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Dynamic System State Modeling for iEEG Signals Using Weighted Least Squares
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Objective: We investigate the effectiveness of linear time-invariant (LTI) models in characterizing the dynamic behavior of multichannel intracranial EEG (iEEG) data in epilepsy patients and evaluate optimization strategies for robust modeling. Background: Epilepsy is a neurological disease that affects nearly 1% of the world's population. The disease is marked by recurrent and unprovoked seizures, which are transient events of irregular neural activity that often cause motor and cognitive impairments and occasionally death. Modeling and understanding epileptic networks are crucial for seizure onset zone localization and neuromodulation therapies. The ability to reliably reconstruct brain signals without the need for extensive recording is necessary. Dynamic LTI state space models, x[t+1] = Ax[t], where x[t] is a vector of recorded iEEG signals, could reliably reconstruct short-term brain activity given only initial state conditions. The classical method to estimate the model's transition matrix A is by using the least squares approach. Unfortunately, this method is sensitive to outliers and initial conditions, and the signal reconstruction quality significantly degrades with time. Therefore, we investigated whether a weighted least squares approach could reduce the effect of outliers and initial conditions on the reconstructed signal. Methods: We constructed LTI models and estimated A matrices to characterize the dynamics of the brain data in epilepsy patients using ordinary and weighted least squares methods in sliding time windows of iEEG data. To assess the effectiveness of each method in capturing the underlying dynamics, the state vector x[t] was reconstructed using the initial iEEG state conditions x[0] and the estimated A matrix. The reconstructed state vectors for the ordinary and weighted least squares models were computed, and the root mean square error (RMSE) between the original iEEG signal and each reconstruction was then calculated to compare the accuracy of the models. The weights were modified piecewise linearly to produce minimal error. Also, outliers were identified, and their weight was reduced. Results: Experiments with three different weight profiles show improvement in root mean squared error between the ground truth signals and the reconstructed signals. Given the automated detection of outliers, their effect on the reconstruction could be eliminated by using appropriate weights. Conclusion: Using the weighted least squares method to estimate dynamical brain signal properties allows more reliable reconstruction of brain signals in longer time windows. Optimization of weight parameters might significantly reduce the effects of outliers and initial conditions on the model estimation.

The Art of Brain Signals: Unlocking Real-World Insights Through Advanced EEG Analysis
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The analysis of multimodal data stands at the forefront of uncovering the complexities of brain functions and enhancing neurorehabilitation techniques. This study introduces a pioneering methodology for the meticulous cleaning and processing of multimodal data, incorporating video, raw electroencephalography (EEG), electrooculography (EOG), and acceleration metrics, tailored to advance neurorehabilitation research and practice. Our comprehensive cleaning pipeline is designed to address the multifaceted nature of noise and artifacts inherent in neurological data. Initial stages involve a dual-review process—combining visual inspection and expert analysis—to identify noise-laden segments. Subsequent technical review, leveraging advanced data labeling and visualization tools, ensures the precise demarcation and removal of these segments. This is critical for maintaining the integrity of the data for further analysis. The artifact removal process is central to our methodology, encompassing three key stages: eye artifact removal, motion artifact removal, and the elimination of artifactual dipoles. Eye artifacts, predominantly originating from blinks and eye movements, are mitigated through a combination of robust re-referencing and bandpass filtering techniques. Motion artifacts, resulting from the subject's physical movements, are addressed using specialized motion artifact filtering methods. Lastly, the removal of artifactual dipoles, through dipole fitting and independent component analysis, is vital for isolating and excluding brain activity unrelated to the primary signals of interest. Beyond cleaning, our analysis extends to a suite of sophisticated techniques aimed at unraveling the intricacies of brain function. K-means clustering aids in identifying patterns within the cleaned data, while bispectrum analysis facilitates the examination of nonlinear interactions between brain signals and functional connectivity estimation are then employed to assess brain synchrony and the architecture of brain networks. These techniques collectively enable a deeper understanding of the brain's functional dynamics and its interaction within and across neural networks. The versatility and efficacy of our methodology have been demonstrated through its application in analyzing brain synchronization within diverse artistic and creative contexts, including music, acting, and dance. These applications not only serve to validate the approach but also highlight its potential to contribute significantly to various domains within neurorehabilitation and beyond. By offering a systematic and comprehensive approach to multimodal data cleaning and analysis, this study paves the way for advancing our understanding of brain function and improving outcomes in neurorehabilitation. The methodology holds promise for facilitating the development of targeted interventions and enhancing the efficacy of rehabilitation strategies, thereby contributing significantly to the fields of neuroengineering and BCIs.

Neural circuits underlying estrous cycle regulation of state-dependent emotional memory
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Women are twice as likely as men to be diagnosed with post-traumatic stress disorder (PTSD), and among people that are diagnosed, women report more severe and longer-lasting symptom profiles. These gender differences are partially explained by cycling ovarian hormones across the menstrual cycle, as low levels of ovarian hormones are associated with worsened PTSD symptoms. Here, we tested the hypothesis that ovarian hormone fluctuations across the reproductive cycle contribute to state-dependent learning, a phenomenon in which memory encoding and recall occur most efficiently during the same physiological state. Using cued threat conditioning, the most well-established model of emotional memory, we compared male mice to female mice that underwent training and retrieval under the same or opposite ovarian hormone state. We focused on high (proestrus, P) and low (diestrus, D) hormone states for a total of 5 experimental groups: male, P P, P D, D D, D P. Cued memory recall was indistinguishable between males and females that were both trained and tested in P. Remarkably, all other females exhibited increased cued memory recall. Next, we investigated brain regions involved in these hormonal state-dependent effects on memory, using c-fos expression as a marker of neural activation following cued threat conditioning in males and females in P or D. Analysis of 114 brain regions revealed hormone state-dependent activation in a limited number of regions, including several known to be involved in

threat memory processes such as the lateral part of the central amygdala, zona inserta, nucleus reuniens, periaqueductal gray, and motor portion of the superior colliculus. The most prominent differences, however, were observed in the robust engagement of the rostral part of the lateral septum (LS)—a region not historically considered necessary for cued threat memory, but one that is notably sensitive to steroid hormones—specifically in P females. We next sought to identify neuronal populations within the LS involved in these effects. We performed single nucleus sequencing of the LS in na ve males and na ve and trained proestrus females. Results indicate 52 transcriptionally distinct cellular clusters. Of these, only two neuronal clusters exhibited immediate early gene activation in response to cued threat conditioning: one population expressing both somatostatin and neurotensin, and the other population expressing corticotropin-releasing hormone receptor 2. Ongoing work will anatomically validate these findings with fluorescent in situ hybridization. Future directions will investigate the role of these specific LS neuron populations in regulating state-dependent emotional memory and examine the impacts of hormone states on neural networks engaged during threat memory retrieval. Together, findings demonstrate strong influences of ovarian hormone states in modulating threat memory processes and suggest novel female-specific emotional memory circuitry.

Left Inferior Frontal Gyrus and Superior Temporal Sulcus Activity Underlies Self-Paced Reading Pauses at Phrase Boundaries
Bryant Barrentine; Christophe Smith; Nicole Bentley, M.D.; Harrison Walker, M.D.; Matthew J. Nelson, Ph.D.

Self-paced reading tasks are a common methodology for studying how patients dynamically process sentences using the response time as a stand in for processing effort (King Just, 1991). Pairing this technique with intracranial neural recordings, which to our knowledge has never before been done, is a potentially powerful way to understand the neural processes underlying that processing effort. In this study, we look at the relationship between self-paced reading single word response time during a sentence and intracranial neural activity of the left-hemisphere language network measured with extraoperative stereoelectroencephalography (sEEG) in epilepsy patients. Patient participants performed a one word-at-a-time self-paced reading task with three sentence types: object-relative sentences (“The cat that the dog chased was brown”), subject-relative sentences (“The cat that chased the dog was brown”), and control sentences (“The brown cat chased the dog”). Participants showed a marked peak in per-word response times at the phrase boundary of object-relative sentences that correlated with neural activity in the left inferior frontal gyrus (IFG) and the left superior temporal sulcus (STS). Specifically, trials with faster phrase boundary word RTs saw higher IFG activity preceding the phrase boundary word and less IFG activity after the phrase boundary word, suggesting that anticipatory IFG activity led to the shorter phrase boundary RT. Trials with slower phrase boundary word RTs saw decreased IFG activity before the word onset and increased activity after the word onset during the increased pause at that word, suggesting that what underlies the pause is the need for the processes in this area to “catch up” on trials lacking anticipatory activity. Activity in the left STS prior to phrase boundary word onset did not correlate with phrase boundary word RT, but STS activity after the phrase boundary word onset did positively correlate with phrase boundary word RT. This suggests that the phrase boundary word RT does not depend on anticipatory activity in the STS, but that elevated STS activity after the phrase boundary word does underlie “catching up” during slow phrase boundary word RTs along with IFG activity. These results provide novel details about the processes happening at phrase boundaries during sentence reading, and neural evidence of the interactions between language and domain general cognitive systems underlying pauses during self-paced reading.

Unilateral subthalamic nucleus deep brain stimulation effects on self-reported physical function in Parkinson’s disease
Sarah A. Brinkerhoff, PhD, Frank G. Robinson, Victor A Del Bene, PhD, Roy C. Martin, PhD, Christopher L. Gonzalez, MS, J. Nicole Bentley, MD, Barton L. Guthrie, MD, Harrison C. Walker, MD

BACKGROUND: Parkinson’s disease (PD) is a neurodegenerative disease characterized by motor symptoms such as bradykinesia, tremor, rigidity, balance impairment, and dexterity loss, alongside nonmotor symptoms including cognitive impairment, fatigue, pain, and sleep disturbance. Deep brain

stimulation (DBS) improves motor and some non-motor symptoms related to PD. Patient-perceived experience can be assessed in a cost- and time-effective manner and is relatively neglected in DBS studies. METHODS: We studied 30 PD patients undergoing unilateral subthalamic nucleus (STN) DBS. Patients completed validated self-reported inventories (PROMIS and NEURO- OL) assessing symptoms before surgery and at 2-, 4-, and 6-month post-operative visits. Linear mixed effects regressions, accounting for baseline scores and individual variability, assessed the impact of unilateral STN DBS on overall physical function, upper extremity function, lower extremity function, cognition, fatigue, pain interference, and sleep disturbance. Additional linear mixed effects regressions determined if MDS-UPDRS part III scores predicted outcomes across all time points. RESULTS: Patients reported improvements in overall physical function, upper extremity function, cognitive function, fatigue, and sleep disturbance following unilateral STN DBS. Improvements in fatigue lasted up to 2 months after surgery for DBS (2 months = 4.4 T-score units). Improvements from baseline in self-reported overall physical function (2 months = 2.2 T-score units, 4 months = 2.2 T-score units), upper extremity function (2 months = 3.6 T-score units, 4 months = 2.8 T-score units), and sleep disturbance (2 months = 3.9 T-score units, 4 months = 3.4 T-score units) lasted up to 4 months after surgery for DBS. Post-operative lower extremity function and pain did not improve significantly, although most patients did not have significant gait deficits prior to surgery. MDS-UPDRS III scores were associated with self-reported upper extremity function (-1.5 upper extremity function T-score units per 10-unit increase in MDS-UPDRS III) and cognitive function (-1.3 cognitive extremity function T-score units per 10-unit increase in MDS-UPDRS III) but did not correlate with other outcomes. CONCLUSIONS: PD patients reported improvement in motor function after unilateral STN DBS, aligning with the procedure's targeted outcomes. The PROMIS and NEURO- OL inventories exhibited effectiveness in capturing motor changes, particularly in upper extremity function. Additionally, self-reported improvements in fatigue and sleep disturbance concurred with prior findings. This study supports the utility of PROMIS and NEURO- oL inventories as efficient assessments for individuals with PD, offering comprehensive insights into patient-reported outcomes both before and after interventions. The computer adaptive nature of these tests, coupled with their brief completion time (less than 15 minutes each), underscores their practical value in evaluating diverse aspects of the PD patient experience.

