THE UNIVERSITY OF ARIZONA.

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sLORETA REVEALS RESTING ANTERIOR CINGULATE THETA BAND POWER DIFFERENCES IN HIGH vs. LOW OBSESSIVE COMPULSIVE SYMPTOMOLOGY

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Abstract

❖ A hyperactive cortico-striatal circuit has been proposed to underlie the obtrusive thoughts and repetitive behaviors which comprise Obsessive-Compulsive (OC) symptoms.

❖ Larger Error-Related Negativities (ERNs) generated from the Anterior Cingulate Cortex (ACC) have been proposed to reflect this hyperactive cortico-striatal circuit in OCD, as well as across OC symptom scores in non-patients.

❖Since ERN amplitude has been shown to predict reinforcement learning accuracy specific to losses ('NoGo' learning; Frank et al., 2006, 2007), we sought to investigate if individuals who score high on an OC scale show a bias to learn from punishment cues.

❖ Study I revealed that there were no differences in 'NoGo' learning between students with high vs. low OC symptom scores, although the high group had <u>smaller</u> ERNs (defined as responses to suboptimal choices).

❖ These effects were replicated in Study II, which also revealed that the high OC group had <u>larger</u> ERNs in a Flankers task during motor errors-of-commission.

❖ Resting brain activity was investigated as a predictor of this OC-related task dissociation in ERN amplitude. Since OC groups differ in ACC Theta power (high OC: ↑rACC, ↓dACC), it is hypothesized that tonic differences in these brain areas may underlie this task-specific dissociation in ERN amplitudes.

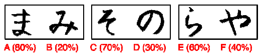
Methods

Participants

- ❖ Each study recruited from > 1200 undergraduates scoring over the range of Obsessive-Compulsive Inventory – Revised (OCI-R) scores (Foa et al., 2002).
- ❖ The OCI-R score of > 21 is considered clinically meaningful, and was used as a cut-off point for creating high and low groups: (**OCI > 21** = '**High OC**'; **OCI < 21** = '**Low OC**')
- ❖ Participants were excluded for drug use, regression to the mean out of their 'group'.
- ❖ **Study I**: N = 74 run, 60 eligible (16 High OC, 44 Low OC)
- ❖ **Study II**: N = 60 run, 53 eligible (24 High OC, 29 Low OC)

Probabilistic Learning Task

- ❖ A probabilistic learning (PL) task was used to elicit response ERNs when participants choose suboptimal stimuli in a forced choice (Frank et al, 2004).
- ❖ During the **training** phase, three pairs of symbols ought to be learned based solely on the feedback provided after each forced choice. The feedback is probabilistic and will reinforce the correct choice only 80%, 70% or 60% of the time, depending on the stimulus pair:



- ❖ In a subsequent **test** phase, each symbol is paired with one of all six symbols and participants must choose amongst all possible choices without feedback.

Flankers Task

- ❖ A modified Flankers task was used to elicit motor error-of-commission ERNs in Study II.

EEG recording and Task Order for Studies I & II

- ❖ NeuroScan SynAmps², 64 Channels, 500X gain, 500 Hz sample, filtered offline [1.5 -15 Hz, 96 dB/oct], re-referenced offline to linked mastoids prior to ERP averaging.
- ❖ **Study I**: Four minutes of rest and two PL tasks were run for each subject.
- ❖ **Study II**: Six minutes of rest, one PL task, and one Flankers task were run

ERP Creation

- ❖ 'Correct' and 'incorrect' responses to the optimal and suboptimal reinforcement choices were averaged for the PL **test** phase. Correct and incorrect responses during the Flankers task were averaged. **All ERPs reported contained > 29 epochs**.
- ❖ The ERN Amplitude was defined as peak-to-peak difference between the highest negative deflection at Cz between 0 and 120 ms after the response, subtracted from the preceding trough (defined as 0 – 80 ms preceding the peak). **Thus more positive values reflect larger ERN amplitudes.**

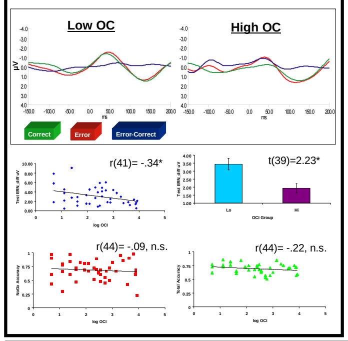
sLORETA

- ❖ sLORETA analysis procedures largely followed the methods of Pizzagalli et al. (2006).
- ❖ Non-overlapping 2.048 second epochs of rest data were cleaned of artifacts using ICA.
- ❖ Study I used 2 minutes of eyes-closed data, Study II used 6 minutes of open and closed. Voxel-wise correlations were run in the non-parametric sLORETA stats package between theta band (4-8 Hz) current density power and OCI-R scores.
- ❖ ROI analyses were also run: all 6239 sLORETA voxels were normalized for the theta band within each subject to a total power of '1' and then log transformed. Voxels were averaged within ACC Brodmann Area (BA) ROIs thought to correspond to affective (rostral) and cognitive (dorsal) functions (Dorsal ACC = Z > 15 and Y < 35; else rostral):

