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Shared Cortical Language Networks With Convergent Hierarchical Network Dynamics for Lexicosemantic Processing in Comprehension and Naming

Kathryn Snyder; Kiefer Forseth; Oscar Woolnough, PhD; Elliot Murphy; Gregory Hickok; Nitin Tandon, MD

INTRODUCTION: Theoretical models suggest that spoken and written language engage a shared lexicosemantic processing network in perception and production, yet convergent neural mechanisms are unclear.

METHODS: 65 ECoG patients completed auditory (AN) and orthographic (ON) naming. We analyzed gamma activity (70-115Hz) with mixed-effects multilevel analyses to identify the lexicosemantic processing network during comprehension and naming. We mapped network dynamics using autoregressive hidden Markov models (ARHMM). We used direct cortical stimulation (DCS) to attribute causality to critical nodes.

RESULTS: At speech onset, activation of superior temporal gyrus (pSTG) was followed by superior temporal sulcus (pSTS) and middle temporal gyrus (pMTG). For each written word, visual cortex activity was followed by activation of lexical (fusiform gyrus, Fus; pSTS; pMTG) and phonological (intraparietal sulcus, IPS; pSTG) reading routes. Both modalities engaged posterolateral temporal cortex (pLTC) for comprehension, and activity was correlated with phrasal composition (p<0.01) implicating it in compositional semantics. The last word activated a shared network (pLTC; Fus; IPS; pars triangularis, pTr) for naming. ARHMM isolated 5 states for AN and 6 for ON with 3 convergent states. The first convergent state occurring at stimulus offset was characterized by outflow from pLTC, Fus, IPS, and pTr, and state duration was correlated with reaction time (p<0.001) implicating it in lexical access. Lastly, during stimulus presentation, DCS of Heschl's gyrus disrupted listening, while DCS of planum temporale and pLTC disrupted listening and reading. At stimulus offset, DCS of pLTC, Fus, IPS, and pTr disrupted AN and ON.

CONCLUSIONS: Juxtaposing network dynamics of multimodal lexicosemantic processing in speech perception and production informs our understanding of specialized and shared language networks providing new insights to facilitate designs of neural prosthetics for language disorders.

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Stimulation Pattern-Specific Modulation of Epileptiform Biomarkers During Short-Term Stimulation of the Anterior Nucleus of the Thalamus in Medication Refractory Epilepsy Patients

Bobby Mohan; Teryn Johnson; Behrang Fazli; Amir Mbonde; Chris Harris; Amy Crepeau; Katherine Noe; Joseph Drazkowski; Matthew Hoerth; Cornelia Drees, MD;

Richard S. Zimmerman, MD; Justin Cramer; Ichiro Ikuta; Kai Joshua Miller, PhD, MD, PhD; Gregory A. Worrell; Nuri Ince; Jonathon J. Parker, MD, PhD INTRODUCTION: Anterior thalamic (ANT) deep brain stimulation (DBS) can reduce seizure frequency by 75% in patients with medication-resistant focal epilepsy. However, a third of patients experience <50% seizure reduction and 10% no measurable reduction. Accurate mammillothalamic tract (MTT) targeting does not explain most observed seizure suppression variability. We suggest uniform application of high frequency (145 Hz) regularly spaced stimulation pulses may not be effective for all patients. A systematic investigation of alternative patterns, including irregularly spaced stimulation pulses (hypothesized to weaken hyperexcitability) is needed.

METHODS: Patients were consented and underwent a research thalamic stimulation protocol after completion of seizure mapping and anti-epileptic medication resumption. Bipolar continuous ANT rhythmic (RS) or non-rhythmic stimulation (NRS) was delivered spanning the two contacts closest to the MTT during 18-minute blocks. Rates of high frequency oscillations (HFOs) and epileptic spikes were detected, quantified, and compared using the KS test (p-value <0.05).

RESULTS: ANT stimulation was performed on three subjects (n=2 right ANT, n=1 left ANT). Rhythmic stimulation modulated HFO rates in 4.8%, 1.5%, and 1.5% of channels and epileptic spike rate in 68%, 49%, and 2% of channels across subjects, respectively. Non rhythmic stimulation modulated HFO rates in 2.4%, 2.6%, and 2.5% of channels, and modified epileptic spike rate in 45% and 6% of channels in subjects 2 and 3, respectively. In a seizure onset zone (SOZ) specific analysis, we found differential effects of RS and NRS on HFO and spiking rates.

CONCLUSIONS: Epileptiform biomarkers are modulated in a significant fashion by short-term thalamic stimulation. Ongoing studies will explore an expanded library of non-rhythmic stimulation patterns to identify those with optimal epileptiform activity suppression. Future clinical trials of chronic thalamic stimulation directed by short-term trial stimulation are needed to validate this approach.

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Association Between Intraoperative Local Field Potentials, Lead Location, and Motor Outcomes in Patients Undergoing Deep Brain Stimulation of the Subthalamic Nucleus for Parkinson's Disease

Kalman Katlowitz, MD; Luciano Branco; Michelle Case; Nuri Ince; Ashwin Viswanathan, MD

INTRODUCTION: Local Field Potential (LFP) biomarkers of disease states in Deep Brain Stimulation (DBS) can help guide patient care. However, even small variations in lead location can significantly affect signal content and therapuetic index.

METHODS: 10 patients with Parkinsons Disease were implanted with bilateral Subthalamic Nucleus (STN) leads and awake intraoperative resting state LFP was captured. Lead locations and volume of neural activation (VNA) were defined using the SureTune platform. UPDRS Part III scores were recorded preoperative and at 6 months post operatively. Beta (14-32 Hz) and High Frequency Oscillation (HFO, 200-400Hz) power was defined for each electrode as the weights to the main projected source of Beta and HFO oscillations.

