

isolated from human blood and plasma samples via direct immunoprecipitation using biotinylated antibodies for proteins known to be expressed in neurons (Contactin-2, i.e.) and astrocytes (glial-glutamate-aspartate-transporter, i.e., GLAST). Once isolated, protein concentrations in the EV samples were analyzed via ELISA assay, EV abundance was measured using ViewSizer Nanoparticle Tracking analysis, and EVs were visualized via Transmission Electron Microscopy. EVs were then analyzed for metal contents using a Perkin-Elmer NexION 350S via an ICP-MS/MS dynamic reaction cell method. RESULTS/ANTICIPATED RESULTS: Preliminary results demonstrate that it is feasible to quantify the metal contents of these CNS-derived EVs, particularly in terms of toxic metals known to be associated with neurodegenerative disorders, including copper, zinc, lead, aluminum, manganese, and iron. DISCUSSION/SIGNIFICANCE: CNS-derived EVs isolated from peripheral blood draws show promise as a potential biomarker of real-time metal load in the brain and spinal cord, with promising applications in predicting future development of neurodegenerative disorders (i.e., ALS) among patients with relevant elevated CNS metal loads.

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Interest in and Perceived Effectiveness of Contingency Management Among Alcohol Drinkers Using Behavioral Economic Purchase Tasks^{*,†}

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OBJECTIVES/GOALS: The purpose of this study was to develop behavioral economic purchase tasks to assess interest in CM as a function of treatment cost and perceived effectiveness of CM as a function of abstinence incentive size in alcohol drinkers. Additionally, these purchase tasks are being assessed for their clinical utility in an ongoing clinical trial. METHODS/STUDY POPULATION: Alcohol drinkers recruited from Amazon Mechanical Turk completed behavioral economic purchase tasks measuring demand for CM based on targeted abstinence intervals and treatment effectiveness and alcohol use disorder severity assessments. Nonlinear mixed effects modeling was used to fit demand curves and assess the relationship between individual characteristics and demand metrics for CM. Ongoing analyses involve administering the same behavioral economic purchase tasks in heavy alcohol users in the ongoing clinical trial, which is aimed at reducing alcohol use through remotely implemented CM. RESULTS/ANTICIPATED RESULTS: Mechanical Turk participants reported higher probability of abstinence when offered larger incentives and required larger incentives when duration of abstinence required to earn the incentive was increased. Additionally, willingness to pay for treatment increased as effectiveness of treatment increased. It is anticipated that these patterns will be observed in the clinical trial participants. DISCUSSION/SIGNIFICANCE: Abstinence interval and treatment effectiveness are important features to consider when developing effective CM for widespread use, as these variables affected participants likelihood of being abstinent and their interest in treatment. We are currently working on verifying the results of these assessments in clinical trial participants.

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Resting state fMRI connectivity in individuals with aphasia and the role of the inferior frontal gyrus

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OBJECTIVES/GOALS: This poster will explore lesion-symptom mapping and resting state functional magnetic resonance imaging (rsfMRI) in participants with aphasia. This analysis aims to reveal the behavioral impact of distinct lesions to the left inferior frontal gyrus (LIFG) and the potential for rsfMRI to provide evidence of cortical reorganization. METHODS/STUDY POPULATION: The analyses will be conducted on a small sample of approximately six participants with post-stroke language impairment (i.e., aphasia) recruited as part of an ongoing study. Lesion load in the anterior LIFG (aLIFG), consisting of the orbital (BA 47) and triangular (BA 45) parts, and the posterior LIFG (pLIFG), consisting of the opercular part (BA 44) will be correlated with performance on tasks of semantic and phonological processing. Functional connectivity will be determined between regions of interest (i.e., anterior superior temporal, posterior middle temporal, angular, and supramarginal gyri) in the left and/or right hemispheres based on rsfMRI data. RESULTS/ANTICIPATED RESULTS: Lesion load in the aLIFG is expected to correlate to performance on the semantic task, whereas lesion load in the pLIFG is expected to correlate to performance on the phonological task. For participants whose behavioral performance exceeds expectations based on lesion load (e.g., larger aLIFG lesion load, yet better semantic task performance), rsfMRI connectivity is expected to be greater (e.g., between the posterior middle temporal and angular gyri), suggesting cortical reorganization. DISCUSSION/SIGNIFICANCE: If our hypotheses are supported, our results will corroborate evidence of a functional spectrum (i.e., semantic-phonological) in the LIFG. Future work will compare rsfMRI connectivity to neurotypical controls and sites of connectivity may be used as targets in studies of non-invasive brain stimulation as an adjuvant to behavioral therapy.

