A Novel Method Assessing REM Sleep Without Atonia in Parkinson's Disease Using the Waveband, an At-Home EEG Sleep Monitoring Device

Timothy C. Sheehan[1], Nurkurniati Tjiptarto[1], Dave Samuelson[1], Jayne Nerrie[1], Jay Pathmanathan[1], Jordan Dubow[2], Jacob Donoghue[1], Sagar Vaidya[3], David W. Matthews[1]

1 Beacon Biosignals, Boston, MA; 2 CLINTREX Research LLC, Sarasota, FL; 3 Cerevance Beta Inc.

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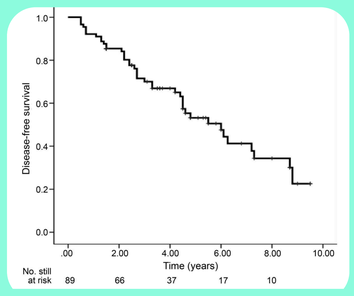
Introduction

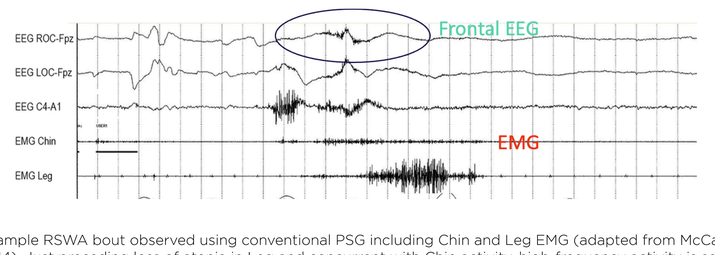
Background

- Traditional RBD assessment relies on detecting REM sleep without atonia (RSWA) using polysomnography (PSG) with electromyography (EMG) leads.
- Automated detection of muscle artifacts during REM sleep using an at-home EEG-based sleep monitor may enable identification of RSWA.
- Because RBD often goes undiagnosed for many years, early detection from accessible at-home measures is essential for improving patient outcomes and for stratifying early- vs late-stage PD patients in clinical trials.



In patients with RBD, conversion risk to neurodegenerative synucleinopathy (including PD) is 30% at 3 years and 66% at 7.5 years. Survival curve (adapted from Postuma et al., 2015) above.

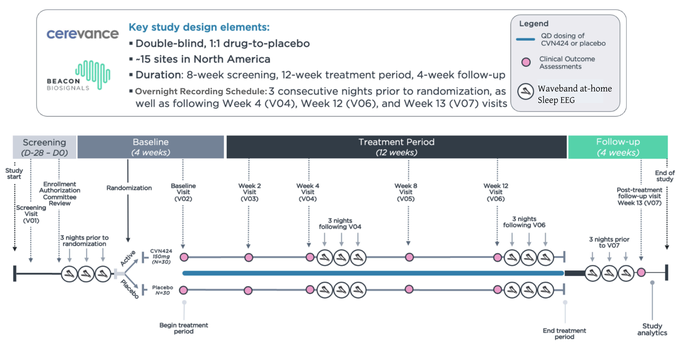
Conventionally, diagnosis of RSWA or RBD requires in-clinic PSG including chin, arm, and leg EMG. While in conventional PSG leg and chin EMG activity provided the most reliable signals of muscle activity during REM, concurrent muscle artifact on anterior EEG channels also revealed a strong signal.



Example RSWA bout observed using conventional PSG including Chin and Leg EMG (adapted from McCarter et al. 2014). Just preceding loss of atonia in Leg and concurrent with Chin activity, high-frequency activity is seen in frontal electrodes.

Methods

Longitudinal sleep EEG data was obtained from patients with Parkinson's disease who participated in the CVN424-203 Phase II study (n=30, 245 nights). This patient population has an elevated incidence of RSWA with 5 having a prior RBD diagnosis. REM sleep was automatically identified using an FDA-cleared sleep staging algorithm.



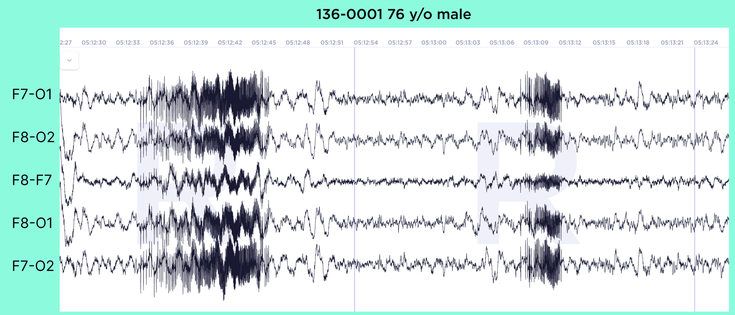
Trial schematic for Phase II study. Overnight at-home EEG was collected in sets of three consecutive nights at baseline, across two visits during the treatment period, and during follow up.

Waveband headband montage includes two frontal and two occipital contacts and is optimized for sleep comfort.

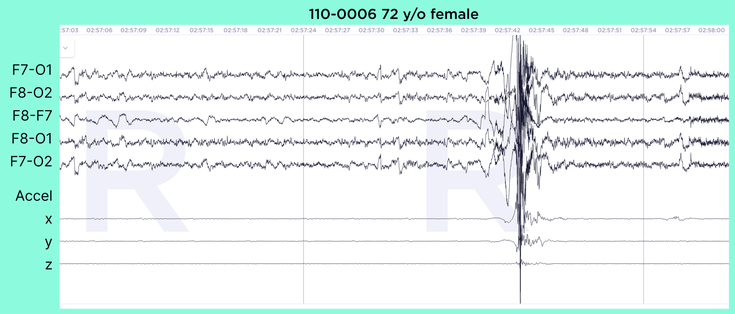
Examples of muscle artifacts during REM

Example data recorded using the Waveband from two participants diagnosed with RBD. During REM sleep, as classified by sleep staging algorithm, we identify RSWA featuring either tonic muscle artifact on EEG channels (top) or clear evidence of movement artifact captured on both EEG and accelerometer channels (bottom).

