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symptoms(features) then to carry on-demand or modulate stimulus-parameters. This study enhances DBS modus-operandi with a variety-of-methods, encapsulates prime-disputes (tasks and tests) for progress of efficient adaptive-closed-loop DBS(ACL-DBS) therapeutic-efficacy. Model-paradigms of basal-ganglion (BG) circuitry disorders pathogenesis, computational enhancement for standard (open-loopDBS), also candidate neural and non-neural neuronal/non-neuronal features of Parkinson`s plus associated management-strategies for ACL-DBS. We determine key-operative tests concerning ideal-DBS, for instance, precise-target point, (ii) better stimulus spatio-temporals-region, building(constructing) the in-silico tests-for-DBS, (iv) detecting detailed motoric-feature-markers, specifically measuring in what way field-potential (i.e.,LFPs) oscillations correlate to developmental-dysfunctions, and simplify how stimulus involves cortico-basal-ganglion thalamic-net-work to create ideal stimulus-signatures. Using ACL-DBS method every Parkinson will experience an early calibration-measurement-period in which parameter-values of management-policy shall be adjusted/fine-tuned to different-qualities. In this connection, strength of neuro-bio-markers in excess-of-time will be of vital-consequence. These neuro-markers can be capable of coping over long-timescale through mystifying-factors as consequent treatment, Parkinson-aging, cycle of the disease. Our study to improves the stimulus-linked neuro-modulatory-plans. Once markers setting is done, the management-strategy must be customized stimulus-patterns corresponding to daily activities plus patients-behavior. In fact, understanding subject-behaviors like gripping, gait, speaking, napping can be improved beyond the purpose of optimum stimulus-model-paradigm. Like, higher-tremor Parkinson`s need lower stimulations while they are in sleep mode, and this is due to the lesser conditional problems. The Parkinson symptoms of disease can be altered marginally, nonetheless dopamine-cells even die; its evolution endures inevitably—inexorably to halt cell-death. The advent of available human-neuron assemblies in organoids possibly will offer a clearer log-on to the means inherent neuronal-downfall with the help of the adaptive closed loop deep brain stimulation devices.

P34.10

Characterizing Parkinson's clinical features in black americans and measuring the effect of non-impact lower body exercise on neuroimaging biomarkers and motor and gait function.

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This study is a collaboration between neuroscientists and exercise scientists to characterize Parkinson's Disease (PD) clinical features in Black Americans and measure the effectiveness of short bouts of eccentric exercise training on reducing PD motor symptoms. The collaboration includes a 12-week exercise intervention with pre-and-post MRI scans on Black Americans recruited by a community research accelerator. The study expects differences in PD clinical features including functional connections between the Substantia Nigra (SN) and the peripheral vagus nerve, the primary connection from the heart to the brain. The study expects that eccentric training will be acceptable to both Black and white participants and will similarly reduce motor and gait symptoms, supported by communication between the Substantia Nigra (SN) and the cerebellum enabled by increased peripheral vagus nerve activity, measured through heart function health.
Conflicting findings on the prevalence and clinical features of PD in the Black community may be due to underrepresentation or may inform researchers how healthy autonomic nervous system (ANS) function is disrupted in PD. Our group has shown eccentric training to reduce PD motor and gait symptoms. We hypothesize this is mediated by engaging the heart-brain axis to enhance SN structure and function.
In this study, 20 Black participants (10 with Parkinson's Disease, 10 age-sex-matched healthy controls) will attend 24 training sessions over 12 weeks, with 2 sessions per week. During the training, participants will have motor and gait symptoms and success in training continuously accessed and later compare for differences between Black and white populations. In controlled studies, such training has improved gait and balance outcomes for 20+ white participants with PD over the past 4 years. Through nonimpact eccentric movement, the reACT trainer engages the lower body, targeting the quadriceps, as individuals safely balance on an oscillating platform holding onto support rails, keeping themselves in an upright fixed position. The study will compare the effects of eccentric training and features of PD neuroimaging biomarkers for Black and white participants, enabling more appropriate representation and generalization of the preliminary behavioral findings and their neural bases in the SN.

P34.11

Predicting progression of Parkinson's disease motor outcomes using a multimodal combination of baseline clinical measures, neuroimaging and biofluid markers

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PD is heterogenous, with diagnosis reliant on clinician assessment, corresponding to subjectivity and consequent high rates of misdiagnosis. Furthermore, forecasting disease progression on an individual basis is limited, contributing to a lack of personalised treatment strategies. Therefore, objective biomarkers of PD progression are critically needed, but must be validated prior to clinical deployment. We assessed the utility of various clinical, neuroimaging and pathological marker measures to predict motor outcome progression up to 5-years follow-up in early PD.
Data was extracted from the Parkinson's Progression Markers Initiative. As a proxy marker of substantia nigra (SN) integrity, manual masking of T2-weighted MRI scans was used to delineate the hypointense region adjacent to the SN. Enhanced hierarchal clustering was performed on Unified Parkinson's Disease Rating Scale (UPDRS) motor outcomes at 5-year follow-up. Models to predict cluster membership were developed via logistic regression and a stratified cross-validation machine learning pipeline comparing various classifiers. The utility of a multi-modal assessment was assessed by comparing two models: 1) only baseline motor assessments as predictors; and 2) incorporating additional measures including prodromal assessments (sleep, olfactory and autonomic function), neuroimaging (proxy SN volume, striatal DaT binding) and biofluid (CSF alpha-syn, p-tau, a-beta, and serum IGF-1) markers at baseline.
Two clusters were identified, with the second cluster (n=79) demonstrating higher rigidity, lower DaT binding, worsened cognitive and motor outcomes and increased mood dysfunction at 5-year follow-up compared to the first cluster (n=221), which displayed tremor dominance. Logistic regression determined that membership in the rigid-dominant cluster was predicted by higher difficulty in motor aspects of living, automatic dysfunction, and p-tau, along with lower smell and alpha-syn: predicting 49.1% of variance