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Investigating the Architecture of Speech Processing Pathways in the Brain

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OBJECTIVES/GOALS: Speech production requires mapping between sound-based and motor-based neural representations of a word – accomplished by learning internal models. However, the neural bases of these internal models remain unclear. The aim of this study is to provide experimental evidence for these internal models in the brain during speech production. METHODS/STUDY POPULATION: 16 healthy human adults were recruited for this electrooculography speech study. 20 English pseudowords were designed to vary on confusability along specific features of articulation (place vs manner). All words were controlled for length and voicing. Three task conditions were performed: speech perception,

covert and overt speech production. EEG was recorded using a 64-channel Biosemi ActiveTwo system. EMG was recorded on the orbicularis oris inferior and neck strap muscles. Overt productions were recorded with a high-quality microphone to determine overt production onset. EMG during was used to determine covert production onset. Neuroimaging: Representational Similarity Analysis (RSA), was used to probe the sound- and motor-based neural representations over sensors and time for each task. RESULTS/ANTICIPATED RESULTS: Production (motor) and perception (sound) neural representations were calculated using a cross-validated squared Euclidean distance metric. The RSA results in the speech perception task show a strong selectivity around 150ms, which is compatible with recent human electrocorticography findings in human superior temporal gyrus. Parietal sensors showed a large difference for motor-based neural representations, indicating a strong encoding for production related processes, as hypothesized by previous studies on the ventral and dorsal stream model of language. Temporal sensors, however, showed a large change for both motor- and sound-based neural representations. This is a surprising result since temporal regions are believed to be primarily engaged in perception (sound-based) processes. DISCUSSION/SIGNIFICANCE: This study used neuroimaging (EEG) and advanced multivariate pattern analysis (RSA) to test models of production (motor-) and perception (sound-) based neural representations in three different speech task conditions. These results show strong feasibility of this approach to map how the perception and production processes interact in the brain.

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Loop-mediated isothermal amplification for the detection of cytomegalovirus infection and drug resistance at the point of care[†]

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OBJECTIVES/GOALS: To develop a loop-mediated isothermal amplification (LAMP) assay for the detection of cytomegalovirus (CMV) infection and drug resistance. METHODS/STUDY POPULATION: We designed core and loop primers sets utilizing the NEB LAMP Primer Design Tool. Each set contained four or six primers targeting major-immediate early genes – essential for viral entry/replication – or regions known to confer resistance to the antiviral drug ganciclovir. Optimization of reactions conditions was achieved employing DNA reference materials. Reactions were visualized through a change in color as amplification reactions accumulated. Successful reaction conditions were selected based on specific amplification products in less than 60 minutes. Limits of detection were evaluated as the main performance outcome. RESULTS/ANTICIPATED RESULTS: Genomic data were extracted and used to design a series of LAMP primers (48 total) that aimed to detect specific genomic regions of CMV. Using this strategy, we successfully designed and identified eight primer sets that showed high 100% sensitivity and 100 % specificity, when detecting $> 1.00 \times 10^5$ copies/mL of CMV gDNA. We are in the process of characterizing a new set of primers to determine the diagnostic utility of a LAMP

assay in detecting selected single-nucleotide mutations at the UL97 loci. The expected outcomes at completion include: (1) the identification of LAMP primers to detect drug-resistance mutants, (2) defining optimal conditions for successful reactions, and (3) determining limits of detection for subsequent validation with clinical specimens. DISCUSSION/SIGNIFICANCE: CMV infection remains one of the most dangerous infectious agents for immunocompromised hosts, newborns, and unborn children. This study will describe a proof-of-concept LAMP assay for the genotypic detection of drug resistance in CMV-infected individuals and hence, create new avenues for selection of effective therapies to treat CMV disease.

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Computational methods for predicting drug combinations for targeting KRAS mutations relevant to non-small cell lung cancer

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OBJECTIVES/GOALS: Our goal is to develop a cost-effective approach for precision medicine treatment by providing computational predictions for new uses of currently available FDA approved, and experimental drugs for NSCLC. METHODS/STUDY POPULATION: Cell Lines: A549 (ATCC- CCL-185) Human epithelial Lung Carcinoma cells, H1792 (ATCC-CRL-5895) Human Lung Carcinoma cells. In Vitro Cytotoxicity Assay: A Vybrant[®] MTT Cell Proliferation Assay was used. Colony Formation Assay: NCI-H1792, A549 cells were seeded at a density of 500 cells/ dish, then treated with ARS-1620, Osimertinib. The Computational Analysis of Novel Drug Opportunities (CANDO): Herein, we employed the bioanalytic docking (BANDOCK) protocol within CANDO to calculate the compound-protein interaction scores for a library of 13,218 compounds from DrugBank against a library of 5,317 protein structures from the Protein Data Bank, resulting in a proteomic interaction signature for each compound, and identified Osimertinib as the most likely EGFR/ErbB inhibitor to synergize with ARS-1620. RESULTS/ANTICIPATED RESULTS: ARS-1620 and Osimertinib in combination displays potent anti-tumor activity as evident by a decrease in cell viability with cytotoxicity assays, as well as reduced number of colonies in the colony formation assay for both A549 and H1792 cells. By using CANDO, and cross-referencing the obtained rankings with known experimental information, we have obtained drug predictions within the context of precision medicine. Our preliminary data indicates that EGFR inhibitor Osimertinib may be most structurally similar to KRAS G12C inhibitors overall, compared to other ErbB/ EGFR inhibitors. Validations with human cancer cell lines A549 and H1792 have confirmed that Osimertinib in combination with KRAS G12C inhibitor ARS-1620 may exhibit a synergistic effect in decreasing cellular proliferation and colony formation. DISCUSSION/SIGNIFICANCE: This suggests that this innovative drug combination therapy may help improve treatment outcomes for KRAS G12C(H1792) and KRASG12S(A549) mutant cancers. Cell migration and cell invasion studies in response to treatment with Osimertinib and ARS-1620 are currently ongoing.