Directional and ring unilateral subthalamic nucleus deep brain stimulation effects on mood and quality of life in Parkinson's disease

Frank Robinson; Sarah A. Brinkerhoff, PhD; Victor A Del Bene, PhD; Roy C. Martin, PhD; Christopher L. Gonzalez, MS; J. Nicole Bentley, MD; Barton L. Guthrie, MD; Harrison C. Walker, MD

BACKGROUND: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms that impact cognition, sleep, anxiety, and depression. Deep brain stimulation (DBS) is a neuromodulation therapy that targets function in brain circuits that primarily serve movement. Some work however suggests that subthalamic nucleus (STN) DBS can improve aspects of non-motor function, as well. Prior studies typically use omnidirectional (ring) configurations for stimulation rather than the greater spatial precision of newer segmented lead architectures. Here we contrast the effects of ring and directional stimulation on patient-reported mood and quality of life following unilateral STN DBS for PD. METHODS: We used a randomized, double-blind crossover design with thirty participants undergoing unilateral STN DBS for PD. Stimulation settings were optimized at 2 and 4 months with either directional or ring stimulation in random order. Each participant completed self-reported inventories (PROMIS, Neuro- oL, PD 8), as well the Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) preoperatively, and at 2, 4, and 6 months postoperatively. Linear mixed effects regressions evaluated the effect of time on self-reported mood symptoms and social measures, accounting for pre-operative baseline scores and interindividual variability. Additional linear mixed effects regressions evaluated the effect of stimulation type (directional versus ring) on self-reported outcomes, accounting for interindividual variability. RESULTS: Self-reported qualify of life (PD 8), satisfaction in social roles and activities, and depression (PROMIS) all improved after unilateral STN DBS. There were no post-operative changes in depression (BDI), anxiety (BAI, PROMIS), communication, emotional / behavioral control, wellbeing, stigma, social participation, or overall mental health. Worse pre-operative symptoms and oL predicted larger improvements in every outcome measure except somatic symptoms of depression. There were no significant differences between ring and directional stimulation on any measure. CONCLUSIONS: Self-reported quality of life, mood, and satisfaction in social roles improved after unilateral STN DBS, and the

CONCLUSIONS: Self-reported quality of life, mood, and satisfaction in social roles improved after unilateral STN DBS, and the degree of improvement was predicted by the severity of pre-operative symptoms.

Time-Frequency Analysis of Spectral Responses to SPES to Localize the Epileptogenic Network
Helen E. Brinyark, Ben Cox, Joshua LaRocque, Erin Conrad, Rachel J. Smith

Resection or ablation of the seizure onset zone (SOZ) has been proven to reduce or eliminate seizures that are not controlled with medication in patients with epilepsy. However, a range of 20-70% of patients undergoing this invasive surgery do not become seizure free, and this is partly because no biomarker of the SOZ exists. Intracranial EEG recorded during single-pulse electrical stimulation (SPES) can be analyzed to localize the SOZ. It has been shown that cortico-cortical spectral responses (CCSRs) that are evoked during SPES hold promise for SOZ localization. In this preliminary study, we analyzed CCSRs in seven epilepsy patients across four frequency bands: theta (4-7 Hz), alpha (8-12 Hz), beta (13-30 Hz), low gamma (30-50 Hz). Intracranial EEG monitoring and SPES were performed on patients with drug-resistant epilepsy prior to surgical treatment. A short pulse was applied at 1 Hz to all adjacent pairs of electrode contacts, with 30 trials performed per pair. Convolution was performed using the MATLAB function cwt to perform a continuous Morse wavelet transform of each trial. The CCSR for each contact pair was calculated by squaring the absolute value of the average wavelet transform result and converted to decibels. A Gaussian CDF fit to the baseline distribution (450-150 ms before the stimulus) at each frequency was used to calculate p-values for each post-stimulus time-frequency power value at that frequency. P-values were corrected for multiple comparisons using the Benjamini-Hochberg procedure. For each contact pair, the number of significant power values during the N1 peak time (10-50 ms after the stimulus) and during the N2 peak time (50-250 ms after the stimulus) intervals were totaled for each frequency band and normalized by the number of time-frequency points within the time-frequency zone (TFZ). For each stimulus-response electrode pair, the significance value for each TFZ was compared to the significance value over the whole response (15-900 ms after the stimulus) for the electrode pair. The significance values for each electrode pair were recalculated by randomly shuffling significance values 500 times and taking the average. The proportion of the most responsive electrode pairs (top 0.1-10%) that contained clinician identified SOZ electrodes were calculated for the randomized and true significance values for each TFZ and the whole response. In 5 out of 7 patients, the proportion of most responsive electrodes that are SOZ is greater than random chance in the gamma-N2 TFZ and across the whole response. Our preliminary results suggest that contacts with significant spectral responses over the whole response correlate with the SOZ better than significant responses in any TFZ (AUC = 0.37). These findings corroborate the use of whole CCSRs as a candidate biomarker for the SOZ. In the future, we will expand our analysis to include more patients across multiple centers and compare the clinician identified SOZ with post-surgical outcome data. In conclusion, this preliminary analysis suggests that CCSRs can be used to improve SOZ localization and increase success rates for those seeking surgical treatment for epilepsy.

Characterizing the role of the paraventricular nucleus of the thalamus during outcome-based predictions
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The ability to learn associations between cues and future outcomes is critical for survival. As such, individuals learn which neutral stimuli (e.g., cues) lead to rewards (e.g., food) and which cues predict harm and should be avoided. This ability to add ‘meaning’ or incentive value to neutral stimuli is known as “incentive salience.” However, the neural mechanisms mediating these causal associations or incentive salience are poorly understood. Previous research from the lab has shown that the paraventricular nucleus of the thalamus is a brain region critical for motivated behaviors. Specifically, we have shown that PVT neurons can be classified into two major distinct subpopulations that diverge based on their genetic, connectional, and functional identity. These subpopulations can be differentiated by the presence or absence of the dopamine D2 receptor (D2R+). In addition, they play dissociable roles in motivated behavior. Particularly, PVT(D2R+) neurons were shown to increase their activity only when mice approached a maze zone associated with reward delivery. These increases in activity by PVT(D2R+) neurons were not observed either during regular locomotion across the maze or when mice were approaching a different zone in the maze that had not been associated with reward delivery. As such, these strongly suggest that PVT(D2R+)

neurons might play a critical role in the learned associations between environmental cues and their outcomes. To test this, we used bulk calcium imaging and fiber photometry to measure the activity of PVT(D2R+) neurons (using Drd2-Cre mice and Cre-dependent GCaMP6s) while hungry mice learned to perform a foraging-like reward task. In this task, mice need to learn through trial and error to run back and forth from one end of a linear maze, the trigger zone, to the opposite end of the maze, the reward zone, to obtain food rewards. We found that at the beginning of the training in the task, there were no significant changes in the activity of PVT(D2R+) neurons during the approach to the reward zone. However, as mice learned to associate the reward zone with the delivery of the reward, we observed a learning-dependent effect on the activity of these neurons. Furthermore, changing task contingencies, such as the type of outcome delivered or the relevant cues that signaled reward, also modulated PVT(D2R+) neurons. Altogether, these data highlight that PVT(D2R+) neurons play a critical role in learned associations to make outcome-based predictions by adding subjective value to neutral stimuli.

Meta-analysis on ketamine pharmacological induced neuromodulation to increased burst mode
Brad Caldwell

This meta-analysis explores a few notable publications to explore a correlation between (1) ketamine's downstream effects via HCN/T–channels which increase burst mode, and (2) reported segmentation of perceptual experience into discrete frames. Also postulates other pharmacological agents (NMDA–antagonists: alcohol, cannabis, sleep–deprivation; GABA–agonists: muscimol, barbiturates; kappa–opioid–agonist: ibogaine) as acting in a similar fashion.

Right Hemisphere White Matter Tractography is Predictive of Bilingual Status
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Prior literature has shown differences in white matter connectivity and executive functioning (EF) performance between monolinguals and bilinguals. (Abutalebi, 2016) However, the exact relationship between white matter connectivity and bilingualism and what structural adaptations might facilitate those differences in executive functioning remain elusive. (Pliatsikas, 2020). In this study, we attempted to examine the relationship between neuroanatomical differences in bilingualism and executive functioning based on a large-scale mono- and bilingual English-Spanish dataset. 3 Groups of 400 monolingual English, (MLE) 451 monolingual Spanish, (MLS) and 335 bilingual English-Spanish speakers (BES) (total n= 1,185) were taken from an existing sample of diverse aging adults. (Mean Age = 63.6, SD = 8.1; 71.3% female; White= 20.4%, Hispanic = 66%, Black = 13.6%). Linear regression was performed to predict executive functioning (EF) task performances (Trails Making Test parts A and B, Digit Span (DSF/DSB/DST), and Digit Symbol Substitution (DSS)) from fractional anisotropy (FA) and language group status. Multinomial logistic regression was performed to predict language groups from fractional anisotropy and EF task scores. The linear regression model showed that DST and DSB scores were positively predicted by the FA of the right uncinate fasciculus (UF) and the right superior longitudinal fasciculus (SLF). The DSS and Trail B scores were related to the FA of the bilateral UF and the right corticospinal tract (CST). The multinomial logistic regression model showed a lateralization effect of the UF in predicting language groups, with lower FA of the left and higher FA of the right being associated with an increased likelihood of being in the bilingual group. Similarly, higher FA of the right SLF was associated with the MLS and BES groups, and lower FA of the left CST was associated with the MLE group. Furthermore, MLS and BES groups were inversely associated with DSF and DSS performance, and positively associated with Trails A performance. These results not only suggest an existing relationship between bilingualism and EF performance, but reveal the role of enhanced white matter integrity of the right UF and SLF as underlying neurological mechanisms supporting the dynamic neural adaptations incurred by bilingual experiences. The dissociation of the bilateral UF in predicting bilingual status indicates that the information exchange between the right inferior frontal gyrus and the anterior temporal lobe may take a dominant role in bilingual processing. The right lateralization of increased white matter connectivity further suggests the contribution of the right hemisphere in bilingualism. . Important limitations to consider are that years of education also emerged as a significant predictor of performance and language group which could play a mediating role. Also, the CST, included as a double dissociation measure to assess for Type 1 error, had miniscule but

significant relations with both language group and EF measures. Nevertheless, these results point to an identifiable neuroanatomical substrate of bilingualism which necessitates further study.

