Home-Based EEG Detection of REM Sleep Without Atonia as a Methodological Biomarker of Neurodegenerative Risk

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Methodological Issue Being Addressed Early manifestations of neurodegenerative disease are difficult to detect, yet sleep pathology is both common and clinically informative. REM dysregulation is one of the most salient manifestations of this pathology, particularly REM Behavior Disorder in, though not limited to, alpha-synucleinopathies. Traditional RBD assessment relies on detecting REM sleep without atonia (RSWA)—a prodromal biomarker of RBD, Parkinson's disease, and other alpha-synucleinopathies— using polysomnography (PSG) with electromyography (EMG) leads. We propose that REM-related disturbances and broader sleep architecture abnormalities can instead be captured using EEG-based sleep monitors that clinical trial participants can operate autonomously at home over extended time periods. Moreover, automated detection of muscle artifacts during REM sleep from these EEG recordings may enable identification of RSWA. This work addresses the methodological challenge of quantifying RSWA from an at-home, wireless EEG wearable device without requiring additional sensors or in-lab visits.

Introduction We propose and evaluate a methodological framework for deriving RSWA metrics from dry-electrode EEG signals recorded in the home environment using an FDA cleared EEG-based sleep monitor. The approach aims to enable longitudinal, low-burden monitoring of RSWA as an early indicator of brainstem dysfunction associated with α-synucleinopathies.

Methods In this preliminary assessment, we evaluated longitudinal sleep EEG data obtained from patients with Parkinson's Disease who participated the CVN424-203 Phase II study (n=30, 245 nights). This patient population has an elevated incidence of RSWA with 6 having a prior RBD diagnosis. REM sleep was automatically identified using an FDA-cleared sleep staging algorithm. Within REM, algorithms were tested to identify EMG artifact. An RSWA Index was computed as the proportion of 3-second mini-epochs exhibiting ≥4x baseline variance in the 30–50 Hz band, reflecting elevated scalp EMG activity (frontalis, temporalis, and occipitalis). Recordings with an RSWA index > 2% were classified as "RSWA-positive" and algorithmic performance was evaluated on all recordings with ≥60 minutes of REM based on prior RBD diagnosis and inter-recording reliability.

Results The RSWA Index achieved modest single night predictive power (sensitivity =63%, specificity=74%, AUC=0.75). Examining cross night reliability (ICC=0.60) we identified 12/24 RBD-negative participants as having perfect specificity (0% RSWA-positive) while 4/24 were identified as likely non-diagnosed RSWA (>80% RSWA-positive). A post-hoc median split on

baseline RSWA index revealed lower MDS-UPDRS scores in the RSWA-negative sub-group across Part I, II, and III. These findings demonstrate the feasibility of estimating RSWA from scalp-derived EMG activity and highlight its potential as a digital biomarker for early neurodegenerative change.

Conclusion This methodological framework enables the use of advanced neurophysiological diagnostics that were previously impossible in decentralized trials. RSWA detection (along with evaluation of other sleep pathologies) offers insight into the dysfunction of deep sleep networks, providing a scalable means of identifying prodromal sleep-related dysfunction in a variety of neurodegenerative diseases. Leveraging multi-night recordings can improve overall sensitivity and specificity in diagnosing RSWA over single night “gold-standard” PSG. Such at-home monitoring could improve trial stratification with a precision approach to patient subtype-specific treatment effects, facilitate longitudinal tracking of early neurodegenerative processes, and support large-scale observational studies targeting the preclinical window of disease evolution.

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Disclosures TS, NT, DS, JN, JP, JD, and DM are employed by Beacon Biosignals. JD is employed by Clintrex. SV was employed at Cerevance Beta when this work was performed