revealed that performance plateaued after one week of actigraphy. Best single feature "short immobile bursts" achieved an AUC of 0.958, a sensitivity of 94.3%, and a specificity of 78.6%. In this population, RBD-I item 3 best discriminated between groups with an AUC of 0.892, a sensitivity of 91.4%, and a specificity of 85.7%. The combination of a positive RBD-I item 3 and a positive actigraphy-based classification achieved a sensitivity of 88.6% and a specificity of 96.4%.

Conclusion: High-frequency actigraphy using machine learning detects iRBD with high accuracy. Addition of a single RBD question to this procedure increased specificity. These results need to be validated in a larger sample and lay the groundwork for an ambulatory screening paradigm in the general population.

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PROTEOMIC APPROACH FOR UNDERSTANDING THE MECHANISMS OF PERIODIC LIMB MOVEMENTS AND RESTLESS LEGS SYNDROME

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Introduction: Periodic limb movements (PLMs) are episodes of involuntary, repetitive muscle movements that are highly associated with restless legs syndrome (RLS). Although PLMs and RLS are reportedly two separate phenomena, both are tightly correlated and may result from a similar pathology. The present study profiled plasma protein biomarkers of PLMs and RLS to contribute to the identification of mechanisms associated with each disorder/trait.

Methods: The SomaScan highly multiplexed aptamer assay was used to profile 5,000 proteins in 24–48-hour old EDTA plasma samples from the Stanford Technology Analytics and Genomics in Sleep (STAGES) study. PLMs per hour (PLMI) were derived from overnight polysomnography and RLS was classified based on affirmative responses to questions of the Alliance Sleep Questionnaire. Three linear regression models were conducted to examine significant protein markers of 1) PLMI in the sample as a whole; 2) PLMI controlling for the presence of RLS; and 3) RLS without PLMs (i.e.,PLMI<5). All models included log2-normalized relative protein expression as the dependent variable and important covariates such as age, gender, BMI, sample storage time, and blood draw period. False discovery rate (FDR) to control for multiple testing was applied with an a-priori p-value of 0.05 for identifying significant associations.

Results: PLMI was significantly associated with 253 proteins (219 positive,34 negative). The inclusion of RLS in the model mitigated the significance of most proteins, and only 8 proteins remained significant. Negatively associated proteins (LEAP-1, Ferritin, SELH, Caspase-8) included functions related to iron storage, absorption, and delivery and negative regulation of inflammatory/immune responses. Positively associated proteins (SFRP4, RANTES, CathepsinA, DKK1) included proteins with functions related to immune response, inflammatory response, bone formation, and protein stability. RLS without PLMs was associated with 7 upregulated proteins (megalin, RUFY1, TADBP, ANGL7, LRTM2, SNAPN, STOM) with functions related to vitamin D metabolism, calcium and zinc binding, circadian rhythm regulation, and calcium-dependent neurotransmitter secretion.

Conclusion: These large proteomic analyses identified independent differential protein expressions for PLMs and RLS that suggest different pathophysiological contributions.

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ISOLATED REM SLEEP WITHOUT ATONIA FOLLOWING COVID-19 INFECTION: A CASE-CONTROL STUDY

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Introduction: REM sleep without atonia (RSWA) is the neurophysiological substrate of REM sleep behavior disorder (RBD), a form of prodromal parkinsonism in most older adults. Isolated RSWA (without clinical RBD) elevation was demonstrated recently in older adults following SARS-CoV2 (COVID-19) infection, but comparison to controls was not reported. We aimed to comparatively analyze RSWA between patients with previous COVID-19 infection and COVID-19 negative controls.

Methods: 25 patients with previous COVID-19 infection were compared to 25 age-sex matched controls who tested negative for COVID-19 prior to polysomnography. Patients receiving medications known to increase RSWA were excluded. We reviewed medical records to determine clinical features and quantitatively analyzed RSWA in the submentalis (SM) and anterior tibialis (AT) muscles for phasic, tonic, and "any" muscle activity, phasic burst duration, and the automated REM atonia index. Non-parametric analyses compared clinical and polysomnographic features between groups, with combined SM and AT RSWA as the defined primary outcome. The comparative frequency of COVID-19 positive cases and COVID-19 negative controls who met or exceeded proposed isolated RSWA thresholds was also determined.

Results: COVID-19 patients had significantly greater RSWA than COVID-19 negative controls in the combined SM and AT muscles ($p = 0.00076$). Most other RSWA metrics were also higher in COVID-19 patients than controls ($p<0.03$), except tonic muscle activity, phasic burst durations, and RAI. Isolated RSWA occurred more frequently in COVID-19 (9 patients, 36%) than controls (3, 12%; $p>0.05$). No patients had a clinical history or polysomnographic evidence for parasomnia behavior or a primary neurological condition.

Conclusion: Quantitative RSWA amounts were comparatively greater in COVID-19 patients than in COVID-19 tested-negative controls, suggesting association of previous COVID-19 infection with central nervous system brainstem dysfunction in the region of the dorsal pons and/or ventromedial medulla. Further prospective studies are needed to determine whether RSWA is a predisposing influence to, or consequence of, COVID-19 infection in these patients, and whether COVID-19 survivors might harbor neurodegenerative risk or disease markers.

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