Role of infralimbic cortex inhibitory neurons in the extinction of auditory fear memory
Rodrigo Campos-Cardoso, Zephyr R. Desa, Brianna L. Fitzgerald, Kirstie A. Cummings

The rodent medial prefrontal cortex (mPFC) plays a crucial role in fear modulation, with the prelimbic (PL) and infralimbic (IL) subregions linked to fear promotion and suppression, respectively. While the role of PL inhibitory microcircuit plasticity in fear memory processing has been described recently, the plasticity mechanisms supporting a role for the IL in fear suppression have been less explored. Recent studies have demonstrated that both IL PV- and SST-INs are potentially involved in fear suppression post-extinction training. However, the mechanisms underlying their involvement are not fully elucidated. Moreover, how these IN populations are organized, their in vivo activity dynamics, and learning-related plasticity following extinction training remain unknown. By using whole-cell brain slice electrophysiology, we show that both IL PV- and SST-INs undergo layer-specific experience-dependent synaptic plasticity after auditory fear conditioning and/or extinction training. To begin to reveal the role that each of these IN classes has in shaping behavior, we performed in vivo optogenetic manipulations of IL PV-INs and SST-INs. We observed that the activity of IL PV-INs seems to control fear-related behaviors, where their optogenetic activation and silencing during extinction training impaired and promoted extinction memory expression on the next day, respectively. These results suggest that the dynamic activity of IL INs is required for the extinction of learned fear. Current work is focused on revealing the dynamics of in vivo SST-IN and PV-IN activity during fear memory encoding and extinction to reveal a circuit model describing their involvement.

Dynamics of Dominant Default Mode Network Linked to Processing Speed in Cognitively Healthy Oldest-Old
Hannah Cowart, George C. Ling, Paul D. Stewart, Sara A. Nolin, Kristina M. Visscher

Cognition can vary tremendously among the cognitively-intact “oldest-old” in areas such as executive function, memory, and processing speed. Dynamic brain activity can be clustered on the individual time-point level to produce group-averaged “brain states,” termed “co-activation patterns” (CAPs), which can provide high resolution temporal information about brain function. Here we present the first study conducted in the oldest-old population that attempts to describe the relationship of brain dynamics to cognition. 146 cognitively-unimpaired participants aged 85-years or older provided 8-minute, 2.4-second TR, 3T resting-state functional magnetic resonance imaging (rs-fMRI) and completed neurocognitive assessments as part of a 4-site study, the McKnight Brain Aging Registry, a collaboration with UAB, University of Florida, University of Miami, and University of Arizona. CAPs were calculated using a k-means clustering algorithm. Dynamics were defined based on Fraction of occurrence (percentage of time spent in a specific state), persistence (consecutive time spent in a specific state), and transitions (movements from one state to another state).The most stable CAP across models (mean r = 0.92) has highly active DMN (z = 2.2), relatively high activation of the ventral attention network (VAN, z = 1.0) and low activation of every other network (z -0.6). We compared the dynamics of this dominant CAP to 5 aggregate measures of cognitive performance. Strikingly, these dynamics were strongly correlated only to processing speed, where better processing speed related to greater transition entropy, longer persistence, and greater fraction of occurrence. The default mode network was identified as a stable, common group-wide measure in the oldest-old population, regardless of model. Better processing speed was found to correlate to a dominant and persistent default mode network activity. CAPs add a new, dynamic dimension to fMRI and hold promise as a potential biomarker for cognitive intervention in future studies.

Anti-Parkinsonian Drugs Rescue Locomotive Phenotypes in JIP3 Knockout Zebrafish: Implications for Treating Patients with MAPK8IP3-related Disorders
Crowder, C., PhD, Travis, K., MS, Smith, G., MS, Glaze, Amber, Might, M., PhD, Crouse, A., PhD, and Foksinska, A. MS

MAPK8IP3-related disorders are neurodevelopmental conditions caused by variants in the gene Mitogen-activated protein kinase 8 interacting protein 3 that encodes the axonal transport protein JIP3. These

disorders are present in children and characterized by motility issues, intellectual disability, brain abnormalities and global developmental delays. In order to identify treatment options for patients, we conducted behavioral and motility phenotyping in JIP3 knock-out (KO) zebrafish to establish a high-throughput drug screening assay. JIP3 KO larval zebrafish displayed decreased locomotor activity, moved less often, travelled shorter distances and adults displayed decreased fecundity, body length and weight, compared to wild-type clutch mates. We used the artificial intelligence tool, mediKanren, and physician recommendations to prioritize a drug candidate list that we began screening at various concentrations in larval zebrafish to ameliorate the locomotor phenotype. We identified amantadine and levodopa, as promising drug candidates that rescued the locomotor phenotype in JIP3 KO zebrafish. We also demonstrated that overexpression of Spag9/JIP4 rescued locomotor phenotypes in larval zebrafish, indicating an alternative compensatory approach for treatment. We are working with physicians to screen the drug candidates in patients to determine the efficacy of these therapies to treat MAPK8IP3-related disorders hypothesized to result in JIP3 loss-of-function.

Toward comparing scotomas: Using microperimetry paired with cortical magnification factor to quantify retinal functional health in patients with central vision loss.
Elam J Cutts, Marcello Maniglia, Matthew K. Defenderfer, Pinar Demirayak, Dawn K. DeCarlo, Kristina M Visscher

In macular degeneration, the primary cause of vision loss among older adults, photoreceptor death in the retina results in diverse patterns of vision impairment. Complex visual tasks such as reading or navigation require both basic visual sensation (here, ‘low level vision’) as well as neural processes beyond basic sensation (here, ‘high-level vision’). Patients with similar retinal damage can differ widely in their performance on complex visual tasks, suggesting that compensation for this impairment varies between patients. uantification of this compensation is a necessary step to understanding the neural mechanisms underlying compensatory visual strategies. Traditional tests like visual acuity and contrast sensitivity gauge only limited aspects of vision and may not capture the broader visual field, leading to discrepancies between test outcomes and real-world function. To bridge this gap, we developed a method using outcomes from the Macular Integrity Assessment (MAIA), a microperimetry method that evaluates sensitivity across the retina. uantitatively comparing MAIA results across patients has been a challenge, especially given that lesions in central vision lead to worse impairment than peripheral vision. Here we introduce a method to quantitatively account for that difference, using the concept of the “Cortical Magnification Factor” (CMF). Different parts of visual cortex correspond to distinct regions of vision (retinotopic maps), and the CMF describes how much more cortex is devoted to each portion of the visual field. By weighting MAIA scores with CMF, we derived a measure called retinal functional health (RFH). RFH reliably reflects the clinical impression of the severity of a scotoma. RFH was significantly correlated to contrast sensitivity, as well as acuity. Further, models incorporating RFH were better predictors of high level visual processing (aggregate performance on a range of complex visual tasks). These results validate our measure of RFH to compare scotoma severity across participants.

The Result of Developing and Incorporating a Novelty Virtual Interactive Brain Atlas and Virtual Anatomy Lab Website into a Medical Student Neuroscience Curriculum.
Hunter Caroline Davies, M.S.; Jordan George; Inga Kadisha, PhD

Background: With anatomy teaching approaches constantly evolving, the need to incorporate more online supplemental educational resources is evident. Studies have shown that providing students with additional educational resources can be beneficial when given in an organized manner. Specifically, many institutions have begun to create anatomy resources for their students. With neuroanatomy being perceived as one of the most difficult anatomical regions to learn, more online resources need to be provided to help improve students' knowledge and ability to learn its complexity. This study aims to develop a novelty Virtual Interactive Brian Atlas (VIBA) and virtual anatomy lab (VAL) website into the medical student neuroscience curriculum. The VIBA study tool and VAL website aim to improve students’ knowledge of neuroanatomy and provide them with additional educational resources they can self-study at home. Methods: A novelty VIBA and VAL website were created and incorporated into the 2nd-year medical student's Neuroscience module. The VIBA study tool was created using Microsoft PowerPoint. Coronal, midsagittal, whole brain, and

horizontal plastinated brain slices, purchased from van Hagans Inc. in 2018, were embedded within the VIBA study tool, with each slice consisting of detailed descriptions, interactive features, and quiz assessments. In addition, MRI T1-weighted scans were incorporated into VIBA to complement the plastinated brain images. Interactive action settings were added to allow users to navigate through slides in an efficient manner. The VAL website was created using Sharepoint and consists of anatomy resources from both in-house and outside anatomy sources. Results: Both educational resources were created in a six-month timeframe and integrated into the 2nd-year Neuroscience module syllabus. Conclusions: The online brain atlas and website were created in a time-efficient manner, and positive feedback from the faculty was received. Both resources will continue to be integrated into future neuroanatomy courses for students of different health professions.

