https://doi.org/10.5664/jcsm.9722

JCSM | Journal of Clinical Sleep Medicine

COMMENTARY

Subjective-objective sleepiness discrepancy in adult-onset myotonic dystrophy type 1

Commentary on Sansone VA, Proserpio P, Mauro L, et al. Assessment of self-reported and objective daytime sleepiness in adult-onset myotonic dystrophy type 1. *J Clin Sleep Med*. 2021;17(12):2383–2391. doi:10.5664/jcsm.9438

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Myotonic dystrophy type 1 (DM1) is the most common adult-onset muscular dystrophy, caused by the expansion of a cytosine-thymine-guanine (CTG) repeat of the myotonic dystrophy protein kinase (*DMPK*) gene; DM1 is a slowly progressive neuromuscular disease that affects the brain and multiple organ systems.[1] DM1 is characterized by myotonia (delayed muscle relaxation after contraction), skeletal muscle weakness, cataracts, early balding, insulin resistance, cardiac conduction abnormalities, and sleep-disordered breathing (SDB) leading to progressive respiratory failure.[1]

Excessive daytime sleepiness (EDS) is one of the most frequent nonmuscular symptoms reported by patients with DM1.[2] EDS in DM1 can be a presenting symptom that develops years before the weakness or SDB appears and persists after the SDB has been treated. Up to 88% of adults with DM1 have reported EDS,[3] but studies have shown that subjective (self-reported) sleepiness using self-report instruments has a much lower frequency[4] and objective sleepiness using the Multiple Sleep Latency Test (MSLT) often has an even lower frequency.[5]

In this issue of the *Journal of Clinical Sleep Medicine,* Sansone et al[6] conducted a prospective study of the prevalence and features of EDS in 63 patients with adult-onset DM1 using different self-report sleep assessment tools for EDS and fatigue and objective sleepiness using the MSLT. They found a significant subjective (self-reported)–objective sleepiness discrepancy: Far more patients had objective sleepiness on the MSLT (48% had an abnormal mean sleep latency [MSL] < 8 minutes); only 33% had an Epworth Sleepiness Scale (ESS) score > 10. Moreover, concordance between the abnormal ESS and MSLT results was present in only 21% of patients; 40% of patients had discordant results, abnormal in only 1 of the 2 sleepiness measures.

Why is there such a significant subjective–objective sleepiness discrepancy in DM1? Could patients be misidentifying fatigue as sleepiness? Fatigue is another common concern in DM1,[7–9] and some studies have reported that patients with DM1 have difficulty discriminating between fatigue and sleepiness.[10,11] In the current study reported by Sansone et al, data analysis of fatigue (using scales validated for DM1) showed that fatigue was equally common in the patients with or without objective sleepiness on the MSLT (40% vs 42%). However, more patients with self-reported sleepiness (ESS > 10) also reported fatigue than did those with ESS ≤ 10 (49% vs 37%). DM1 over time also affects brain and cognition,[12] but cognitive testing has confirmed that patients can reliably complete the questionnaires. Although SDB (apnea-hypopnea index > 5 events/h) was present in 68% of the study cohort, there were no relationships between SDB and EDS measures in the current study. Other studies have failed to find a direct correlation between sleepiness and SDB or SDB severity in DM1.[5,13–15]

Perhaps an even better explanation for self-reported–objective sleepiness discrepancy in DM1 is that sleepiness is a multidimensional construct, and the self-reported ESS and objective MSLT measure sleep propensity quite differently.[16,17] The MSLT measures physiological sleepiness and the ability of an individual to fall asleep quickly when encouraged to do so, whereas the ESS asks an individual to assess his or her ability to stay awake in soporific situations of varying severity and risk. The ESS is greatly influenced by a person's ability to be aware, recognize, and report sleepiness.[18] A systematic review of the ESS measurement properties in populations with sleep disorders confirmed the correlation between the ESS and MSLT to be weak at best ($P = –.27$).[17] Increasing the pathological ESS threshold to ≥ 13 enhanced the predictability of the correlation with objective sleepiness in a survival analysis.[19]

Sansone et al[6] also provided interesting observations about the clinical, polysomnogram (PSG), and MSLT characteristics in DM1, which are sometimes similar but usually very different from those of narcolepsy type 1. Patients with DM1 more often describe EDS as having features more like those reported by patients with SDB than with narcolepsy. Daytime sleepiness in DM1 occurs mostly in monotonous situations and is not improved by naps. Nine of 30 patients with MSL < 8 minutes and 4 with MSL ≥ 8 minutes had ≥ 2 sleep-onset rapid eye movement (REM) periods (SOREMPs) on the MSLT. Patients

with DM1 who had MSL < 8 minutes on the MSLT had a higher total sleep time and sleep efficiency and lower wake after sleep onset according to PSG. Four patients with SOREMPs exhibited stage 1 sleep (N1) to REM sleep transitions, which are most often seen in patients with narcolepsy type 1.

An earlier case-control study recorded PSG and the MSLT in 40 consecutive adults with DM1 and 40 age- and sex-matched control patients.[5] They found during a structured clinical interview that 80% reported EDS but only 31% had ESS scores > 10, and 13% had MSL < 8 minutes on the MSLT. The number of SOREMPs differed between patients with DM1 and the control patients; at least 1 and 2 or more SOREMPs were present in 47.5% and 32.5% of patients with DM1, respectively, and only 1 control patient had a SOREMP. Higher percentages of slow-wave sleep and REM sleep were found in DM1. Patients with DM1 had significantly more periodic limb movements during wakefulness, periodic limb movements during sleep in both non-rapid eye movement sleep and REM sleep, and periodic limb movements during sleep–associated microarousals. Higher REM sleep density was found in DM1 with similar tendencies for either REM sleep without atonia or phasic electromyography activity. Nocturnal SOREMPs in overnight PSG have been observed in some patients with DM1,[20] another PSG finding thought to be more characteristic for narcolepsy type 1. Cerebrospinal orexin levels are usually normal in patients with DM1 with EDS.[2,5,13,15,21]

Self-reported measures screening for EDS in DM1 are needed because PSG and the MSLT are not readily available to all patients. Identifying EDS in DM1 is important. Cross-sectional studies show that patients with DMI with EDS and fatigue (or EDS alone) are significantly more prone to psychological distress and are less optimistic, active, empathetic, organized, and motivated than those without these symptoms[4] and are also less likely to work.[8,22] A hybrid approach that uses both objective and self-reported measures may improve the quantification of EDS. It is imperative to explore novel and optimal measures to quantify sleepiness in DM1 because EDS can negatively impact the quality of life in these patients.

CITATION

Gorantla S, Blume G, Grigg-Damberger M. Subjective-objective sleepiness discrepancy in adult-onset myotonic dystrophy type 1. *J Clin Sleep Med.* 2021;17(12):2351–2352.

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SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication October 4, 2021
Submitted in final revised form October 5, 2021
Accepted for publication October 5, 2021
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DISCLOSURE STATEMENT

Work for this commentary was performed at the University of Illinois College of Medicine at Peoria. The authors report no conflicts of interest. All authors read and approved the final manuscript.