Rostral ACC: BA24_aff, BA32_aff; Dorsal ACC: BA24_cog, BA32_cog

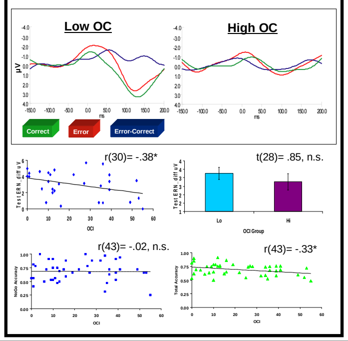
Study I: Investigation

PL Task: ↑ OC Predicts ↓ ERN



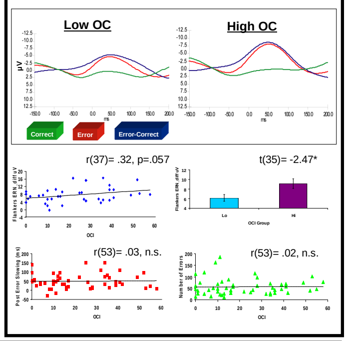
Study II: Replication

PL Task: ↑ OC Predicts ↓ ERN

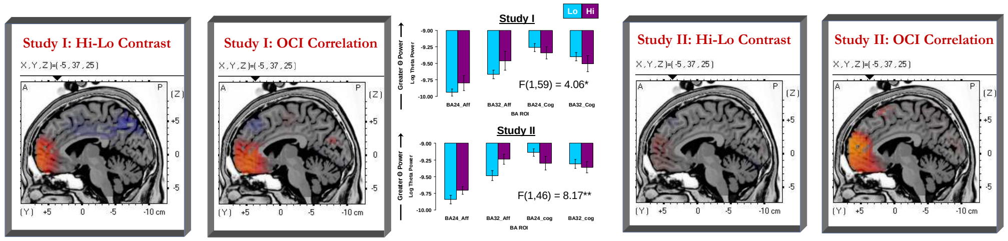


Study II: Extension

Flankers: ↑ OC Predicts ↑ ERN

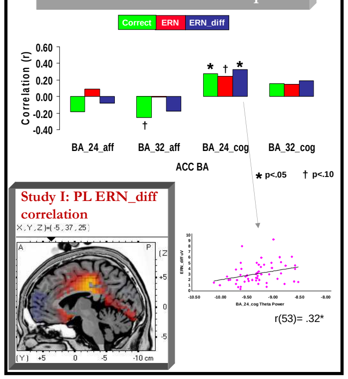


Resting Theta Power Differs As A Function of High OC Score: ↑ rACC Θ, ↓ dACC Θ

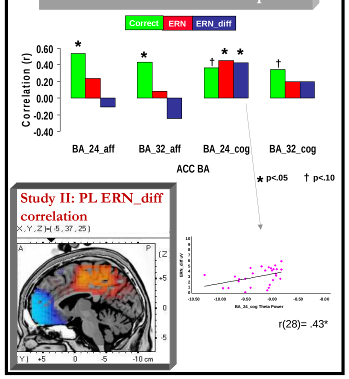


Does ACC Theta Power Predict ERN / OC Task Dissociation?

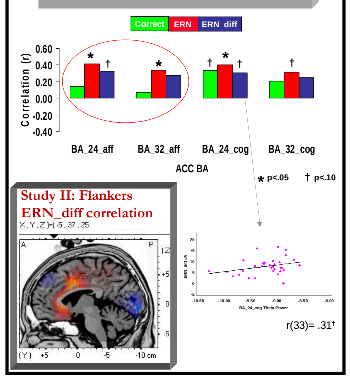
dACC Predicts PL ERN Amplitude



dACC Predicts PL ERN Amplitude

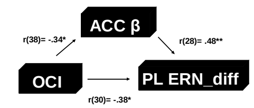


r/dACC Predict Flankers ERN



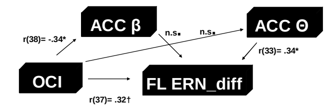
Could ACC Θ Be A Mediator?

❖ Given the differential influence of ACC region on the PL ERN, individual slopes (β) in ACC power (BA_24_aff, BA_32_aff, BA_32_cog, BA_24_cog) were computed to test for a mediating effect between OCI score and ERN amplitude



❖ No effect for mediation has been found with this sample size.

❖ Given the similar influence of ACC region on the Flanker ERN, total ACC power (BA_24_aff, BA_32_aff, BA_32_cog, BA_24_cog) was computed to test for a mediating effect between OCI score and ERN amplitude



❖ Given the lack of correlation between: **OCI → ACC Θ** or **ACC β → Flankers ERN_diff**, mediation may not be implicated in this case.

Conclusion

❖ A task dissociation was found in ERN amplitudes as a function of OC status, where OC symptoms predicted a lower ERN during a probabilistic learning task and a higher ERN during a Flankers task. No major behavioral effects were found.

❖ Given that the OC symptoms predicted a dissociation in relative resting ACC activity in the theta band ("hotter" rostral ACC, "cooler" dorsal ACC), these areas were hypothesized to contribute differential variance towards the ERN in different tasks.

❖ Although statistical tests of mediation were either non-significant (PL task) or not conceptually supported (Flankers task), future analyses may be able to address these issues.

Future Directions

❖ sLORETA source localization of the task-dependent PL and Flankers ERNs may: 1) provide more sensitive tests of the neural systems underlying ERN generation, and 2) reveal tonic vs. phasic activity differences in the ACC as a function of OC symptoms.

❖ Given the resting differences in OFC / VMPFC areas, other tasks which do not involve the intake of information or monitoring of performance may be more sensitive tests of altered neural systems in OCD. Preliminary evidence from Study II implicates reversal learning to be specifically compromised as a function of OC symptom score.

Foa et al., 2002, Psychological Assessment 14(4): 485-496
Frank et al., 2004, Science 306(5703): 1940-1943
Frank et al., 2006, Neuron 47: 495-501
Frank et al., 2007, CABN 7: 297-308
Pizzagalli et al. ,2006, Human Brain Mapping 27: 185-201

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Handouts available: www.psychofizz.org / Contact: jimcav@email.arizona.edu