Causal evidence for the network involved in theory of mind
Kaitlyn E. Davis, Benjamin C. Cox, Jerzy P. Szaflarski

Forming supportive bonds with others is a fundamental human need that has enabled us to thrive as a social species. A vital component of connecting with others is the ability to infer their thoughts and feelings, i.e., having a theory of mind (ToM). This ability is supported by a distributed network with the dorsomedial prefrontal cortex (dmPFC) and temporoparietal junction (TPJ) serving as key components. While much is known about the areas associated with ToM, far less is understood about their interactions. A major limit to our understanding of the dynamics of this network is the lack of causal evidence identifying the interactions necessary for ToM. To address this, we are utilizing intracranial electrical stimulation (iES) to disrupt ToM performance by modulating the dmPFC and TPJ. Prior intracranial electroencephalography (iEEG) findings demonstrated activity in the dmPFC and TPJ predicted performance on a ToM task. As a preliminary step, we examined the impact stimulating these regions had on ToM performance in a single participant to ensure we are disrupting this ability. We expected inhibitory stimulation to increase reaction time and decrease accuracy. The participant was a 45 year old male undergoing stereotactic EEG (sEEG) for localization of drug resistant epilepsy with electrodes implanted in the right mesial temporal lobe. He completed the False Belief task that consists of 40 brief stories describing a protagonist's belief about a situation or control stories describing a photograph of a scene (presented for 10s), followed by a True/ False question (presented for 5s). To demonstrate ToM, the participant must recognize when the story describes a character with a false belief, as opposed to a photograph depicting an outdated scene. The task was presented on a laptop and answers were selected using the keyboard. Stimulation was not administered during the first 10 trials (5 Belief, 5 Photograph) to collect baseline data. For the next 30 trials, inhibitory stimulation was applied first to the TPJ for 15 trials and then to dmPFC for 15 trials (16 Belief, 14 Photograph). Stimulation was applied for the duration of the 5s True/False questions at 20Hz and 2mA using 250 us pulse trains. We computed linear regression analyses to determine the effect stimulation (Levels: No Stimulation, TPJ Stimulation, dmPFC Stimulation) had on ToM performance (Dependent Variables: reaction time and accuracy). Results from the linear regression analysis indicated the stimulation condition affected reaction time (p 0.001) but not accuracy (p 0.5). Post-hoc pairwise comparisons revealed stimulating the dmPFC increased reaction time compared to the TPJ (p 0.05). However, reaction time did not differ for trials without stimulation, potentially attributable to the limited number of trials (N=10) in this condition.This case study demonstrates causal evidence for the involvement of the dmPFC in ToM task performance, corroborating prior iEEG research. This earlier work not only identified dmPFC activity as a predictor of response time during a ToM task but also showed that the dmPFC is more specifically linked to ToM than the TPJ.

The mouse dorsal peduncular cortex encodes fear memory
Zephyr Desa, Rodrigo Campos-Cardoso, Brianna Fitzgerald, Jace Duhon, Victoria Landar, Alana Moore, Kirstie A. Cummings

The rodent medial prefrontal cortex (mPFC) is thought to exhibit a functional dichotomy, where dorsal areas including anterior cingulate and prelimbic cortex promote fear, whereas ventral areas including infralimbic and dorsal peduncular cortex suppress fear. While the IL has been linked to a role in fear suppression, the DP has been vastly understudied. Due to its anatomical location, the DP has been hypothesized to function similarly to IL in fear suppression, however its role in regulating fear remains

largely unknown. Through cFos immunohistochemistry, whole-cell brain slice electrophysiology, fiber photometry, and activity-dependent neural tagging, we recently demonstrated that DP exhibits cue-dependent activity during both fear memory encoding and retrieval and exhibits evidence of learning-related plasticity. By activating and silencing fear-tagged DP neural ensembles using optogenetics, we were able to both drive promotion and suppression of fear, respectively. In light of our recent findings, in unpublished work, we sought to identify projection populations to DP to highlight how the subregion is engaged and how it fits into the existing fear memory framework. By performing retrograde circuit tracing, we identified a prominent projection from the basolateral amygdala (BLA) to DP. Optogenetic silencing of projections from BLA to DP during fear encoding led to a significant reduction in fear memory expression the following day. These results suggest that BLA projections to the DP are likely important for driving fear memory encoding in the DP. Future experiments will employ optogenetic-assisted electrophysiology to reveal whether BLA projections onto DP neurons undergo fear-related plasticity. These results support our recent recharacterization of the role of DP in fear memory encoding and open up new avenues of investigation for how it fits within the established fear memory circuit.

A Pilot Feasibility and Efficacy Study of Transdermal Auricular Vagus Nerve Stimulation for Treating Insomnia in Breast Cancer Patients Receiving Palliative Care
Melissa Do, Alex Evancho, PT, DPT, William “Jamie” Tyler, Ph.D.

Background: While the purpose of sleep is heavily debated, it is widely accepted that quality sleep is essential to the well-being of every individual. It has been shown to decrease stress, improve depressive moods, enhance memory consolidation, reduce inflammation, and improve one’s overall health. Insomnia is a common problem experienced by patients with breast cancer, affecting about 40% of cancer survivors. This is a critical concern with cancer clinicians as it can affect the overall health of those with breast cancer or those recovering from breast cancer. Benzodiazepines are commonly prescribed to treat insomnia in breast cancer patients, but these drugs come with negative side effects and a high risk of abuse. Transauricular Vagus Nerve Stimulation (taVNS) is a non-invasive and non-pharmacologic intervention that could potentially be used as an alternative to treat insomnia. taVNS is safe and well-studied neuromodulation device that delivers low-intensity pulsed electrical currents to the vagus nerve through the external ear. This neuromodulation device has demonstrated efficacy in treating insomnia, stress, anxiety, pain, depression, inflammation reduction, and other diseases. Therefore, this intervention could serve as a safe, critical intervention to aid in breast cancer recovery and issues associated with breast cancer diagnosis. Methods: In this study, we aim to investigate the influence of taVNS to address insomnia in breast cancer patients receiving palliative and supportive care services. Specifically, we aim to evaluate the feasibility of using taVNS to treat insomnia in patients with breast cancer. We also aim to evaluate the efficacy of repeated, nightly taVNS on sleep quality, anxiety, and cancer-related fatigue. Results: We expect that 30 patients with breast cancer and insomnia will be enrolled and undergo taVNS to address insomnia, quantified by various sleep related outcome measures, with an estimated recruitment rate of 70%, eligibility rate of 70%, completion rate of 80%, and follow up rate of 80%. We hypothesize that patients will report significantly improved sleep (minimally clinically significant change of 6 points on the Insomnia Severity Index (ISI)), with possible improvements in anxiety, depression, and cancer related fatigue after one week of taVNS. Conclusion: This study is ongoing and recruitment strategies include recruiting breast cancer patients who have an active diagnosis or have had a diagnosis of Stage I-IV breast cancer and have cancer-related insomnia, as defined by having a Insomnia Severity Index of 8.

Combining Vagus Nerve Stimulaton with Large Amplitude Movement Therapy for individuals with Parkinson s Disease
Alexandra Evancho, DPT and Jamie Tyler, PhD

Introduction: Parkinson's Disease (PD) is a neurodegenerative disease characterized by the progressive loss of dopaminergic neurons, leading to both motor and nonmotor symptoms, which negatively impact quality of life. While there is no cure for PD, exercise potently attenuates disease progression, and is commonly prescribed to treat the symptoms of PD. This study explores the feasibility and preliminary efficacy of using innovative neuromodulation methods to enhance the treatment effect of exercise interventions for individuals with PD. We are exploring the combination of transcutaneous auricular vagus

nerve stimulation (taVNS), a non-invasive neuromodulation method, and Large-Amplitude Movement Therapy (LAMT), an evidence-based exercise intervention, to target motor and cognitive function in this population. These synergistic, low-risk interventions could potentially increase the therapeutic benefits of exercise in PD patients, ultimately improving quality of life. Methods: This study utilizes a randomized controlled trial design, where individuals with idiopathic PD (n=30) are divided into two groups receiving either active taVNS + LAMT (n=15) or sham taVNS + LAMT (n=15). The intervention's feasibility and tolerability are assessed, alongside its impact on motor and cognitive functions, through various standardized assessments conducted over the course of the study. Results/Discussion: This study is ongoing. So far, we have recruited 15 individuals with idiopathic PD to participate in the study. Five (5) individuals have completed the study protocol, with no adverse events reported. Significance: This study will provide insight into the feasibility and preliminary efficacy of using taVNS to enhance physical therapy care for individuals PD. Further research could lead to the development of more effective, personalized treatment strategies, contributing significantly to the field of neurorehabilitation.

Analysis of brain-wide projections to the dorsal peduncular cortex
Brianna L. Fitzgerald, Victoria Landar, Jace Duhon, and Kirstie A Cummings, Ph.D.

The rodent medial prefrontal cortex (mPFC) is important for cognitive activity including working memory, emotions, and behaviors as they relate to environmental conditions. The dorsal areas, anterior cingulate 1 (Cg1) and prelimbic (PL) cortex, have been implicated in fear promotion while the ventral areas, infralimbic (IL) and dorsal peduncular (DP) cortex, have been implicated in fear suppression (extinction). We recently discovered that, in contrast to its hypothesized role, the DP paradoxically participates in fear memory encoding and not extinction. However, the long-range projections that may engage the DP during fear memory encoding and retrieval are largely unknown. Moreover, whether the DP and PL might be engaged by the same or distinct brain regions/cells populations to cooperatively encode fear memory is also unknown. Here, we performed circuit tracing experiments to investigate how the DP is interconnected with other fear-related brain regions. Our results generate several hypotheses regarding the engagement of DP in fear memory encoding as well as potential differences in PL and DP circuitry. Future work will test the contributions of projections to the DP in mediating the behavioral and physiological correlates of fear memory encoding in the region.

Behaviors associated to autism-linked dopamine transporter genetic variants
Hunter Goffinett and Aurelio Galli

Dopamine (DA) is a neurotransmitter involved in motor function, motivation, and reward pathways. The human dopamine transporter (hDAT) is a pre-synaptic transporter protein responsible for the release and reuptake of DA from the synaptic cleft. Genetic variations in hDAT have been associated to impaired DA homeostasis, a complication linked with several brain disorders, including Parkinson’s and autism spectrum disorder (ASD). Although the causes of ASD are unknown, characterizing the functions and associated behaviors of ASD-linked hDAT variants may lead to the identification of the underlying mechanisms of ASD, discovery of ASD genetic markers, and help guide therapeutic developments. The Galli lab has previously identified several missense and in-frame deletion variants of the hDAT gene (SLC6A3) in individuals with ASD. These variants were associated to aberrant hDAT function resulting in impaired DA clearance. Our laboratory uses Drosophila as an animal model to express these hDAT genetic variations in the appropriate neurocircuits in order to determine impairments of specific behaviors. In this poster presentation, we show how expressing hDAT genetic variants in Drosophila disrupts DA-associated behaviors including increased fear, impaired social interactions, and increased locomotion. These results implicate hDAT variants as a potential risk factor for ASD and highlight the utility of the Drosophila model in assaying DA dysregulation. However, more research into the effects of ASD-related hDAT genetic variants on motor coordination and complex behaviors is needed. To observe how ASD-linked hDAT variants disrupt behaviors with high temporal resolution (msec), we will utilize a high-speed camera capable of 50,000 frames per second. This camera could capture the effects these variants have on motor coordination during behaviors requiring high sensory integration such as flight take-off. Additionally, high-speed recording of Drosophila may be able to capture the impacts ASD-related hDAT variants have on other complex behaviors, such as fear, repetitive behaviors, as well as social interactions. High-speed cameras have the potential to identify the associated

roles hDAT mutations have on the underlying mechanisms and behavioral paradigms of ASD.

