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

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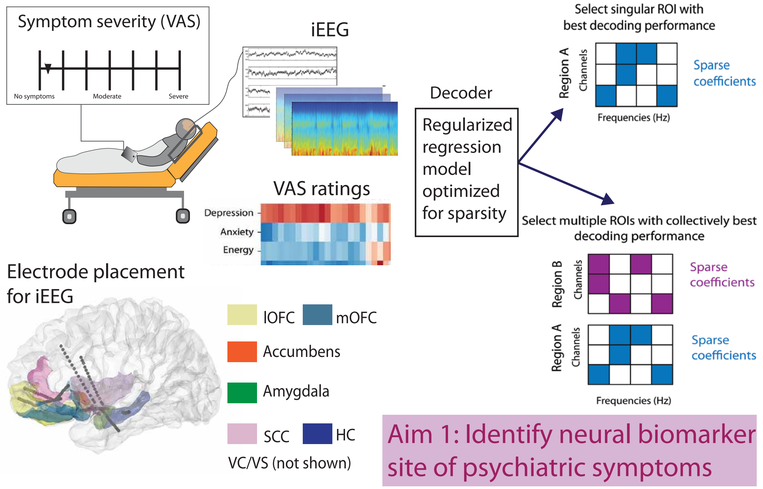
BACKGROUND

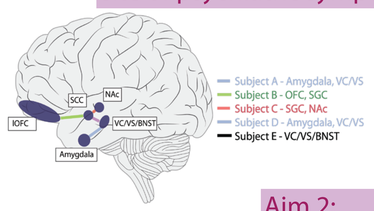
The variability and heterogeneity of depressive symptoms and their response to DBS can make treatment challenging. Identifying dynamic neurophysiological biomarkers is key to understanding the neural basis of depression and enabling adaptive, personalized DBS.

METHODS



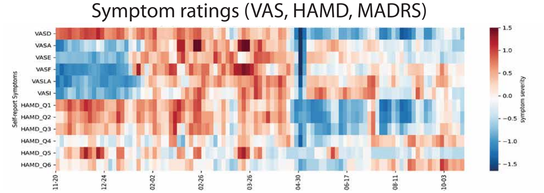
Aim 1: Identify neural biomarker site of psychiatric symptoms

Summary of personalized targets for stimulation and sensing in closed-loop DBS

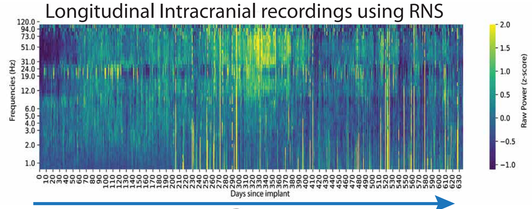


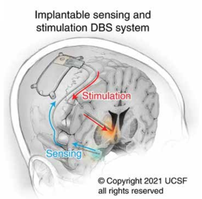
Aim 2: Track dynamic encoding of behavioral symptoms with neural recordings

Symptom ratings (VAS, HAMD, MADRS)



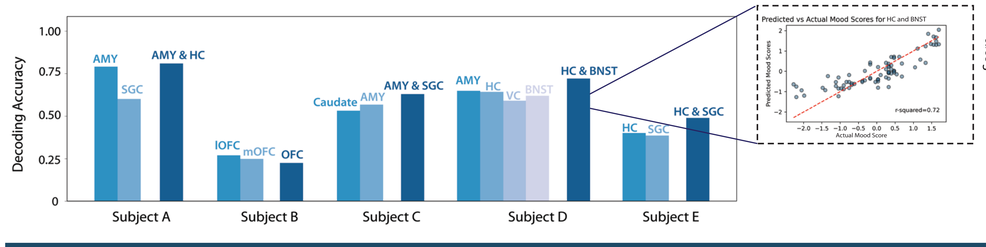
Longitudinal Intracranial recordings using RNS

