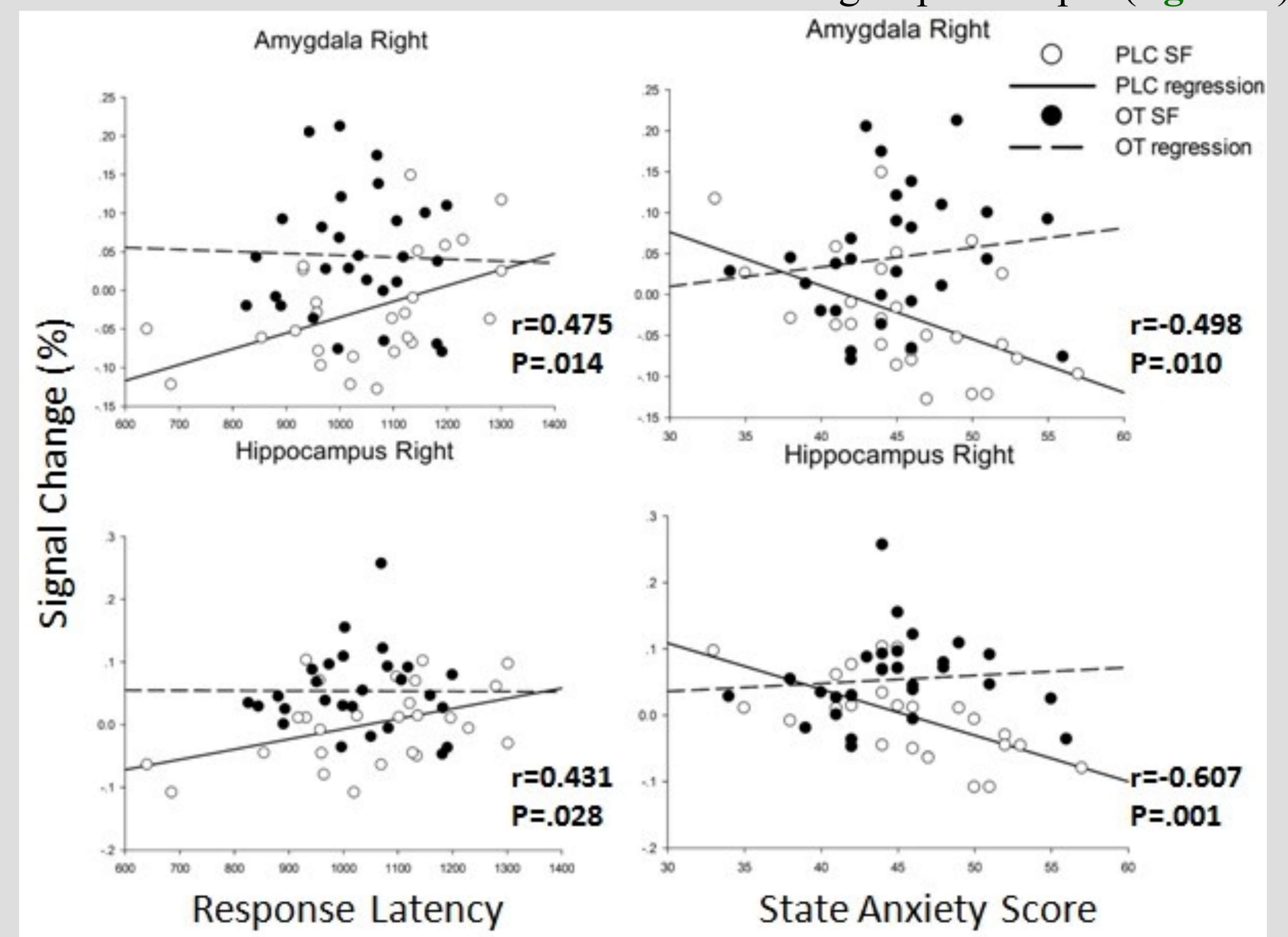

Figure 5. Under PLC, but not OXT, % BOLD signal changes in these ROIs are positively correlated with response time but negatively correlated with state anxiety only in the social feedback condition.

