CLINICAL REVIEW

Sleep propensity in psychiatric hypersomnolence: A systematic review and meta-analysis of multiple sleep latency test findings

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A R T I C L E   I N F O

S U M M A R Y

Hypersomnolence plays a sizeable role in the course and morbidity of psychiatric disorders. Current sleep medicine nosology is reliant on the multiple sleep latency test (MSLT) to segregate hypersomnolence associated with psychiatric disorders from other central nervous system causes. However, the evidence base regarding sleep propensity in psychiatric hypersomnolence as measured by the MSLT has not been systematically evaluated, which is vital to clarify the utility and validity of current nosological schema. In this review, the use of sleep propensity assessed by the MSLT in patients with psychiatric hypersomnolence is systematically evaluated, using both qualitative and quantitative assessment. Findings demonstrate high heterogeneity and potential for bias among studies, with a pooled estimate of sleep propensity among patients with psychiatric hypersomnolence similar to normative values. Additionally, approximately 25% of patients with psychiatric hypersomnolence demonstrate a mean sleep latency below 8 min, the current cutpoint to define pathologic sleepiness. These data underscore the limitations of the MSLT in segregating psychiatric hypersomnolence from other central nervous system hypersomnias. Further research is warranted to evaluate novel measures and biomarkers of excessive sleepiness to advance clinical practice, as well as dimensional approaches to classification of hypersomnolence disorders.

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Introduction

Hypersomnolence, broadly defined as excessive daytime sleepiness (EDS) and/or excessive sleep duration, commonly occurs in patients with psychiatric disorders. Hypersomnolence plays a significant role in the course of psychiatric illness, particularly mood disorders, and is associated with treatment resistance, symptomatic relapse, increased risk of suicide, and functional impairment [1—6]. Despite its importance, there has generally been limited research on hypersomnolence in psychiatric disorders, particularly related to objective measures of sleepiness in these patients.

The multiple sleep latency test (MSLT) is widely considered the gold standard measure of daytime sleepiness, and as such, it is commonly used in the practice of sleep medicine for diagnostic purposes [7,8]. It is generally accepted that there is no objective evidence that patients with mood disorders have abnormal mean sleep latency on the MSLT [9]. As a result, nosologies central to the practice of sleep medicine have emphasized that psychiatric hypersomnolence is characterized by sleep latencies that are often within normal limits, in contrast to other central nervous system (CNS) hypersomnias [8,10].

However, despite the importance of hypersomnolence in psychiatric disorders and the reliance on the MSLT to guide diagnostic classification in sleep medicine, there have been no systematic reviews conducted to synthesize the literature and estimate objective sleep propensity in this patient population, a vital component of evidence-based medicine [11]. Thus, the primary aim of this review was to systematically analyze the available literature regarding sleep propensity in psychiatric hypersomnolence as measured by the MSLT, with the intention that such a synthesis would inform clinical practice and further refine the nosology of sleep disorders.

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Abbreviations

ADHD	attention deficit hyperactivity disorder
ASDC	Association of Sleep Disorders Centers
BDI	Beck depression inventory
CES-D	Center for Epidemiologic Studies depression scale
CNS	central nervous system
DSM	diagnostic and statistical manual
EEG	electroencephalogram
EDS	excessive daytime sleepiness
ESS	Epworth sleepiness scale
F	female
HRSD	Hamilton rating scale for depression
ICD	International classification of disease
ICSD	International classification of sleep disorders
IH	idiopathic hypersomnia
M	male
MINORS	methodological index for non-randomized studies
MSLT	multiple sleep latency test
MSL	mean sleep latency
MWT	maintenance of wakefulness test
NR	not reported
PRISMA	preferred reporting items for systematic reviews and meta-analyses
PVT	psychomotor vigilance task
RDC	research diagnostic criteria
PSG	polysomnography
REM	rapid eye movement
SD	standard deviation
SEM	standard error of the mean
SOREM	sleep onset rapid eye movement

Methods

Criteria for considering studies of this review

Types of participants

Studies that employed the MSLT to assess sleep propensity in patients or research subjects with psychiatric disorders were included. Since MSLT protocols utilized in research and clinical settings can vary [7], the operationalized definition of an MSLT utilized in this study required multiple repeated nap opportunities occurring within the same day, during which the participant tried to fall asleep, and latency to sleep was quantified. Studies were limited to those assessing adults, as there are limited normative data for the MSLT in pediatric populations [7].