RESULTS: There was an average of 54% reduction in the UPDRS score. The final UPDRS score was significantly anti-corelated with percent overlap of the VNA for each clinically selected electrode with the

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STN (p=0.008 F-test of linear model) but not the Zona Incerta (ZI) (p=0.9). Similarly, Beta and HFO power were significantly higher for electrodes overlapping with the STN (p=0.004 and 0.02, respectively) but not ZI (p>0.4 for both). The UPDRS response corresponded to the maximum amplitude of the Beta power source (p=0.001), but not HFO power (p=0.1). Interestingly, the strength of the pathological cross frequency coupling (CFC) between Beta and HFO oscillations was related to electrode position within ZI (p<0.05 for both), but not STN (p>0.2 for both)

CONCLUSIONS: There is a strong correlation between electrode location, clinical outcomes, and clinically relevant signals. Beta and HFO power were localized to the STN but their CFC localized to the ZI. Focused programming strategies based on either imaging or LFP data can facilitate identification of the optimal therapeutic contacts.

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Network-Wide Morphological Dynamics Predict Functional Cognitive Performance

Zane Norville; Michelle Hedlund; Vivek Buch, MD

INTRODUCTION: Learning-related morphological changes in brain connectivity remain poorly understood. Network analysis techniques provide robust interpretation of high-dimensional neural data during skill acquisition. This insight may reveal novel anatomical and personalized targets for restoring performance in individuals with intellectual disabilities, who today possess sparse therapeutic offerings.

METHODS: Task-paired electrode data were collected from 23 subjects undergoing sEEG epilepsy evaluation. Each subject performed several trials of a temporal expectancy task paradigm in which reaction time was assessed following visual stimulus color-change. Subjects were categorized into "Learners" (n = 17; improved at the task) or "Non-Learners" (n = 6; did not improve) based on trial reaction time slopes. During analysis, each sEEG channel represented a node in a graph. Edge weights between each pair of channels were assigned with phase-locking value to form functional connectivity matrices, which were calculated in four frequency bands (alpha, beta, low-gamma, high-gamma). Changes in modularity (a network-wide measure of community segregation) and efficiency (a measure of cross-network navigation ease) over a task session were compared between Learners and Non-Learners for periods prior to the presentation stimulus (pre-trial), go-cue, and response.

RESULTS: Learners demonstrated increased high-gamma modularity in the pre-trial period (p < 0.05), increased alpha efficiency in the gocue period (p < 0.05), and increased alpha and high-gamma modularity in the response period (p < 0.05) relative to Non-Learners.

CONCLUSIONS: Dynamic learning was associated with increases in modular community segregation and brain-wide functional efficiency over the duration of a cognitive task. These network analytical findings demonstrate the potential impact of graph network decoding on understanding dynamic learning and could lead to novel therapeutic control signals for future restoration strategies.

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Distinctive Spatial Distributions of Motor Cortex Oscillatory Dynamics After Subthalamic Nucleus Deep Brain Stimulation in Parkinson's Disease

Min Jae Kim; Qasim Qureshi; Pierce Hunter Davis; Alex Vaz; Elton Ho; Yoon Woo Byun; Benjamin Rapoport, MD, PhD; Bijan Pesaran; Iahn Cajigas, MD

INTRODUCTION: Subthalamic Nucleus Deep Brain Stimulation (STN-DBS) in Parkinson's Disease (PD) involves disruption of motor cortex-STN synchrony of beta-band oscillations. However, precise neural substrates within the motor cortex where such oscillatory fluctuations and their interactions occur are still unknown. Understanding spatialtemporal dynamics shared across cortex and basal ganglia would be crucial for improving DBS surgical targeting strategies.

METHODS: In a PD patient undergoing STN-DBS electrode implantation, the right STN was stimulated with different amplitudes, and respective volumes of tissue activation (VTA) were modeled. The degree of motor STN subregion stimulated (%) from VTA was calculated. In parallel, 1024-contact electrocorticography (ECoG) array was placed on the ipsilateral M1 during STN stimulation. Relative to DBS-OFF condition, changes in ECoG spectral power across five canonical frequency bands (alpha, low-beta, high-beta, gamma) were evaluated. Finally, changes in ECoG power and the degree of motor STN stimulated were correlated, and their correlation-coefficient was mapped across the array channels.

RESULTS: With more motor STN subregion stimulated, the mean power in M1 gamma-band oscillations increased (r=0.61,p=0.04), and a nonsignificant trend of decreased beta-band oscillations was observed (r=0.19, p=0.56 for low beta, r=-0.29, p=0.36 for high beta). Across the entire cortical array, increased STN stimulation was associated with decreased low beta-band power in the medial portion of M1, but in the lateral portion of M1 for high beta-band power. A global increase in gamma-band power was observed across the entire medial-lateral axis of M1.

CONCLUSIONS: Our findings suggest that STN-DBS yields distinctive spatial dynamics of low and high beta-band power. These fluctuations are inverted and varied across the medial-lateral axis of M1. Parcellating the cortical response to STN-DBS can elucidate the precise mechanisms of STN-DBS to augment its clinical efficacy.

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The Past, Present, and Future of Image Guided Technology: A Patent Bibliometric Analysis

Maaria Chaudhry; Nabiha Quadri, MD; Philippe Mercier; Tobias A Mattei

INTRODUCTION: The advent of 3D neuronavigation technologies in the late 1990s changed the practice of modern neurosurgery by allowing surgeons to plan and perform image-guided procedures with reliable intraoperative accuracy.

METHODS: The Lens, a publicly available digital database with access to peer-reviewed articles and patent technologies, was used to perform a bibliometric analysis. Specific criteria including search terms for image guided neurosurgery, neuronavigation, brain and spine were