■ A seed-based connectivity analysis (Psychophysiological Interaction) revealed OXT increased right amygdala to left putamen & left insula connectivity only in the social female condition. (p<0.01 uncorrected) . (**figure 6**).
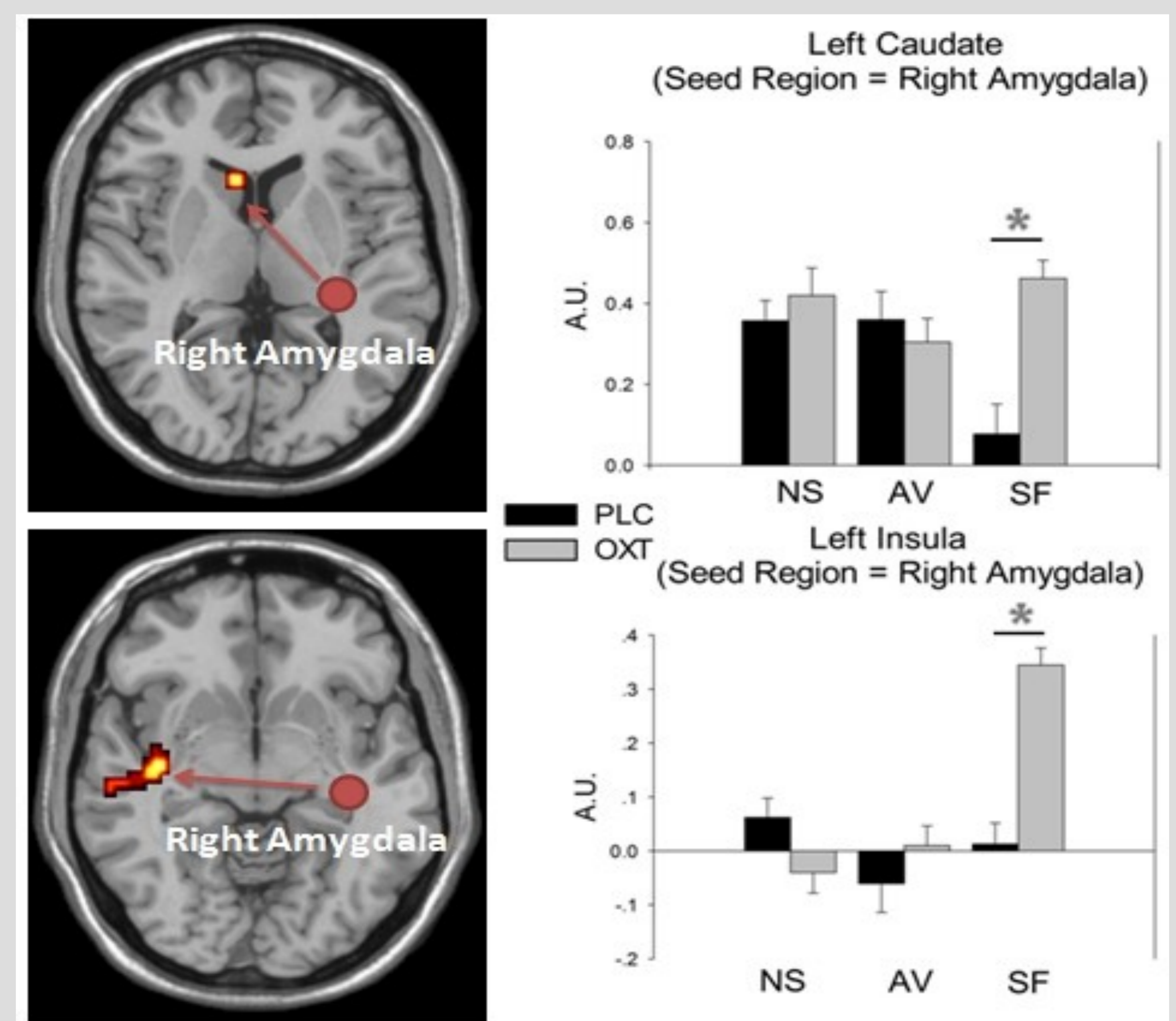

Figure 6. Extracted parameter estimates from left caudate and insula using right amygdala as the seed region. OXT increased connectivity strength in the social female condition. *p<0.05

Conclusions

■ Contrary to findings in male Caucasian subjects[1] in Chinese subjects social feedback with emotional faces does not facilitate learning. However, OXT selectively facilitates learning with feedback using social female faces

■ OXT facilitation of learning with social feedback is associated with increased activity and functional connectivity in regions associated with emotional memory (hippocampus, parahippocampal gyrus, insula and amygdala) and reward (caudate/ putamen).

■OXT also reduces significant associations between signal changes in these regions and response times and state anxiety scores.

■ OXT also reduces deactivation in posterior regions of the default network during learning with both social and non-social feedback.

References

[1] Hurlemann R., Patin A., Onur, O. A., Cohen, M. X., Baumgartner, T., Metzler, S., Maier, W, Kendrick KM (2010). Oxytocin enhances amygdala-dependent, socially reinforced learning and emotional empathy in humans. J. Neurosci. 30, 4999-5007