to determine the fractal patterns. Specifically, the activity fluctuation (around the trend) was computed at multiple timescales (n) ranging from 3-600 min. An exponential function with a variable scaling factor α was used to fit the local fluctuation function with respect to n. The α(n) that represented the temporal correlations was fed into a convolutional neural network (CNN) model whose output was further used as the input of a Cox proportional hazards model to predict the time to incident Parkinsonism. Covariates at baseline considered include age, sex, education, cognition, motor function, chronic health assessment, and actigraphy-derived measures including physical activity level, rest-activity/activity-rest transition probabilities, interdaily stability, and intradaily variability.

Results: There were 412 subjects who developed parkinsonism (in 4.75±3.13 [SD] years from baseline). Based on the gradient of hazard function (with respect to α) from the CNN model (estimated feature importance), the α in three timescale regions (i.e., 3-5 min, 12-20 min, and 270-600 min) contributed significantly to the prediction. Consistently, in separate Cox models with adjustment of age, sex, and education, the mean α at timescales 3-5 min was inversely associated with incident parkinsonism (for 1-SD increase, hazard ratio [HR]=0.82, 95% CI: 0.78-0.92, p<0.0001); The mean α at timescales 270-600 min was also inversely associated with incident Parkinsonism (HR=0.87, 95% CI: 0.78-0.96, p=0.008); And the mean α at timescales 10-25 min was marginally, positively associated with incident Parkinsonism (HR=1.10, 95% CI: 0.99-1.22, p=0.08).

Conclusion: Altered temporal correlations at specific timescales in motor activity predicted the risk of Parkinsonism.

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ISOLATED REM SLEEP BEHAVIOR DISORDER IS ASSOCIATED WITH 24-HOUR RHYTHM DISRUPTION

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Introduction: Isolated REM sleep behavior disorder (iRBD), the loss of motor inhibition during REM sleep, is a symptom of prodromal Lewy body disease, with over 80% of iRBD patients eventually phenoconverting to Parkinson's disease or Dementia with Lewy bodies. Rest-activity rhythm disruption, also an established predictor of Parkinson's disease, has not been well characterized in patients with iRBD. Here, we tested the hypothesis that accelerometer-based measures of 24-hour rhythms would indicate greater fragmentation and variability in patients with iRBD relative to matched healthy controls.

Methods: N=36 patients with iRBD recruited from the Stanford Sleep Clinic had 24-hour activity continuously monitored for (mean ± SD) 25.3 ± 8.4 days using an Axivity wristworn device. A control dataset of age, sex, and body mass index matched healthy older adults (N=126) was selected from the UK Biobank accelerometer dataset. Raw accelerometer data were processed using the GGIR, nparACT, and ActCR software packages in R, with a focus on nonparametric and 5-parameter cosinor measures of 24-hour rhythms. Functional PCA analyses (fPCA) were applied to detect overall differences in 24-hour rhythms and during sleep.

Results: Patients with iRBD had lower interdaily stability and higher intradaily variability than controls (IS, Cohen's d=-1.15, Mann-Whitney test p<0.001; IV, d=0.46, p=0.04). Cosine amplitude was lower in iRBD patients (d=-0.22, p=0.001), but mean activity (mesor) did not differ (d=0.03, p=0.31), suggesting differences in rest-activity patterns rather than overall activity levels. A shape naïve approach utilizing fPCA indicated that increased activity during the night may explain overall rhythm differences observed in iRBD.

Conclusion: Multiple metrics of rest-activity rhythms support the hypothesis that 24-hour rhythms are disrupted in iRBD. It remains to be determined whether rhythm fragmentation in iRBD reflects higher activity levels during REM sleep, or if dysfunctional rhythms represent the direct effects of degenerating sleep-wake regulating circuits, indicating the early stages of Lewy body disease.

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THERMONEUTRAL TEMPERATURE EXPOSURE INCREASES SLOW-WAVE SLEEP IN THE 3XTG-AD MOUSE MODEL OF ALZHEIMER'S DISEASE.

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Introduction: There is growing evidence that disordered sleep, which is known to be associated with Alzheimer's disease (AD), may accelerate neuropathology, thus promoting a vicious cycle. Strategies for improving sleep quality may slow disease progression. Here we investigate the feasibility of sleep enhancement through ambient temperature regulation and examine the effect on amyloid pathology.

Methods: Female 3xTg-AD mice (~12 m.o.) were instrumented for EEG/EMG monitoring. After a week-long baseline, one half of the mice (n=8, EXPT) were exposed to stepwise diurnal increases in ambient temperature (Ta) to reach 30oC (thermoneutral for mice) during the light phase while the rest (n=8, CTRL) remained at room temperature (22oC). Vigilance state – i.e., Wake, REM, NREM, and slow wave sleep (SWS) within NREM – was scored in 4-second epochs and sleep metrics were computed.

Results: SWS percentage became significantly greater (p<0.05) in the light phase for EXPT mice over the course of treatment. These effects suggest better sleep consolidation and greater sleep depth with thermoneutral warming. After four weeks of treatment, the animals were euthanized, and the brains removed to assay amyloid pathology by ELISA. We found that thermoneutral warming caused a significant reduction in both Aβ40 and Aβ42 in the hippocampus, but not in the cortex.

Conclusion: These data imply that thermoneutral warming might have some regional specificity in its effects. The effects appear to be specific to some brain areas more than others, with implications for the cognitive and neuropathologic changes found in AD. Furthermore, since SWS and REM support memory, future studies should investigate the effects of thermoneutral enhancement of SWS and REM on cognition.

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