A more inclusive IoT Ecosystem with Brain Computer Interfaces
Jose Gonzalez-Espana, Lianne S nchez Rodríguez, Maxine Annel Pacheco Ramírez, and Jose L Contreras-Vidal

In this presentation is described two approaches to make IoT more inclusive by empowering individuals that could face marginalization due to challenges like technical literacy barriers or mobility and communication limitations: The NeuroExo BCI System and an Emotion recognition headset.The NeuroExo was developed to address the challenges of using scalp EEG signals for brain-computer interfaces (BCIs) in real-time control of end effectors, such as exoskeletons, for stroke rehabilitation. This system focuses on providing low-cost, interoperable, and easy-to-use solutions for home neurorehabilitation. It features a one-size-fits-most EEG headset with dry comb electrodes. The system is being validated at home with stroke survivors, and healthy subjects using a WiFi-enabled robotic arm as the end effector in closed-loop BCI operation. It utilizes a user-specific trained machine learning model for intent detection with real-time interaction with participants.The emotion recognition EEG headset builds upon the hardware foundation of the NeuroExo, enhancing it with a camera and smartwatch to create a platform that monitors emotion and harnesses IoT to improve the emotional well-being of the wearer. These components are integrated through an iOS mobile application developed in Swift, which interfaces with a Firebase database to store mobile app data and video context awareness information. This application is designed for user interaction and has the potential to assist physicians in enhancing the emotional health of the participants.These system's significance lies not only in bringing BCIs into the IoT ecosystem, but also in its potential to democratize BCI systems, making them accessible for various applications beyond clinical rehabilitation, such as robust BMI control, video games, and more immersive classrooms, among others.

Adaptive control involves oscillatory dynamics in human prefrontal cortex
Anas Khan and Colin Hoy, Robert T Knight, Nicole Bentley

An important skill in human life is the ability to overcome habitual response tendencies to choose the response that is in line with the current goal. Coactivation of more than one response pathway leads to conflict. The brain consists of specialized areas that monitor for this conflict, and generally, a need for cognitive control. Such brain areas reside in the medial prefrontal cortex: anterior cingulate, mid cingulate, dorsomedial prefrontal cortex. These areas have been shown to be activated when a need for control arises. Particularly, midline theta power increases during these moments. Once conflict is detected, conflict monitoring theory suggests (dorso)lateral prefrontal cortex (dlPFC) is recruited to allocate attentional resources to resolve the conflict. In fact, dlPFC is also activated when preparing for control-demanding tasks and when adapting behavior to improve response efficiency and efficacy. The medial and lateral PFCs become synchronous in the low frequency band after errors and during conflicts. Yet, it remains unclear what specific mechanisms involving these two brain regions contribute to preparing for conflict adapting to it. According to the expected value of control theory, previous exposure to conflict should increase control at present. Behaviorally, this manifests as faster responses to conflict following conflict trials and lower theta responses. We predicted this increased control would manifest as directed information flow in the theta band from the lateral to medial PFC. To that end, we recorded intracranial EEG activity from surgical epilepsy patients while they performed a modified color-word Stroop task. We found that conflict trials following conflict involved lateral PFC Granger causing low frequency oscillations in medial PFC greater than the other way around. This effect was not present in conflict trials that followed no-conflict trials, emphasizing the importance of proactive recruitment of cognitive control resources in processing conflict. Our data add to the established cognitive control literature by showing how medial and lateral PFC dynamically interact depending on previous contexts and current goals.

Age-Related Variability in GABA-A Receptor Sensitivity and the Pharmacodynamics of Midazolam
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Background: Aging is associated with various neurophysiological changes, including alterations in the function and sensitivity of GABA-A receptors. This study aimed to investigate the short-interval intracortical inhibition (SICI) as a measure of GABA-A receptor-mediated inhibitory neurotransmission in young and older adults before and after the administration of midazolam, a benzodiazepine that targets these receptors. Methods: This cross-sectional study included 15 young adults and 16 older adults. SICI was measured using transcranial magnetic stimulation (TMS) at baseline and after the administration of midazolam. Due to methodological considerations, a higher-than-standard conditioning pulse was used. Results: At baseline, SICI was absent in older adults, whereas it was present in younger counterparts. After midazolam administration, SICI was abolished in younger adults, suggesting heightened pharmacological sensitivity. In contrast, older adults showed no change, possibly indicating age-related loss of receptor sensitivity or altered pharmacokinetics. Conclusion: The findings suggest significant age-related differences in GABA-A receptor function and benzodiazepine sensitivity, with potential implications for the clinical use of benzodiazepines in different age groups. Further research is warranted to explore the underlying mechanisms of these differences and to evaluate the impact of methodological variations in SICI measurement protocols.

dlPFC theta oscillations exhibit a rostral-caudal gradient during response inhibition
Anas U Khan, Zachary T Irwin, Adam Goodman, Robert T Knight, Kristina Visscher, Harrison Walker, Anna Roller, Barton Guthrie, Nicole Bentley

Executive control of movement enables inhibiting impulsive responses critical for successful navigation of the environment. Circuits mediating stop commands involve prefrontal and basal ganglia structures with fMRI studies demonstrating increased activity during response inhibiton in dorsolateral prefrontal cortex (dlPFC) often ascribed to maintaining task attentional demands. Using direct intraoperative cortical recordings, we investigated oscillatory dynamics along the rostral-caudal axis of dlPFC during a Go/No-go task, probing components of both proactive and reactive motor control. Oscillatory and BOLD activity is known to be rostro-caudally distributed based on level of rule abstractness. Recent studies suggest this gradient may reflect cognitive difficulty with more rostral regions being recruited during more difficult tasks. We assessed whether response inhibition is topographically organized along this axis and observed that theta power increased prominently in rostral dlPFC when inhibiting and delaying responses. We additionally found theta power to correlate with slowing of responses when the expectation of encountering No-go trials was higher, suggesting a possible anti-kinetic proactive control role for theta. These findings provide evidence for a key role for rostral dlPFC theta oscillations in sculpting motor control.

High frequency broad band cortical power better characterizes microlesion during deep brain stimulation surgery for Parkinson's disease
Jeevan Kumar, Joseph Olsen, PhD, Zachary T. Irwin, PhD, Arie Nakhmani, PhD, Christopher P. Hurt, PhD, Christopher L. Gonzalez, MS, Melissa H. Wade, CRNP, Bart L. Guthrie, MD, Harrison C. Walker, MD

Deep brain stimulation (DBS) electrode implant typically elicits acute improvements in contralateral motor symptoms ("microlesion" effects) in patients with Parkinson's disease (PD) and other movement disorders. These temporary symptomatic improvements arise from physical perturbation of the target tissue by the implanted lead, prior to electrical stimulation. Here we investigated changes in cortical field potential dynamics before and after lead implant in association with this well-recognized clinical phenomenon. We measured cortical field potentials and contralateral UPDRS-III sub-scores before and after the lead implant during DBS surgery in 31 PD patients. We computed power spectral density (PSD) at rest and during repetitive contralateral active and passive movements and correlated these measures with changes in UPDRS sub-scores pre- and post-implantation of DBS lead. As expected, UPDRS part 3 scores improved significantly after lead implant, yet beta frequency power increased in dorsal premotor cortex, supplementary motor area, primary motor cortex, primary sensory cortex, and more posterior parietal areas. Primary motor cortex displayed peak frequencies in the beta range (18±4 Hz) at rest, whereas the peak

frequencies for other cortical areas were in the alpha range (10±4 Hz). Interestingly, high frequency broadband power (100 – 400 Hz) decreased in all cortical regions following lead implant during rest and at both active and passive contralateral upper extremity movements. Although beta power, high frequency broadband power, and UPDRS motor scores all changed significantly pre- versus post-DBS lead implant. Only, change in high frequency broad band spectra power in the cortical local field potentials significantly correlated, with the magnitude of UPDRS change. These preliminary results suggest a potential role for aberrant oscillatory activity in high frequency broadband signals in the pathogenesis of motor symptoms of Parkinson's disease. Better understanding of this cortical field potential dynamics could inform novel adaptive stimulation strategies with next generation closed loop deep brain stimulation devices.

Co-Activation Patterns are Linked to Cognition Across Schizophrenia and First-Degree Relatives from the Psychosis Human Connectome Project
George C. Ling, Paul D. Stewart, Scott R. Sponheim, Kristina M. Visscher, Junghee Lee

Brain activity is known to be dynamic, dependent on individual and condition, in ways that are not fully described by static, spatial connectivity. Relatively recent work has shown that dynamic brain activity can be clustered on the individual time-point level, termed "co-activation patterns" (CAPs), giving faster temporal resolution compared to sliding window techniques that average data over seconds. Here we present novel brain-behavior links using data from the Psychosis Human Connectome Project.
151 participants with psychotic disorders, 89 first-degree relatives, and 52 controls provided 1,156, 6.5-minute, 0.8-second TR, 3T resting-state fMRI scans and completed Brief Assessments of Cognition in Schizophrenia (BACS). Preprocessed images were parcellated into 12 networks as described by Gordon et. al., 2016. CAPs were produced trans-diagnostically using k-means method from Janes et. al., 2020. k=7 was selected based on silhouette scores. Biologically relevant CAPs represented a high default state (CAP1), sensorimotor state (CAP3), and high-default/low-motor state (CAP5). No group differences in CAP measures reached significance. BACS composite scores were correlated to several CAP measures (Pearson's correlation, Bonferroni-corrected p-values): CAP entropy ($r = 0.2$, $p = 0.002$), persistence (CAP1: $r = 0.19$, $p = 0.03$; CAP3: $r = 0.23$, $p = 0.003$; CAP5: $r = 0.18$, $p = 0.04$), and transition entropy (CAP6: $r = 0.23$, $p = 0.003$). Significant links between dynamic measures of whole-brain states and cognition were found across groups. CAPs add a new, high temporal resolution dimension to fMRI and holds promise as a potential biomarker for cognitive intervention in future studies.