136-0001 76 y/o male



110-0006 72 y/o female



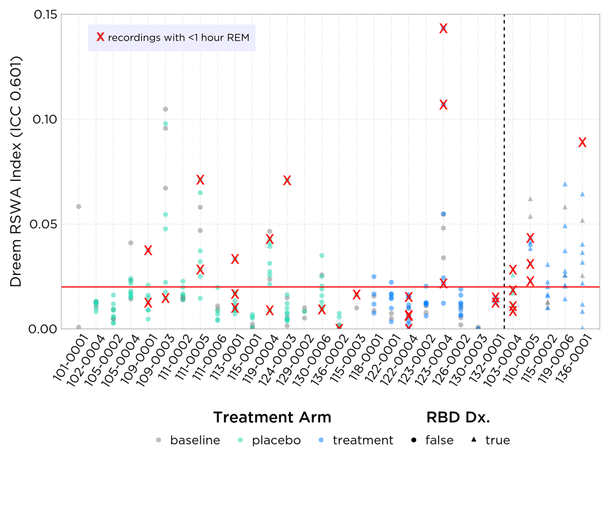
Procedure

An RSWA-index was calculated based on AASM criteria:

- F7-O1 and F8-O2 EEG were filtered to the 30-50 Hz band (4th order Butterworth)
- Variance was computed in 3 s windows
- For each contiguous REM period:
  - Baseline variance was defined as the 30th percentile
  - The mean % of 3 s periods that exceeded 4x baseline was counted
- The average % across all REM periods in a recording is the RSWA index

For analysis purposes, all recordings with an RSWA index >2% RSWA positive were considered RSWA+. Performance was more reliable on nights with >1 hour of REM sleep and analysis was focused on this subset of recordings.

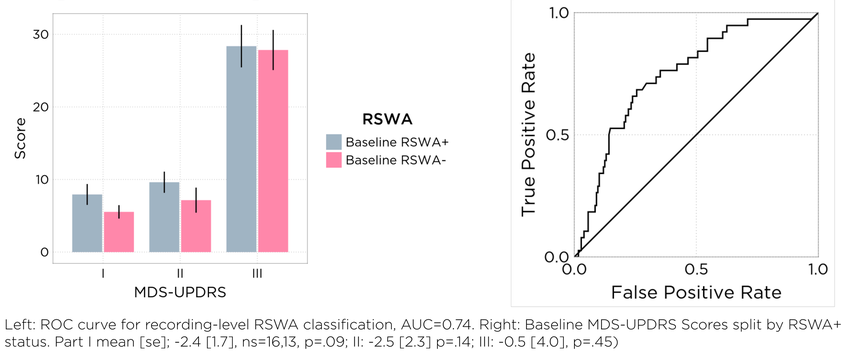
Results



The RSWA Index achieved reliable performance including:

- **Single-night classification:** sensitivity 63%, specificity 74%, AUC 0.75
- **Cross-night Reliability:** ICC 0.60 across nights
- **Stable Phenotyping of RBD-:**
  - 12/25 consistently RSWA−
  - 4/25 likely undiagnosed RSWA (>80% RSWA+ nights)

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 (differences not significant). 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.



Left: ROC curve for recording-level RSWA classification, AUC=0.74. Right: Baseline MDS-UPDRS Scores split by RSWA+ status. Part I mean [se]; -2.4 [1.7], ns=16,13, p=.09; II: -2.5 [2.3] p=.14; III: -0.5 [4.0], p=.45)

Discussion

This study found:

- At-home EEG allows detection of muscle artifact indicative of RSWA. This RSWA index:
  - Was associated with prior RBD diagnosis as well as baseline disease severity
  - Was consistent and potentially prognostic, with 4/24 non RBD patients showing reliable RSWA.
- At-home sleep monitoring can be used for patient stratification and repeated measures can improve sensitivity and specificity.

Limitations:

- Home-based EEG sleep monitoring allows decentralized and longitudinal monitoring of RSWA, but scalp muscles may be less sensitive than muscles monitored on gold standard PSG (including chin and arm/leg channels). Future work must look at sensitivity and specificity differences between EEG methods and PSG with EMG leads.

Future Directions:

- RSWA detection from sleep EEG may be useful for initial diagnosis, clinical trial enrichment, or as a treatment response biomarker.
- Validation work leveraging simultaneous PSG could improve predictive power.

Conclusions

- **RSWA can be directly observed in high-frequency activity in both in-clinic PSG and ambulatory dry EEG.**
- **A derived RSWA index was predictive of RBD status and was reliable across repeated measures from an at-home, reduced-montage EEG device.**
- **Post hoc subgroup analysis by RSWA status revealed baseline differences in disease severity, which may inform response to treatment.**

References

1. Postuma, Ronald B., et al. "Parkinson Risk in Idiopathic REM Sleep Behavior Disorder: Preparing for Neuroprotective Trials." Neurology, vol. 84, no. 11, Mar. 2015, pp. 1104–13
2. McCarter SJ, St Louis EK, Duwell EJ, Timm PC, Sandness DJ, Boeve BF, Silber MH. Diagnostic thresholds for quantitative REM sleep phasic burst duration, phasic and tonic muscle activity, and REM atonia index in REM sleep behavior disorder with and without comorbid obstructive sleep apnea. Sleep. 2014 Oct 1;37(10):1649-62. doi: 10.5665/sleep.4074