Dissecting the functions of lateral OFC networks

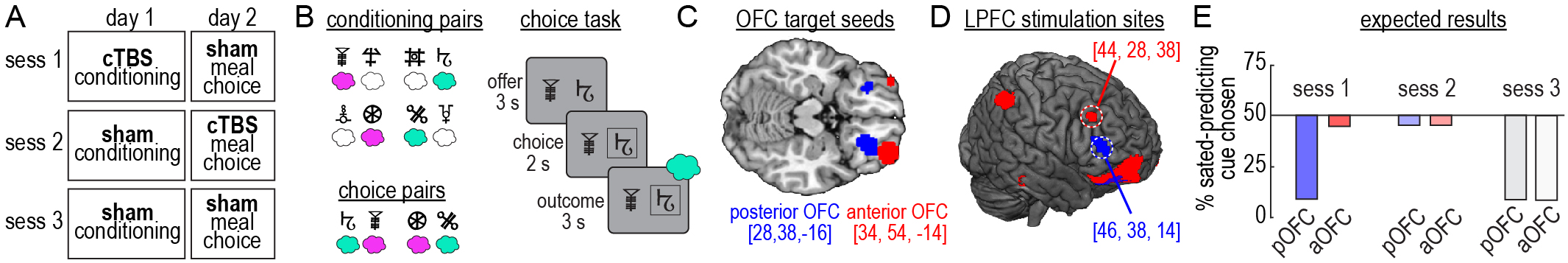
Our previous work has shown that lateral OFC represents expectations about the identity of future rewards1, 2, 3, 4, and that disruption of lateral OFC-network activity impairs the ability to make adaptive choices when they require the consideration of reward identity, e.g., after devaluation of specific outcomes5. Why is the OFC necessary in this case?

It is possible that the OFC contributes to (a) selectively updating the value of a specific outcome during the meal (i.e., devaluation), or (b) representing the associative task structure (i.e., cue-outcome associations) that is necessary for inferring the updated value of the option when making a choice. Given that lateral OFC is a large and heterogeneous region6, 7, particularly in primates7, 8, 9, it is possible that these functions are carried in different subregions. Indeed, previous work in non-human primates suggests that while posterior OFC (pOFC, area 13) is required for value updating, anterior OFC (aOFC, area 11) is required for accessing this updated value during choice10.

We are currently running a 3-session x 2-day TMS experiment to address these questions (**Fig. 4A**). On day 1 of each session, subjects (n=48) learn associations between pairs of visual cues and food odors, such that one cue predicts a sweet or savory food odor, and the other cue predicts no reward (**Fig. 4B**). On day 2, subjects eat a meal corresponding to the sweet or savory food odor (counter-balanced) and then make choices among cues that predict the sweet or savory food odors (**Fig. 4B**). To target the anterior and posterior portion of the lateral OFC (in different groups of subjects, **Fig. 4C**), we individually select stimulation sites in the LPFC that are maximally connected to the aOFC and pOFC (**Fig. 4D**).

In different sessions (order counterbalanced), sham or active cTBS is applied either before learning cue-outcome associations on day 1 or before the meal on day 2 (**Fig. 4A**). We hypothesize that aOFC and pOFC networks make disparate contributions to decisions that require consideration of reward identity, such that aOFC is required for learning and representing specific cue-outcome associations, whereas pOFC is required for value updating. Consequently, we predict (**Fig. 4E**) that cTBS targeting aOFC on day 1 (Sess1-aOFC) will disrupt learning of specific cue-outcome associations, such that on day 2, information about reward identity is not available to infer their updated value after devaluation. In contrast, we predict that targeting pOFC on day 1 (Sess1-pOFC) will have no effect on choices on day 2.

Conversely, we predict that cTBS targeting pOFC on day 2 (Sess2-pOFC) will disrupt value updating during the meal and thereby impair adaptive choices in the task. Moreover, we predict that targeting aOFC on day 2 (Sess2-aOFC) will disrupt signaling of expected reward identity and hence also disrupt adaptive choices on day 2 (**Fig. 4E**). This work will provide insights into the specific functional contributions of OFC networks to decision making.

**Figure 4. Dissecting the functions of lateral OFC networks.** **A.** Experimental design. **B.** Left: Cue pairs and associated odor rewards during conditioning and choice task (purple: sweet food odor; green: savory food odor; white: clean air). Right: Example trial of choice task. **C.** Functional connectivity of posterior (blue) and anterior OFC networks (red). **D.** Stimulation sites in LPFC based on resting-state fMRI connectivity with pOFC and aOFC (based on neurosynth.org data). **E.** Expected results for % of trials in which the cue predicting the sated odor is chosen.

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