Types of studies

All studies that utilized the MSLT to evaluate hypersomnolence in persons with psychiatric disorders were considered. Studies were included that reported MSLT findings in psychiatric disorders, even if such measures were not a primary aim of the study (e.g., a drug-study evaluating the efficacy of a pharmacologic treatment on sleep propensity would be included, as long as MSLT findings at baseline were reported).

Search strategy

Searches were conducted using PubMed and PsycINFO, as well as "waterfall" and "ancestral" searches of related materials. There were no limitations on year of publication or language of article. The following search parameters were utilized: (psychiatr* OR depress* OR mood OR anxiety OR "attention deficit" OR ADHD OR ADD OR schizophr* OR bipolar) AND (hypersom* OR mslt OR "multiple sleep latency test" OR "mean sleep latency"). Both peer reviewed publications and unpublished literature (meeting abstracts, dissertations/theses, etc.) were considered, since the likelihood of unpublished studies, and thus publication bias, is higher in studies of diagnostic tests [12]. The author conducted all searches. The last search was performed November 3, 2015.

Eligibility

The following criteria were required for inclusion: 1) use of MSLT (according to operational definition) to quantify sleep propensity and 2) evaluation of sleep propensity of patients/subjects with psychiatric diagnoses with clinical symptoms of excessive sleepiness and/or sleep duration. Exclusion criteria included: 1) individual nap opportunities occurring on different days, 2) use of non-electroencephalogram (EEG) based method to derive sleep onset (e.g., self-report, actigraphy), 3) testing performed under experimental conditions that were not standard for the patient/subject (e.g., MSLT performed after sleep deprivation), and 4) insufficient data for qualitative analysis or quantitative meta-analysis.

Data extraction

The author extracted all data (unblinded). Extracted data included: author/journal, year of publication, study design, number of MSLT naps, definition of sleep latency, number and demographics (ages and sex), psychiatric diagnoses, and mean sleep latency. Sleep onset rapid eye movement periods (SOREMs) were also noted, if reported. Study quality was assessed (unblinded) by the author using the methodological index for non-randomized studies (MINORS) rating scale [13].

Analysis

All studies that met inclusion/exclusion criteria were analyzed in the qualitative assessment of the literature on this topic. In addition, since normative data for the MSLT exist for 4–5 nap protocols, studies that utilized fewer naps (i.e., two nap protocols), were excluded from the quantitative meta-analysis. Attempts were made to obtain data from studies that did not report sufficient data for meta-analysis, but might otherwise qualify for inclusion. This included contacting corresponding authors of studies in which the MSLT was employed in psychiatric populations and an assessment of hypersomnolence was obtained in the study (e.g., Epworth sleepiness scale) even if it was not used to segregate groups in the primary study, since this subset of data might be applicable to these analyses.

Meta-analysis was performed using random-effects model (DeSimonian-Laird), utilizing OpenMetaAnalyst, an open-source, cross-platform software for advanced meta-analysis (http://www.cebm.brown.edu/open_meta/) [14]. The primary variable of interest was mean sleep latency on MSLT. Secondary variables of interest were proportions of patients with mean sleep latency (MSL) less than 8 and 5 min, as these cutpoints have been used to define pathologic sleepiness [8,10,15]. I^2 was utilized to assess heterogeneity among studies, with cutoffs 0%, 25%, 50%, and 75% used to define no, low, moderate, and high heterogeneity [16,17]. It was anticipated *a priori* that likely confounders that would affect meta-analysis could include age, sex, MSLT protocol variables (number of naps, definition of sleep latency), psychiatric diagnoses, and definition of hypersomnolence (i.e., excessive sleepiness vs. excessive sleep duration).