

San Francisco

Modulation of network dynamics associated with symptom state in treatment-resistant depression

NIH Blueprint for Neuroscience Research

Subject B

Subject E

Stim ON Subject E



Subject C

Personalized

biomarkers

dentified across all

participants

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BACKGROUND

The variability and heterogeneity of depressive symptoms and their response to DBS can make treatment challenging. Identifying dynamic neurophysiological biomarkers is key to understanding the neural basis of depression and enabling adaptive, personalized DBS.

METHODS Select singular ROI with Symptom severity (VAS) best decoding performance Decode Regularized regression model VAS ratings optimized Select multiple ROIs with collectively best decoding performance Electrode placement for iEEG IOFC mOFC Accumbens Amygdala Aim 1: Identify neural biomarker VC/VS (not shown) site of psychiatric symptoms Summary of personalized targets for stimulation and sensing in closed-loop DBS Aim 2: Symptom ratings (VAS, HAMD, MADRS) Track dynamic encoding of behavioral symptoms with neural recordings Implantable sensing and Longitudinal Intracranial recordings using RNS

Days

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RESULTS: AIM 1 Subject A HC & SGC Subject D Subject A Subject B Subject C Subject D RESULTS: AIM 2 Stim ON Subject C Subject D R-SGC1-2 (bipolar re-referenced channel) All channels L-VC 3-4 (bipolar re-referenced channel) All channels

Symptoms improved with closed-loop DBS (A,E,I). tSNE of neural recordings showed clustering based on symptom state (B,F,j). Spectral power was computed across longitudinal recordings, followed by PCA and HMM modeling with permutation testing to identify symptom-related neural states. Significant state differences were found in Subject C (states 1 vs. 2, p<0.01) and Subject D (states 1 vs. 4, p<0.001). This approach revealed dynamic neural state transitions aligned with symptom fluctuations, with state-dependent shifts in feature importance (C,G,L), suggesting that symptom encoding evolves over time. Anatomical specificity was evident, as not all channels tracked symptom changes (B,F). In Subject E, neurophysiological changes aligned more with energy than depression (J).

SUMMARY

Days since Surgery (Smoothed)

L-VC1-2 (bipolar re-referenced channel)

Our findings indicate a longitiudinal shift in neural encoding osf symptoms. Ongoing work using tractography and unsupervised machine learning may highlight a common, distributed network that can be leveraged for closed-loop across subjects.

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