(n=111). This was significantly higher (P < 0.001) than the model omitting additional measures, which accounted for only 27.4% of the variance. This was supported machine learning, whereby the inclusion of additional assessments corresponded to a classification accuracy of 72%, compared to 65% when omitted.
Utilising a multi-modal strategy demonstrated substantial improvements in prediction of 5-year outcomes, suggesting a combination of prodromal, pathological, and imaging markers can be used in conjunction with current clinical assessments to improve diagnosis and prognosis.

P34.12

Local field potentials in Parkinson's disease: Effect of lead type and target, peak detection, and contact selection

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Introduction: Local field potentials (LFP), recorded by deep brain stimulation (DBS) electrodes, in patients with Parkinson's disease (PwPD) provide biomarkers of motor dysfunction, pathophysiologic insights, and are currently leveraged for adaptive DBS commercially in Japan. However, the effect of electrode type and targeted nuclei on LFP measures, in addition to peak association to therapeutic contact selection, are not fully understood. Therefore, the objective of this study was to determine the difference in LFP peak and band power characteristics between the globus pallidus internus (GPI) and subthalamic nucleus (STN), as well as cylindrical and directional leads. The secondary objective was to determine real-world peak detection and the association of peak contact pairings to stimulation contact selection.
Methods: Real-world DBS and LFP data from 48 PwPD (age: 65.1[56.3-71.8] years, sex: 19 female, disease duration: 12.0[7.8-15.0] years) and 96 total nuclei recordings were collected as part of a prospective, post-market study. Peak characteristics and band power amplitude averages were calculated for each nucleus.
Results: Peaks were detected in a total of 76(81.7%) nuclei with a recording and at least 1 peak was detected in 93.3% of patients with bilateral recordings. Peaks were detected in 30/36 directional nuclei and 46/60 cylindrical nuclei (p=0.288). Peak amplitude (p=0.577) and frequency (p=0.962), as well as band power in the low-beta (p=0.104) and high-beta (p=0.213) ranges were similar between lead types. No differences were found in peak detection (p=0.078), amplitude (p=0.281), and frequency (p=0.506), as well as band power in the alpha (p=0.073), high-beta (p=0.314), and gamma (p=0.464) between targets. Therapeutic contact selection fell in between or on the lower contact of the peak bipolar contact pairing in 94.1% of cases.
Conclusion: Lead type appears to have minimal effect on peak detection and LFP characteristics when deployed in a real-world setting. LFPs were also similar between targets, however, the sample size for GPI was small. Importantly, LFP peaks are prominently detectable in real-world settings and demonstrate association to stimulation contact selection in PwPD. These data provide key insights into the real-world feasibility and interpretation of LFPs in PwPD.

P34.13

Real-world local field potential dynamics in patients with Parkinson's disease

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Objective: Local field potentials (LFP) recorded from deep brain stimulation (DBS) electrodes provide salient biomarkers of pathologic oscillatory activity which could be leveraged for clinical implementation. Despite the large body of work on LFPs in patients with Parkinson's disease (PwPD) the longitudinal evolution of LFPs is less explored. Therefore, we analyzed LFPs recorded at routine follow-up visits to determine spectral peak and band power dynamics over time in PwPD and DBS.
Methods: A total of 26 PwPD (age: 67.0[56.8-73.1] years; sex: 8 females; disease duration: 12.0[7.8-15.0] years) with repeated LFP recordings (days between recordings: 33.9[11.0-65.1] were included in this analysis. PwPD with LFP recordings within 2-weeks of macroelectrode implant were labeled as Acute (N=12). Peak amplitude and frequency, in addition to alpha, low-beta, high-beta, and gamma band power, were calculated for each hemisphere.
Results: Peaks were detected in 41/51(80.4%) nuclei with recordings at the initial session and 43/51(84.3%) nuclei at follow-up. Of the patients with bilateral implants (n=26), 24(92.3%) at visit 1 and 25(96.2%) at visit 2 had at least 1 hemisphere with an identifiable peak. No differences were seen in peak amplitude (left hemisphere: p=0.695; right hemisphere: p=0.162) and frequency (left hemisphere: p=0.320; right hemisphere: p=0.576) between visits for the cohort. Right hemisphere low-beta (p=0.018) and bilateral gamma (left hemisphere: p=0.036; right hemisphere: p=0.014) band power demonstrated a significant increase at follow-up. No differences were found in the relative change of peak amplitude, frequency, or band power between patients with acute and chronically implanted macroelectrodes (p>0.05).
Conclusion: Our findings provide early, real-world evidence of LFP peak and band power stability in PwPD. Importantly, peak amplitudes and frequencies demonstrated no differences between visits or between patients with acute and chronic macroelectrode implants. Moreover, peak detection was stable across timepoints. These findings have fundamental implications as LFP recordings in PwPD are proposed to be a salient biomarker for guiding DBS programing and novel stimulation patterns. Nonetheless, continued research, with large samples sizes, is needed to determine the longitudinal dynamics of LFPs taken in real-world clinical settings.