Role of prefrontal cortex and lateral temporal lobe in healthy and anxious/depressed mental states during the performance of a cognitive control task

Aniruddha Shekara (medical student), BE[1], Angelique Paulk, PhD[2], Sydney Cash, MD, PHD[3], Alik Widge, MD, PhD[3], John Sheehy, MD[1], Ishita Basu, PhD[1] (PI)

[1]University of Cincinnati, Cincinnati, OH; [2]Massachusetts General Hospital, Boston, MA; [3]University of Minnesota, Minneapolis, MN

University of CINCINNATI

Background

- Neuropsychiatric disorders are the foremost cause of disability in the United States[1], and understanding the brain circuitry underlying functional deficits is critical for developing targeted neuromodulation therapeutics
- Cognitive control is often compromised across mood and anxiety disorders and can be estimated with an interference task where subjects must suppress a natural response to overcome response conflict[2].
- Conflict evokes robust electrophysiologic signatures in frontal regions[3-4], however, we do not know much about how anxious/depressed (A/D) mental states modulate these circuits and rhythms.
- The objective of this explorative study is to determine the neural signatures of prefrontal cortex (PFC), anterior cingulate cortex (ACC) and lateral temporal lobe (LTL) modulating cognitive control in healthy and A/D states.

Methods

- We recorded intracranial EEG in frontotemporal regions of 16 human subjects (A/D = 6, healthy control = 10) with intractable epilepsy undergoing invasive monitoring while performing a multi-source interference task (MSIT).
- We estimated power in theta (4-8 Hz), alpha (8-15 Hz), beta (13-30 Hz), gamma (30-55 Hz) and high gamma (65-110 Hz) frequency bands.
- For each frequency band and brain region of interest, we fit a generalized linear mixed effects model (GLME):

Response ~ Conflict + State + (1|Subject)

- We observed temporal differences in PFC and LTL spectrograms of healthy and A/D states, and fit subsequent GLMEs:

*Response ~ Conflict + State +Time + State*Time + (1|Subject)*

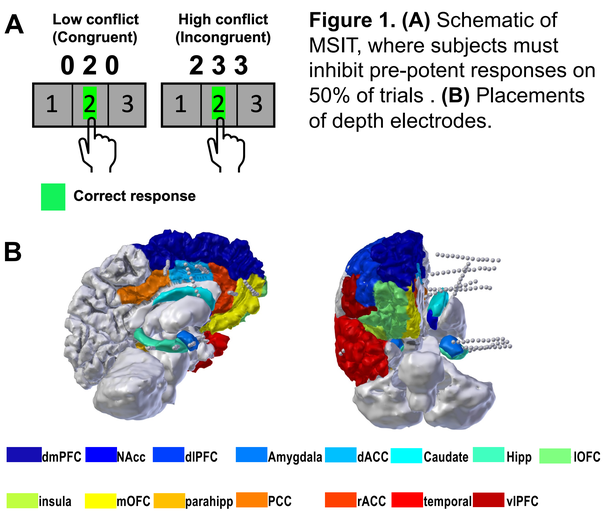

Figure 1. (A) Schematic of MSIT, where subjects must inhibit pre-potent responses on 50% of trials . **(B)** Placements of depth electrodes.