Roles of thalamic reticular nucleus cell types in (1) somatosensory behavior, (2) top-down cortical signaling, and (3) behavioral state transitions: Goals and Strategies
Hero Liu, Christian Puzzo, William Gilbert, Levi Dyson, Scott Cruikshank

The primary sensory thalamic nuclei are widely thought of as "relay nuclei" for bottom-up sensory signals, while the higher-order thalamic nuclei integrate top-down cortical signals. How these two types of pathways work together during sensory processing in live animals is still largely unknown. Here, we focus on the thalamic reticular nucleus (TRN), which can modulate activity in both classes of thalamic cells through feed-forward inhibition. Recent studies have shown that neurons in primary and higher-order sensory thalamic nuclei bidirectionally synapse onto two genetically, anatomically, and physiologically different neuronal subpopulations in the thalamic reticular nucleus (TRN) (Li et al., Nature, Vol. 83, 2020; Martinez-Garcia et al., Nature, Vol. 583, 2020.) Here, we focus on the somatosensory region of TRN, where centrally-located cells expressing calbindin synapse with the primary somatosensory thalamus and the cells along the edges of TRN expressing somatostatin synapse with the higher-order somatosensory thalamus. Ongoing in-vitro studies from our laboratory have determined that these two TRN subpopulations also receive distinct inputs from the neocortex which drive dramatically distinct patterns of activity. To better understand the functional nature of these anatomically and physiologically distinct subcircuits, we are utilizing in-vivo physiological recordings with optogenetic methods for identification and control. In-vivo strategies are essential to assess how sensory processing is affected by TRN subtypes through inhibition of the thalamus, and how this is affected by compounding factors including top-down cortical influences and arousal state. One challenge with in-vivo recordings is the difficulty with preciseidentification of closely adjacent neuronal subtypes embedded deep in the brain. Here we demonstrate strategies using a combination of viral and transgenic mouse-lines to differentially

label the central and edge cells of the TRN while avoiding non-specific labelling in the other parts of the thalamus and nearby structures. These strategies allow us to optogenetically identify and control the different TRN subtypes projecting to distinct relay nuclei which will allow us to probe their sensory and state-dependent functions.

Predicting Muscular Dynamics during Sit-to-Stand Transitions via Electromyographic (EMG) Signal Decoding

Christian Blanco Lopez1, B.S., Saul Gurgua Lopez1*, M.S., Rachel Murphy1*, B.S. Madeline Ragland1*, B.E., and Mark Bolding1,2, PhD.*

Enhancing the quality of life for individuals with impaired muscle engagement presents a significant challenge to approach, however, it also presents an opportunity for research refinement. We intend to establish a predictive model that can accurately forecast activation of muscle movements involved in standing, facilitating mobility for individuals facing difficulties with inadequate muscle engagement of the quadriceps. Our model aims to predict muscle movement of the quadriceps by analyzing electromyography (EMG) signals from separate muscle groups involved in the movement. Through the use of low-cost EMG technology, this research seeks to bridge a crucial gap in neuroengineering applications, offering potential cost-effective avenues for rehabilitation and enhanced autonomy for affected individuals. Our model's outcomes will be evaluated against predefined performance benchmarks, specifically aiming for a sensitivity (true positive rate) of at least 95% to ensure the model's effectiveness in identifying cases accurately. Concurrently, we strive to maintain a false-positive rate of less than 10%, minimizing the risk of incorrect case identification when the participant is not initiating movement to stand. These benchmarks are selected based on industry standards and the critical nature of accurate diagnosis in the area of application, serving as key indicators of our model's success. This research not only highlights the potential of EMG signal analysis in predicting muscle movement but also highlights the importance of interdisciplinary approaches in advancing neuroengineering solutions for mobility impairments. This work is ongoing and satisfies one of the program requirements for the Neuroengineering Graduate Curriculum at the University of Alabama at Birmingham.

Neuroinflammatory protein networks associate with altered decision making and impaired executive functions in the TgF344 Alzheimer's Disease rat model

Macy A. McCuiston, Kristian Davis, Nateka L. Jackson, Lori L. McMahon, Lynn E. Dobrunz, Caesar M. Hernandez

The relative weight that individuals give to rewards and "costs" (such as delay to reward delivery) in making decisions varies significantly across the population and disease states. One aspect of decision making involves weighing the relative benefits and costs associated with immediate versus delayed outcomes. This aspect of decision making is often referred to as temporal discounting (or intertemporal choice) and can be assessed on tasks in which subjects are required to choose between small, immediate rewards and larger rewards delivered after varying delays. Furthermore, intact executive functioning and motivation are foundational to the decision-making process. Recent literature shows there is a great deal of variability in the temporal discounting phenotype between individuals with mild cognitive impairment, frontal temporal dementia, and Alzheimer's Disease (AD), with some showing no differences relative to healthy controls and others showing altered rates of temporal discounting. Even beyond these disorders, individual differences in choice behavior (either maladaptive or normative) in young adults predict a variety of life outcomes, including educational success and socioeconomic status. The current study used a behavioral and molecular approach to determine the effect of genotype on phenotypic differences in temporal discounting, motivation, and executive function and neuroinflammation in the TgF344AD (TgAD) rat model of AD. Young adult (6-7 mo) wild-type (WT; n=6) and TgAD (n=6) were trained on a several operant tasks including temporal discounting (decision making), progressive ratio (motivation), set shifting (cognitive flexibility), and delayed response (working memory) tasks. Basolateral amygdala (BLA), Prelimbic Cortex, and Nucleus Accumbens tissue was then isolated and processed for use in a multiplex ELISA to assess markers of inflammation. Results suggest TgAD rats showed a greater preference for the large, delayed reward relative to WT, however, this preference did not translate to a greater number of total rewards earned. Additionally, TgAD rats were less motivated to obtain the larger reward, were less cognitively flexible, and showed

impaired working memory relative to WT controls. Additionally, AD-associated markers of inflammation were higher in the BLA of TgAD rats relative to WT. Interestingly, young TgAD rats show a similar decision-making and cognitive phenotype as old rats, and these data suggest AD pathology may manifest as maladaptive decision making in addition to impaired executive functions early in life.

Closed-Loop Approaches to Cognitive Training for Enhancing Processing Speed
Ashton Weber and Keith McGregor, Ph.D.

Older adults with greater impairments in visual attention show poorer visual field processing that may impact instrumental activities of daily living such as driving. These deficits may be due to aging-related declines in selective cortical inhibition, particularly in occipitoparietal regions which limit sensory gating of visual stimuli. A proposed mechanism by which the brain selectively inhibits non-relevant (distracting) visual stimuli is through cortical oscillations in the alpha frequency band (8-12 Hz), which can be measured by electroencephalography (EEG). Deficits in visual attention are believed to be related to poorer performance in executive functions, specifically processing speed, which itself may be indicative of dysfunction of cortical inhibition. However, at present, we do not yet understand the relationship between processing speed and occipitoparietal alpha power in the aging brain. The goal of this study is to evaluate the effects of occipitoparietal alpha band neurofeedback using EEG on processing speed measures across age groups. Participants will complete two assessment sessions at the study's outset after giving informed consent. The first session will consist of cognitive and behavioral assessments in which the primary outcome measure is cognitive processing speed. The second session will consist of a visual attention assessment utilizing EEG. Participants will return for three subsequent neurofeedback training sessions involving alpha modulation using EEG. Participants will then repeat the behavioral and visual attention assessments at their sixth and final session. Our Study Aim 1 will determine the relationship between alpha modulation and processing speed. We hypothesize that participants who better modulate alpha will have better measures of processing speed. Further, we hypothesize that younger adults will exhibit better alpha modulation and have better processing speed measures compared to older adults. Our Study Aim 2 will evaluate the effects of alpha modulation neurofeedback training on processing speed measures. We hypothesize that alpha neurofeedback training will improve processing speed, and, after training, older adults will learn to better modulate alpha and will have a greater change in processing speed measures compared to younger adults. The proposed research will advance our understanding of the relationship between alpha modulation and processing speed. This knowledge will contribute to the development of cognitive interventions for older adults, potentially improving their functional performance in instrumental activities of daily living and overall quality of life.

Machine learning reveals mPFC neuronal ensemble dynamics across contingent motivated behaviors
Sierra N. Miller, Carine Lampert, Briana L. Machen, Sheila Subbiah, Lauren E. Assaf, Julia C. Tucker, Morris R. Jackson, Cesar Acevedo, Lucas Pozzo-Miller, B. Sofia Beas

Motivation is a set of complex neuronal processes that enable the initiation, guidance, maintenance, and termination of goal-directed behavior, which are critical for survival. Indeed, many of the most prevalent mental health and neurological disorders display deficits in motivation as one of the main core features. Unfortunately, effective treatment for these disorders is complicated and lacks efficacy, in part due to our incomplete understanding of underlying neuronal mechanisms that regulate motivation. Additionally, several factors influence motivation, such as the internal states (e.g., hunger) of the individual and previous experiences with attaining a particular goal. For the latter, individuals learn to predict rewards based on environmental cues. Moreover, when the environments change, individuals are required to relearn and adapt behavior accordingly. The medial prefrontal cortex (mPFC) is a brain region known to play an important role on motivated behaviors. Particularly, mPFC neurons exhibit distinct responses to cues associated with rewards and during reward approach decisions (Del Arco, et. al., 2017; Moorman and Aston-Jones, 2015). However, how mPFC neuronal ensembles adapt with changes in task contingency is still not fully known. To address this, we use single-cell calcium imaging to characterize the activity of the mPFC neurons while hungry mice perform trials in a foraging task. Once mice were trained to perform this task, different trial contingencies were manipulated. We first aimed to determine how mPFC neuronal

ensembles respond during distinct task events (cue, approach, reward; etc). For this, we implemented and compared three different clustering methods:1) Standard approach (Patel, et. al., 2022); 2) Unsupervised machine learning using K-means clustering with dynamic time wrapping (DTW) algorithm (Kinnunen, et. al., 2021); and 3) Deep machine learning using DTW-Self Organized Maps (Li, et. al., 2021). Then to determine the effects of manipulating task contingencies (e.g., changes in reward type), we used a novel statistical framework based on functional linear mixed models (FLMM) (Loewinger, et. al., 2024 preprint; Beas, et. al., 2024). This robust statistical approach allows for a nuanced trial-level temporal analysis of bulk calcium imaging data. As such, we modified and adopted the FLMM analysis to test the effects of changes in task contingencies on mPFC cells activity dynamics. Our work contributes a meaningful combination of analyses that reveal in high detail the dynamics of both population- and single cell-level activation during a motivated food-seeking behavior.

