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NEURAL DYNAMICS DURING SLEEP IN PARKINSON'S DISEASE PATIENTS

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Introduction: Parkinson's Disease (PD) is a neurodegenerative disease marked by tremor, body tone changes, and cognitive decline with deficits in motor task learning. Characteristic neural patterns during non-Rapid Eye Movement (NREM) sleep have been correlated with learning procedural motor memory tasks. We seek to understand how the neural dynamics of NREM sleep (e.g., sleep spindles and slow waves) interact with motor learning ability in a neurodegenerative disease process. This information might be used to identify electrical biomarkers that could be therapeutically targeted.
Methods: PD subjects and healthy age-matched controls were identified by physician interview, flyering, and medical chart review. Eligibility requirements for subjects precluded severe cognitive decline and untreated sleep disorders. Baseline sleep characteristics were ascertained via survey data collected prior to and on the day of the sleep study. Subjects were fitted with EEG electrodes prior to an all night polysomnogram. Subjects were also fitted with EMG and EOG electrodes for sleep scoring purposes. Motor tasks were performed prior to and following overnight sleep.
Results: Surveys indicated worse sleep quality among PD subjects compared to age-matched controls prior to their sleep session. Sleep macro-architecture of PD subjects showed a smaller percentage of sleep time in N2/N3 stages, and at the spectral level, there were indications of reduced power for slow waves and spindling. Furthermore, we observed aberrant patterns of coupling between slow waves and spindling in PD subjects.
Conclusion: Our study has implications for sleep as a component of motor skill learning and as a marker for a neurodegenerative movement disorder. NREM sleep rhythms such as sleep spindles and slow waves, and their relationships to one another, are thought to be important in motor learning and memory. Aberrations in these rhythms and their coupling may inform potential therapies to enhance motor learning and mitigate the progression of PD.
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SAMELISANT (SUVN-G3031), BASELINE CHARACTERISTICS FROM A PHASE-2 STUDY EVALUATING EFFICACY AND SAFETY IN PATIENTS WITH NARCOLEPSY

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Introduction: Histamine H3 receptor (H3R) antagonists/inverse agonists increase histaminergic neurotransmission and offer a therapeutic option for the treatment of narcolepsy. Samelisant (SUVN-G3031) is a potent H3R inverse agonist and exhibits very high selectivity over other targets. In orexin knockout mice, samelisant produced wake-promoting and anticataplectic effects suggesting its potential therapeutic utility in the treatment of excessive daytime sleepiness and cataplexy associated with narcolepsy. It showed dose-dependent H3R occupancy at efficacy doses. Safety and tolerability studies in animals and healthy human volunteers suggested a favorable risk/benefit profile for samelisant.Samelisant is being evaluated in a Phase-2, multicenter, double-blind, placebo controlled, parallel-group study in patients with narcolepsy with or without cataplexy (ClinicalTrials.gov Identifier: NCT04072380).
Methods: Eligibility criteria for the study include subjects diagnosed with narcolepsy as per ICSD-3, aged between 18 to 50 years with an Epworth Sleepiness Scale (ESS) score of ≥12 and mean maintenance of Wakefulness Test (MWT) time of <12 min. A total of 171 subjects will be randomized into 3 treatment arms (placebo, samelisant 2 mg and samelisant 4 mg) in a fixed 1:1:1. Further, the randomization will be stratified according to the type of narcolepsy (Type-1 or Type-2). Each subject will receive either placebo or study drug once daily for 2 weeks. The primary efficacy endpoint is change in MWT score from baseline to week 2. Secondary endpoints are change in ESS and Clinical Global Impressions of Severity (CGI-S) from baseline to week 2. Safety will be monitored throughout the study by medical monitor and by an independent data safety monitoring committee. Baseline clinical and demographic data for the currently enrolled study is summarized descriptively. Since the study is blinded, a breakdown of baseline characteristics by treatment group will not be available until after completion.
Results: At the data cutoff date of Nov30, 2021, a total of 108 subjects were randomized in the study. The median age of subjects was 30 years (range: 18-50 years) with mean BMI of 26.4 (range: 18.3- 43.1 kg/m2). Overall, 58% subjects were of narcolepsy type-1, 69% were female and 74% were Caucasian. Mean (SD) baseline values of MWT and ESS were 6.20 (4.53) and 17.17 (2.93), respectively.
Conclusion: Baseline characteristics are consistent with the general narcolepsy population. The study is currently enrolling subjects with narcolepsy and the data readout is expected in Q3 2022.
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CHARACTERIZATION OF OBSTRUCTIVE SLEEP APNEA IN ACTIVE-DUTY US MILITARY PERSONNEL RECEIVING INTERDISCIPLINARY CARE AT THE NATIONAL INTREPID CENTER OF EXCELLENCE

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Introduction: Among active-duty service members (ADSMs), obstructive sleep apnea (OSA) is associated with decreased quality of life and military readiness/retention. Limited evidence suggests mild traumatic brain injury (mTBI) patients have increased OSA incidence, but little is known about the underlying physiology. This study aims to characterize OSA in treatment-seeking ADSMs with a history of remote mTBI and/or persistent neurobehavioral symptoms to improve detection and early intervention.
Methods: This is a retrospective analysis of data collected from ADSMs attending the National Intrepid Center of Excellence