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AUTONOMIC REFLEX TESTING CONFIRMS AUTONOMIC DISTURBANCES IN A COHORT OF PATIENTS WITH IDIOPATHIC HYPERSONMIA
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Introduction: Symptoms suggestive of autonomic nervous system (ANS) dysfunction have been previously described in patients with idiopathic hypersomnia (IH), however, objective ANS reflex testing data has not been reported. We aimed to better quantify symptoms of ANS dysfunction in a cohort of patients with IH through the use of standardized ANS reflex testing.

Methods: Patients diagnosed with IH based on ICSD-3 criteria using overnight video polysomnography and multiple sleep latency testing (MSLT) were consecutively enrolled in our study, regardless of ANS symptoms. All patients underwent ANS reflex testing, including measures of parasympathetic (heart rate variability with deep breathing and Valsalva ratio) and sympathetic adrenergic function (Valsalva blood pressure response and 10-minute head-up tilt at an angle of 70 degrees) with continuous blood pressure and heart rate monitoring. Eleven patients also underwent measures of sympathetic cholinergic function (quantitative sudomotor axon reflex testing). All medications that affect ANS function were held prior to ANS testing, including wake-promoting medications and sodium oxybate.

Results: Twenty patients with IH were enrolled. Fifty percent (10/20) were long sleepers (>11hrs). Mean sleep onset latency and number of sleep onset REM periods (SOREMs) on MSLT were 6.9 (± 3.1) mins and 0.2 (± 0.4), respectively. Mean duration of IH symptoms prior to the date of ANS testing was 6.3 (± 8.1) yrs. Eighty-five percent (17/20) of patients had abnormal ANS testing. Of these, 75% (15/20) had sympathetic adrenergic impairment, 64% (7/11) had sympathetic cholinergic impairment, and 5% (1/20) had parasympathetic impairment. Fifty-five percent (11/20) of patients were diagnosed with postural tachycardia syndrome (POTS), 45% (5/11) with small fiber neuropathy, 5% (1/20) with inappropriate sinus tachycardia and 15% (3/20) with neurally-mediated syncope. Seventy percent (14/20) of patients reported orthostatic intolerance regardless of autonomic diagnosis.

Conclusion: ANS dysfunction was common and severe in our cohort of IH patients, affecting all domains of ANS reflex testing, with more prominent impairment in sympathetic domains. POTS was the most common comorbid diagnosis, and most patients reported orthostatic intolerance. There was no association with IH disease duration, though our sample size was limited. Future studies will focus on ANS testing in larger cohorts of IH patients, specifically on shared pathophysiological mechanisms of hypersomnia and ANS dysfunction.

Support (If Any):
(SXB) and experiences with the second nightly SXB dose in patients who switched from twice-nightly SXB to ON-SXB.

Methods: Participants enrolled in the open-label extension/switch study (RESTORE) were aged ≥16 y with a confirmed diagnosis of narcolepsy type 1 or 2 from the phase 3 REST-ON trial or receiving stable doses of twice-nightly SXB for ≥1 month. Initial ON-SXB doses for switch patients were equivalent/closeto their previous total nightly SXB dose. Patient preference questionnaires were completed by switch patients 3 months after switching and nocturnal adverse event (AE) questionnaires at baseline.

Results: At an interim data cutoff date of November 22, 2021, 46 participants completed patient preference questionnaires; 93.5% (43/46) preferred ON-SXB to twice-nightly SXB. Nocturnal AE questionnaires were completed by 76 switch participants. In the 3 months before switching to ON-SXB, 62% (47/76) had unintentionally missed their second twice-nightly SXB dose, with 86% experiencing worse narcolepsy symptoms the next day. Forty percent (30/76) reported taking their second twice-nightly SXB dose >4 h after the first dose, with 47% reporting being somewhat, quite a bit, or extremely groggy/unsteady the next morning. For 76% (58/76), taking a second nighttime dose was somewhat, quite a bit, or extremely inconvenient. Additionally, 91% (69/76) reported that they had arisen from bed after the second dose; of these, 5 reported associated falls, and 3 had injuries. Anxiety (25%) and the need for someone else to wake them (21%) were also reported. One participant reported that the medication was missing when they awoke for the second dose.

Conclusion: These interim data indicate that individuals with narcolepsy and prior experience taking SXB prefer ON-SXB to twice-nightly SXB. Treatment burden from the second nightly SXB dose may be alleviated with ON-SXB.

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SLEEP ONSET REM PERIOD (SOREMP); BEYOND THE DIAGNOSTIC MARKER
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Introduction: Shortened mean sleep latency and multiple Sleep Onset REM Period (SOREMP) on MSLT has been used as a characteristic marker for narcolepsy and incorporated in all editions of the International Classification of Sleep Disorders. Epidemiologic studies have shown that SOREMP could occur in general population especially those with sleep insufficiency and shift work. However the physiological meaning of SOREMP besides the diagnostic marker is not well clarified. We searched for subjective and objective sleep variables independently associated with the number of SOREMPs.

Methods: Participants were 769 consecutive sleepy patients or controls who gave written informed consent and underwent PSG followed by MSLT in Seiwa Hospital or Koishikawa Tokyo Hospital from October 2014 to November 2021. We excluded those with obvious nocturnal sleep disturbances (AHI>10, PLMI>15), with medication affecting sleep and with severe first-night effect at the time of PSG. We analyzed data from resultant 580 participants (male/female=312/268, age 25.3±8.4 years old, BMI 21.6±3.3). They were subdivided into 4 groups according to the number of SOREMPs on MSLT (used as ordinal scale). Subjects with 3 or more SOREMPs were merged into one group to increase number enough for statistical analyses. We dichotomized participants into narcolepsy type 1 (NT1) (n=50) and others (n=530) to adjust the effect of NT1 diagnosis. Epworth Sleepiness Scale (ESS) as well as conventional sleep variables on PSG and MSLT were compared by ANOVA and variables associated with the number of SOREMPs were further analyzed by regression analyses to determine the independent association after adjustment of covariates (age, sex, BMI and dichotomized diagnosis).

Results: Number of SOREMPs on MSLT was positively associated with ESS score (p=0.010), Total Sleep Time (TST) (p=0.03), REM %TST(p<0.001), and negatively associated with Sleep Latency (p<0.01), REM Latency (p<0.001), MSLT mean Sleep Latency (p<0.001) and MSLT REM Latency (p<0.001) and subjective sleep latency on PSG night.

Conclusion: Our data indicate that the number of SOREMPs have physiological significance besides narcolepsy diagnosis. More SOREMPs reflect higher sleep propensity and REM propensity as well as subjective sleepiness. The number of SOREMPs can be a marker reflecting one aspect of sleepiness. Our study will also contribute to better understand the meaning of SOREMP in diagnostic criteria of central disorders of hypersomnolence.

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