Self-paced reading pauses tied to phrase boundaries during sentence comprehension
Jenna Hooper; Christophe Smith; Matthew J. Nelson

The node-tracking framework for sentence comprehension (Nelson et al. 2017) provided a novel plausible mechanistic account of the comprehension of syntactic structure in the brain, on a level at which there are few other competing models. The framework was derived from observations of key neural events happening at the major phrase boundary of sentences during sentence comprehension. To investigate a potential behavioral correlate of that framework, here we performed a self-paced reading experiment in healthy participants and examined the connection between word response times during reading and the phrase boundaries of sentences. Participants read sentences one word-at-a-time, making a key press to advance to each next word of the sentence at their desired pace. Participants were presented with three sentence types: object-relative sentences (“The cat that the dog chased was brown”), subject-relative sentences (“The cat that chased the dog was brown”), and control sentences (“The brown cat chased the dog”), with object-relative sentences known to be the most difficult of the three sentence types. After each sentence, participants were presented with four pictures and tasked with choosing the picture that corresponded to the sentence they had just read. The four pictures presented varied the patient-agent assignment of the two nouns in the sentence (e.g. who was chasing whom in this example sentence) and the complement-noun assignment (e.g. who was brown) independently in a 2x2 design. Preliminary results show a strong and robust peak in per-word reaction times at the phrase boundary word for object-relative sentences relative to other sentence types, and a moderate peak at the phrase boundary word for subject-relative sentences. Participants made the highest proportion of errors on object-relative sentences as expected. On these sentences, participants unexpectedly showed a consistent tendency to make simultaneous patient-agent and complement-noun errors in their responses, which yields insight into the processes occurring when participants errantly comprehend these sentences. Altogether these results provide behavioral evidence of the importance of phrase boundaries in sentence comprehension, corroborating previous neural results of the node-tracking framework.

Beta frequency activity reflects sensory processing in the human subthalamic nucleus
Joseph W. Olson, Marshall T. Holland, J. Nicole Bentley, Harrison C. Walker, and Zachary T. Irwin

The role of the subthalamic nucleus (STN) in sensorimotor circuits remains unclear, as does its significance within Parkinson’s disease (PD) pathophysiology. In particular, how sensory information is processed in STN is understudied even though STN responds to tactile and proprioceptive stimuli, and patients with PD have impaired sensory processing. Here, we recorded intracranially from the dorsolateral STN and sensorimotor cortex from patients with PD undergoing deep brain stimulation (DBS) surgery to investigate the response of STN to simple vibratory stimuli (100 Hz and 200 Hz) of the arm and to hand opening-closing. We studied both single-unit activity with STN micro-electrode recordings (MER) and local field potentials using a directional DBS electrode in the STN and electrocorticography (ECoG) in cortex. Spike rasters from STN MER, aligned to vibratory stimuli onset, show spike-LFP phase locking in the beta frequencies (13-35 Hz) without significant changes in firing rate itself. This transient response, lasting a couple hundred milliseconds after vibratory onset, is independent of vibratory stimulus frequency. A similar response is observed in event-related spectral perturbations (ERSPs) in the local field potentials. Both STN and sensory cortex display a robust response in the beta band after vibratory onset. This response

occurs in cortex before STN and is again independent of vibratory frequency. The ERSP (average) response seems to arise primarily from signal phase alignment (over trials) rather than changes in signal amplitude, paralleling the observations from single-unit recordings. This can be interpreted as a frequency-specific phase reset which has been observed to occur in other brain regions in response to auditory and visual stimuli. Patients also performed hand opening-closing tasks both with and without simultaneous vibration. We rendered ERSPs aligned to electromyography (EMG) peaks and observed STN beta responses on directional contacts similar to those from vibratory stimuli alone. However, movement related beta responses were weaker than those from vibratory stimuli. Neural responses were further attenuated during simultaneous movement and vibration. Our findings suggest that STN and cortical beta synchronization relates to both motor intention and sensory signals such as vibrations. This sheds light on the role of the beta band in sensorimotor circuits, which, despite not being understood, is being used as a control signal in closed-loop DBS. Our findings also indicate that multiple signals may interfere with each other, possibly due to sensory gating mechanisms. Together, these observations may help explain previous findings of beta band's unreliable connection to parkinsonian symptoms such as rigidity.

Brain-to-Brain Communication and Neural Dynamics during Dance Performance through EEG, Hyperscanning and Mobile Brain-Body Imaging Techniques
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Objective. Hyperscanning and Mobile Brain-Body Imaging (MoBI) are important and useful techniques broadly used in the neuroscience field. This study aims to shed light over the neural dynamics during social interactions present in an artistic performance, the project seeks to uncover the brain dynamics and the brain-to-brain synchronization development between dancers over a 5 month period, as well as the functional connectivity in this complex, social and natural setting. Approach. A unique methodology was implemented in order to incorporate and process the electroencephalography (EEG) recordings with the acceleration (IMU) and video to analyze the data. The EEG data collected during live dance performances was denoised by removing physiological and non-physiological artifacts using a pipeline based on adaptive H-infinity filter, Artifact Subspace Reconstruction (ASR), and Independent Component Analysis (ICA) using Matlab and EEGLAB. Once the signals were cleaned and processed the dipoles from both dancers were estimated using the sources from the ICs, clustered and only shared dipole sources across the two dancers were retained, centroids were estimated and located according to corresponding Brodmann areas (BA), subsequent analyses incorporate the calculation of metrics, including bispectrum for evaluating brain synchrony, along with the analysis of functional connectivity. Main Results. Analysis revealed a progression in brain activity over time as results showed an increased efficiency in neural communication over the course of the public performances while dancers refined the movements in the choreography producing a gradual decrease in brain activations. Findings further reveal distinct patterns of neural synchronization that correlate with varying degrees of collaborative and physical interactions, as results show higher brain synchronization levels between dancers while having eye contact, physical touch and improvising during the choreography. Moreover, functional connectivity analysis showed brain consolidation between the visual and motor areas of the brain suggesting an enhanced communication and coordination between the visuomotor networks, contributing to a more synchronized and harmonious performance. Significance. These insights contribute to a deeper understanding of the neural dynamics that are present during human social interaction and collaboration within the field of arts, neural dynamics during social interaction have the potential to be used as a diagnostic tool in developmental and clinical social neuroscience including the design of clinical interventions for individuals with different brain disorders.

Photoreceptor resolved temporal contrast encoding in LGN neurons during ongoing stimulation
Keaton Ramsey, Philipp Tellers, Cyril N.A. Nyankerh, Alexander Meadway, Lawrence C. Sincich

The response properties of neurons in the lateral geniculate nucleus (LGN) are typically studied with large full-field stimuli that do not probe vision at the scale of cone photoreceptors or in the presence of other stimuli. To understand how LGN cells respond to stimuli covering small portions of the receptive field during ongoing stimulation, we examined spike activity changes resulting from contrast steps occurring in fine-grained noise stimuli. We recorded extracellularly from 63 LGN cells in 2 anesthetized macaques with

receptive fields located 0.5°-4° from the fovea. An adaptive optics scanning laser ophthalmoscope was used with an infrared (842±25 nm) channel to image the retina, while red (711±12 nm) and green (543±11 nm) channels delivered binarized white noise movies. Each color was modulated independently over a 0.32° stimulus field. A movie pixel subtended 0.6 arcmin (~3 m), just smaller than a single cone photoreceptor. Spike-triggered averaging was used to map receptive fields and classify cells by color and ON or OFF preference. To examine response characteristics, we determined a cell's baseline average spike probability across all stimulus movie frames. We then computed spike probability changes during specific conditions for the pixel located at the receptive field center's peak. Conditions included single frame stimuli (ON or OFF), temporal contrast stimuli (ON-to-OFF or OFF-to-ON), and recovery in the subsequent frame for all these scenarios. Of the cells recorded, 26 OFF and 24 ON cells showed a change in spike probability from baseline. In these cases, the single frame pattern of the preferred stimulus increased the mean spike probability by 20% (±17% SD). Notably, for both cell types the single frame patterns led to spike probability changes that were equal in magnitude, but opposite in polarity, for preferred and non-preferred stimuli. Temporal contrast patterns produced higher changes in spike probability than single frame patterns, but differed in magnitude for preferred (27±21%) versus non-preferred (25±21%) stimuli. During the recovery frame, spike probability also differed from baseline with equal magnitude for the single frame condition regardless of preference (5.4±6.5%), while the temporal contrast conditions changed probability differentially (4.7±11% for preferred, 2.3±9.2% for non-preferred). Our results suggest that single frame conditions lead to symmetric changes in spike rates in ON and OFF conditions, while temporal contrast patterns drive asymmetric responses weighted toward preferred stimuli. Thus, contrast encoding in time shows a history dependence detectable even at a cone resolved level in LGN neurons.

Vagus Nerve Stimulation for treatment of aphasia and dysarthria
Alibek Sartayev, Alex Evancho, Keith McGregor, Jamie Tyler

Being able to communicate with others is undoubtedly one of the most important features defying quality of life. Sadly it is often caused by stroke, brain injury or various progressive neurological conditions, so there are at least 15 million people with aphasia worldwide and 2 million in U.S. The therapy helps most people but there are not many neurological interventions to accelerate the process. This study is about applying Transcutaneous Auricular VNS (taVNS) in therapy for stroke patients who has symptoms of aphasia, apraxia, and/or dysarthria. We also are going to use Electropalatographic(EPG) measurements to record the progress of the movements of the tongue.

Alzheimer's Disease and Normative Aging Neuropathology in the Basolateral Amygdala of the TgF344 Rat
Sherine A.G. Skjefte, Pheven A. Yohannes, Juan P. Carcamo Dal Zotto, Macy A. McCuiston, Caesar M. Hernandez

Alzheimer's disease (AD) is a progressive neurodegenerative disease affecting millions worldwide. AD causes cognitive defects, such as memory loss, and is characterized by specific pathology such as amyloid-beta plaques, tau neurofibrillary tangles (NFTs), neuroinflammation associated with gliosis, and neurodegeneration. However, the role of aggregates and tangles in the basolateral amygdala (BLA) in AD has not been well studied. In this study, we aim to elucidate the pathology trajectories which diverge between normative aging and AD in the BLA. Using immunohistochemical approaches, we measured amyloid, tau, microglial, and astrocyte activation (using Iba1 and GFAP, respectively) to determine pathology progression in BLA nuclei ranging from young, 3 months old, to aged, 24 months old, wildtype rats and transgenic Fisher-344 AD (TgF344-AD; TgAD) rats. Immunostaining highlighted pathologies of interest, including amyloid beta aggregates, tau NFTs, gliosis, and neuronal cell count. Preliminary results suggest early amyloid and tau pathology is observable in the BLA. Additionally, we report greater activated microglia and astrocytes within the BLA of young TgAD rats. In TgAD rats, aging is associated with greater amyloid and tau accumulation. In the older WT rats, we also see increased activated microglia and astrocytes irrespective of genotype. These results highlight the effectiveness of the TgF344 rat model at simulating AD pathology in humans and show the BLA as an epicenter of early AD pathological changes.