Results

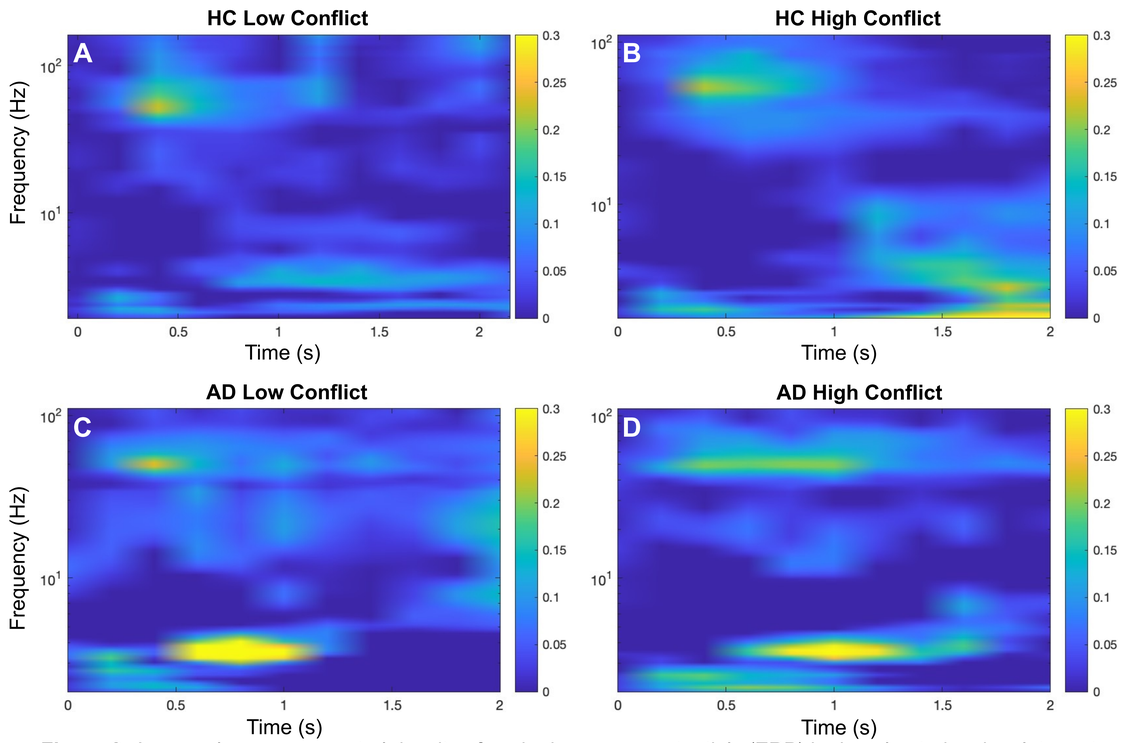

Figure 2. Average log power spectral density of evoked response potentials (ERP) in dorsal anterior cingulate cortex (dACC) of healthy controls **(A, B)** and A/D **(C, D)** subjects during low and high-conflict trials.

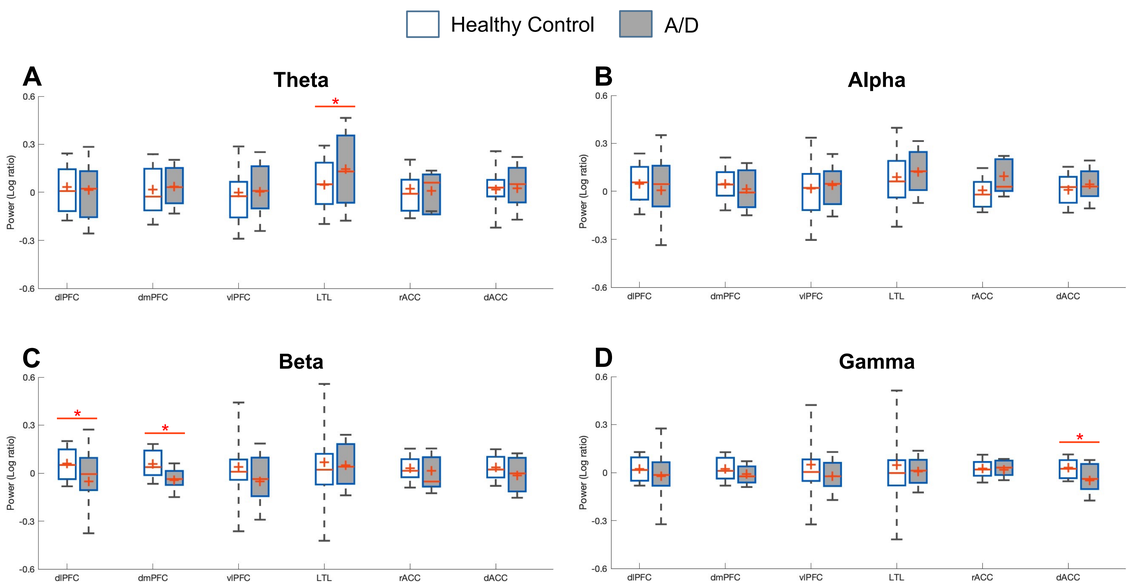

Figure 3. Log power ratio between low and high conflict trials of healthy control and A/D subjects in Theta **(A)**, Alpha **(B)**, Beta **(C)**, and Gamma **(D)** frequency bands. + represents mean, * represents p < 0.01.

GLME Results

Region	Frequency Band	Predictor	β	p
dlPFC	Theta	Conflict	0.022	0.002
dmPFC	Theta	Conflict	0.038	0.002
dmPFC	Alpha	Conflict	0.041	<0.001
dmPFC	Beta	Conflict	0.020	0.043
LTL	Theta	Conflict	0.043	<0.001
dACC	Alpha	Conflict	0.030	0.014
dACC	Beta	State	-0.091	<0.001

Table 1. Significant predictors of Log power in GLME with Conflict (high, low) and State (Healthy Control or A/D) predictors.

Region	Frequency Band	Predictor	β	p
dlPFC	Theta	State x Time2	-0.137	<0.001
dlPFC	Theta	State x Time3	-0.193	<0.001
dmPFC	Alpha	State x Time2	-0.093	<0.001
dmPFC	Alpha	State x Time3	-0.128	<0.001
LTL	Theta	State x Time2	-0.045	<0.001
LTL	Theta	State x Time3	-0.047	<0.001
dACC	Theta	State x Time2	-0.164	<0.001
dACC	Theta	State x Time3	-0.178	<0.001
dACC	Alpha	State x Time2	-0.239	<0.001
dACC	Alpha	State x Time3	-0.231	<0.001

Table 2. Significant State*Time interactions predictive of Log power in GLME with Conflict (Low, High), State (Healthy Control, A/D), and Time (Time1 = 0.5-1s, Time2 = 1-1.5s, Time3 = 1.5-2s).

Conclusions

- A/D states modulate oscillations in PFC and LTL regions during conflict processing
- Our results demonstrate roles of PFC and LTL conflict encoding independent of mental state.
- A/D state influences temporal features of PFC and LTL response
- Further exploration of time-dependent effects of mental state on conflict-evoked oscillations is necessary to elucidate mechanisms of cognitive processing in the PFC-LTL network in healthy and A/D states

Acknowledgements

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