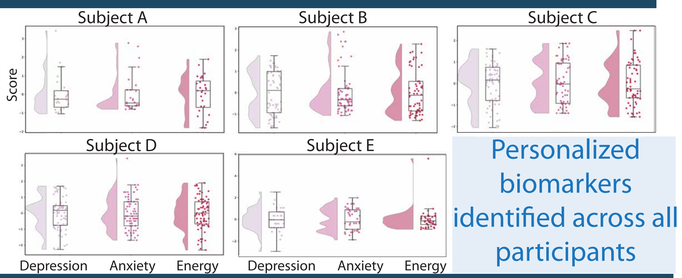




Scangos, et al. 2020

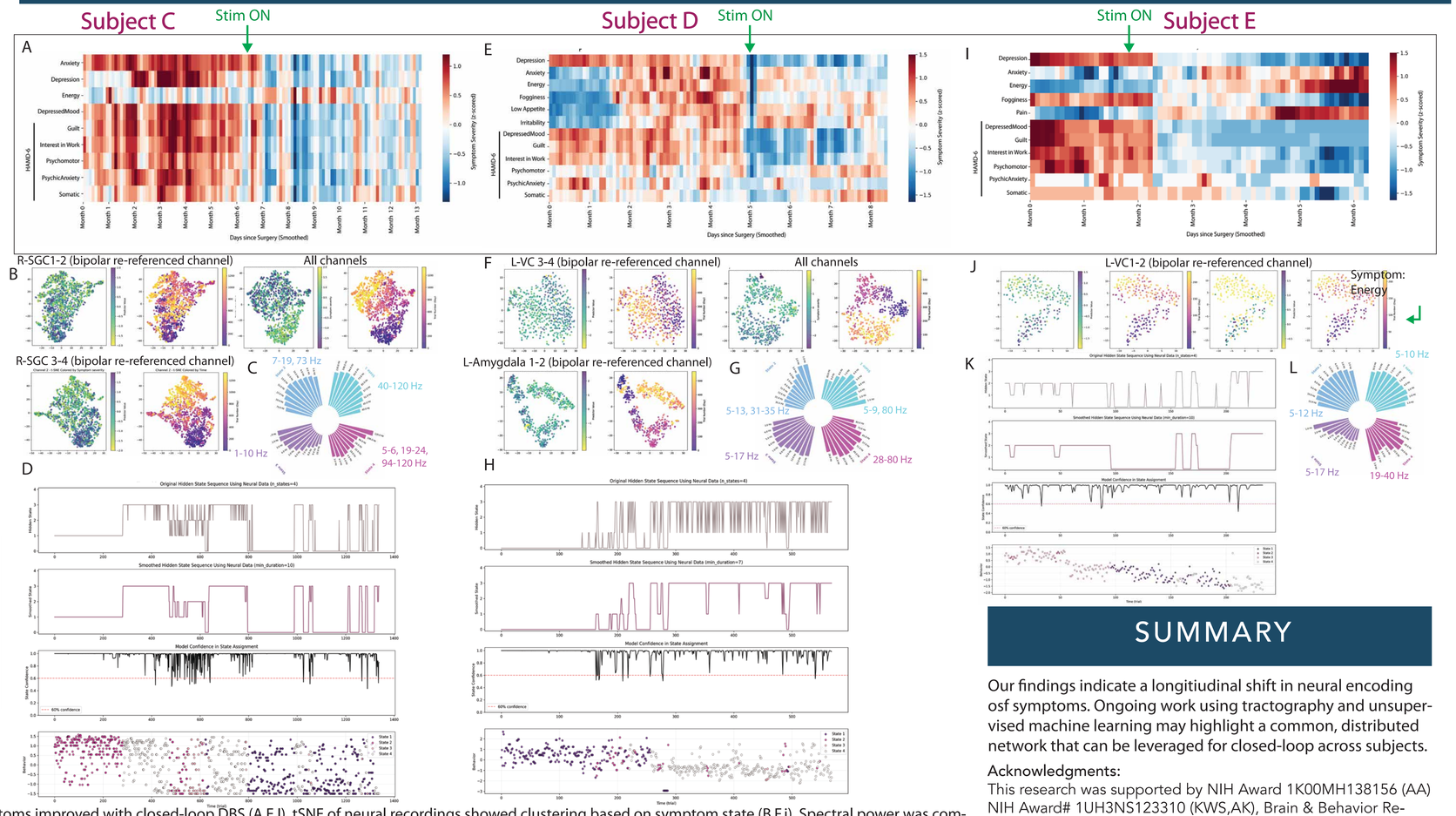
RESULTS: AIM 1





Personalized biomarkers identified across all participants

RESULTS: AIM 2



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

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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