Decoding semantic information from intracranial recordings
Christophe Smith, Nicole Bentley, Harrison Walker, Matthew Nelson

An emerging technology for the treatment of speech deficits due to motor paralysis is the language brain-computer interface (BCI). Most research to develop a BCI focuses on recording and decoding activity from the speech sensorimotor cortex (Moses et al., 2021). This approach decodes the kinematics of attempted speech and can be used to determine the phonetic components of language. Although this has been effective it does not consider other components of speech production and comprehension which may improve the decoding accuracy. Decoding other linguistic features could improve the accuracy of BCI decodes by supplying it with information about the meaning of the word. Our study fills this gap by decoding semantic information from neural activity recorded directly in cortical language centers. Volunteer epilepsy patients performed tasks involving semantic processing for both language production and comprehension while we recorded their intracranial neural activity using stereoelectroencephalography (sEEG). Recordings also included microwires specifically targeting the anterior temporal lobe (ATL), thought by many to be the apex of the semantic system in the brain (Mesulam et al., 2015). The stimulus items in the tasks were concrete nouns spanning a range of 15 semantic categories, which included across-category superordinate groupings (e.g. animate vs. inanimate objects). Early analyses using support vector machines for direct decoding from neural activity have shown above chance accuracy for decoding the semantic category of an item on a given trial (19.3% accuracy achieved with a chance level of 6.7%). The ATL and inferior frontal gyrus (IFG), a known important node in the semantic network (Binder et al., 2009), were found to contribute the most to the decoding performance. As this work progresses we will investigate different machine learning techniques, as well as the use of semantic models to provide intermediate representations as decoding targets as opposed to directly decoding categories from neural activity. These models allow us to probe how semantics may be represented in the brain, expanding the fundamental knowledge of how language is represented in the brain. These models are expected to improve decoding performance as has been shown in the decoding of speech on a phonemic and sensorimotor basis from the sensorimotor cortex (Anumanchipalli et al., 2022).

Preventing Spinal Cord Injury Induced Muscle Atrophy with Muscle-Specific PGC-1α Overexpression
Serenah E. Smith, Drue Benefield, Glenn C. Rowe

Spinal cord injury (SCI) resulting from damage to the vertebral column leads to dramatic decreases in muscle mass. The decreases in muscle mass is associated with the development of comorbidities and poor outcomes. Therefore, identifying factors that are able to preserve muscle mass after spinal cord injury is important to improving recoveries. One of the proposed contributors to the development of muscle atrophy after SCI is the occurrence of mitochondrial dysfunction within skeletal muscle. The mitochondrial dysfunction results in elevated levels of reactive oxygen species (ROS) and reduced PGC-1α expression levels. PGC-1α is a potent regulator of mitochondrial function and has been shown to regulate an anti-ROS system. We therefore wanted to test whether overexpression of muscle PGC-1α was able to prevent the development of SCI induced muscle atrophy. We performed full spinal cord transections or laminectomy-only (sham) surgeries at the T9 vertebra of mice that overexpress PGC-1alpha under the control of the muscle-creatine kinase promoter (MCK-PGC-1αTg) or littermate controls. We measured grip strength and movement (BMS), body weight, and muscle weights 3 days post injury. We also performed qPCR and western blots to measure levels atrophy markers and protein synthesis. Analysis of the muscle weights revealed a decrease in muscle weight for the control transection group, compared to the control shams, and a possible preservation of muscle mass in the MCK-PGC-1αTg, however, more time after injury is needed to explicate this difference. The MCK-PGC-1αTg groups also showed similar levels of atrophy markers and protein synthesis levels compared to the control sham group. Taken together these results

suggest that muscle overexpression of PGC-1α is able to blunt the development of atrophy compared to control groups.

Dissociable encoding of motivated behavior by parallel thalamo-striatal projections
Alexa Tellez, Briana Machen, Carine Lampert, Isbah Khan, Claire Gao, Emma Macdonald, Sofia Beas

Motivated behaviors enable individuals to pursue goals that are essential for survival. However, the mechanisms that underlie these behaviors are still not fully understood. Previous research has identified the paraventricular nucleus of the thalamus (PVT) as a brain region that integrates bottom-up interoceptive signals with top-down cortical information and sends robust glutamatergic projections to the NAc. Furthermore, we identified two major distinct subpopulations of neurons in the PVT (Type1PVT and Type2PVT) that differ in their genetic identity, connectional features, and functionality. However, very little is known about the involvement of these thalamic inputs to the NAc in mediating motivational processes. Here, using fiber photometry, we investigated the in vivo dynamics of these two parallel thalamo-striatal pathways in mice performing a reward foraging task. Collectively, our findings show a novel dissociation between the Type1PVT–NAc and Type2PVT–NAc pathways and identify a specific neuronal subpopulation of the PVT that signals motivational states.

Clinical Trials in Neuromodulatory Treatment of Drug-Resistant Hypertension: A Systematic Review
Garrett Thrash, Elijah Wang, Yifei Sun, Marshall T Holland, Bryan Becker

Introduction: Drug-resistant hypertension (DRH) affects somewhere between 9-18% of the U.S. hypertensive population. Recognized as hypertension (HTN) that is resistant to three or more medications, DRH can lead to fatal sequelae, such as heart failure, aortic dissection, and other vast systemic disease. The disruption of the homeostatic mechanisms that stabilize blood pressure (BP) can be treated procedurally when medication fails. These procedures include carotid body stimulation, renal denervation, sympathectomies, dorsal root ganglia (DRG) stimulation, and more recently spinal cord stimulation (SCS) have all been utilized in the treatment of DRH. Results: Renal denervation and carotid body stimulation have both shown promising results with multiple clinical. trials, while sympathectomies have mostly been retired due to the irreversible adverse effects caused. DRG stimulation showed varying success rates while SCS stimulation showed a potential lowering of BP. Discussion/Conclusion: SCS stimulation is a novel treatment of DRH that shows promising results but requires further investigation and prospective studies of the treatment to provide guidelines for future DRH treatment. This review summarizes the clinical trials for neuromodulatory treatment of DRH following PRISMA guidelines and suggests future directions in the treatment of DRH.

Intracranial Recordings of Cognitive Control during Conflict Trials and its Progress towards Brain Mapping: A Systematic Review
Garrett W. Thrash, Yifei Sun1, Kailey Walters, Rebecca Billings, Victor A Del Bene,, J Nicole Bentley

Response inhibition allows regulatory loci of the brain to mediate action responses through the motor cortex while performing tasks that require abrupt stopping. This has been extensively studied in the cortical areas involved with cognitive control, but the subcortical regulatory regions are not as well investigated due to the invasive nature of the recording. Intracranial recordings, such as stereo-electroencephalogram (SEEG) and electrocorticograms (ECoG) allow for investigate of the subcortical areas, and also provide greater temporal acuity than other techniques. We summarize response inhibition using tasks of inhibitory control, such as the stop-signal task, Go/ No-Go task, Stroop task, and Flanker Test. The findings were mainly heterogenous due to the lack of data available. However, it was found by multiple studies that the subthalamic nucleus and inferior frontal gyrus took command of the motor cortex during response inhibition through executive control to prevent action. There were also reports of sex and age differences in response inhibition, such that the ability of impulse control increases with age in adolescence yet began to decrease with age in elderly populations. Females exhibited a higher rate of inhibitory processing speed as well as a decrease in error commission. The relationship of other neuroanatomical with response inhibition is discussed in further detail in the review. This review provides the first summarization of intracranial recordings in patients with Parkinson's disease (PD), epilepsy, and other indications for deep brain

stimulation (DBS) with focused effort on brain mapping the temporal and spatial aspects of the anatomy responsible for cognitive control.

Comparing Resting State and Stimulation Evoked Network Connectivity Using Dynamical Systems Modeling

Caila Coyne, Helen Brinyark, Ben Cox, Sridevi V. Sarma, Arie Nakhmani and Rachel J. Smith

Introduction: The aim of this study is to develop a framework for comparing resting state connectivity networks to stimulation evoked networks in drug resistant epilepsy patients. Recently, single-pulse electrical stimulation (SPES) has become increasingly used to investigate functional and pathological connectivity in epilepsy and to probe cortical excitability. It has been found that the stimulation-evoked responses, cortico-cortical evoked potentials (CCEPs), often differs in magnitude in epileptogenic and healthy brain regions. However, SPES is still not a part of routine clinical care as the process can be long, tedious and may provoke unwanted seizures. Consequently, by mapping the resting state network to the stimulation evoked network, we can investigate whether similar information about epileptogenic connectivity can be obtained from resting state intracranial EEG (iEEG) data alone. Methods: The resting state iEEG recordings were preprocessed by high pass filtering to remove DC drift, re-referencing to a bipolar montage and rejecting artifactual channels and epochs. The stimulation artifacts in the CCEP data are removed using a method that avoids introducing discontinuities in the time series. For the resting state connectivity network, linear time invariant (LTI) state-space models in the form: $x[t+1]=ARSx[t]$, are constructed with interictal recordings divided into 500 ms windows where $x[t]\in Rnx1$ represents the state vector describing the neuronal activity recorded from each of the n contacts, and $ARS\in Rnxn$ is the state transition matrix. Each ARSij element of the state transition matrix describes how the present activity of contact j influences the future activity of contact i. The matrix is estimated by solving a system of linear equations using the least squares method. To estimate the state transition matrix for CCEP data, an exogenous perturbation term is added to the model to account for the electrical stimulation introduced into the network: $x[t+1]=ACCEPx[t]+Bu[t]$. ACCEP and B are then estimated simultaneously using average CCEP waveforms as the state vector. Results: We first show that dynamical network models built from both the resting state and CCEP data adequately capture the underlying dynamics of the system through recursive reconstruction of the respective data used to build the models. To quantify similarity in connectivity between resting and stimulated networks, the A matrices are vectorized and we calculate a transformation matrix T where $ARS = TACCEP$ and $ARS\in Rn^2x1$ and $ACCEP\in Rn^2x1$. We then calculate the L2 norm of T to define network similarity. We expect that the norm of T will be minimized with greater similarity between the resting state and stimulation-evoked network.