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REVIEW ARTICLE

# Hyperhidrosis in sleep disorders – A narrative review of mechanisms and clinical significance

Juan Idiaquez[1] | Juan Carlos Casar[1] | Erna S. Arnardottir[2,3] | Elias August[2,4] | Julia Santin[1] | Rodrigo Iturriaga[5]

[1]Departamento de Neurología, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

[2]Reykjavik University Sleep Institute, School of Technology, Reykjavik University, Reykjavik, Iceland

[3]Internal Medicine Services, Landspitali, The National University Hospital of Iceland, Reykjavik, Iceland

[4]Department of Engineering, School of Technology, Reykjavik University, Reykjavik, Iceland

[5]Laboratorio de Neurobiología, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile, Santiago, Chile

**Correspondence**
Juan Idiaquez, Departamento de Neurología, Facultad de Medicina, Pontificia Universidad Católica de Chile, diagonal Paraguay 362, Santiago, Chile.
Email: idiaquez@123.cl

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## Summary

Hyperhidrosis is characterized by excessive sweating beyond thermoregulatory needs that affects patients' quality of life. It results from an excessive stimulation of eccrine sweat glands in the skin by the sympathetic nervous system. Hyperhidrosis may be primary or secondary to an underlying cause. Nocturnal hyperhidrosis is associated with different sleep disorders, such as obstructive sleep apnea, insomnia, restless legs syndrome/periodic limb movement during sleep and narcolepsy. The major cause of the hyperhidrosis is sympathetic overactivity and, in the case of narcolepsy type 1, orexin deficiency may also contribute. In this narrative review, we will provide an outline of the possible mechanisms underlying sudomotor dysfunction and the resulting nocturnal hyperhidrosis in these different sleep disorders and explore its clinical relevance.

**KEYWORDS**
hyperhidrosis, insomnia, narcolepsy, periodic limb movement, restless legs syndrome, sleep apnea

## 1 | INTRODUCTION

The presence of excessive sweating beyond what is needed for thermoregulation is termed hyperhidrosis, and it is associated with sympathetic cholinergic hyperactivity. It can be observed under some physiological conditions, as a symptom secondary to several disorders, or as a pharmacological side-effect, but it may also constitute a primary isolated condition (Nawrocki & Cha, 2019). Sleep disorders are often an overlooked cause of secondary hyperhidrosis. Obstructive sleep apnea (OSA), insomnia, restless legs syndrome/periodic leg movement disorder (RLS/PLMS) and narcolepsy type 1 (NT1) are among the sleep disorders that may manifest themselves with this symptom (Arnardottir et al., 2013; Klein et al., 2014; Mold et al., 2006). In these disorders, nocturnal hyperhidrosis is common, accompanied or not by diurnal hyperhidrosis, and is associated with a reduction in quality of life. The mechanisms involved in excessive sweating in OSA, insomnia, RLS/PLMS and NT1 are not completely understood.

The scope of this review is to provide an overview of sweating mechanisms, and the resulting hyperhidrosis associated with OSA, insomnia, RLS/PLMS and NT1. We will first give a brief overview of normal autonomic sudomotor function during sleep and the methods to evaluate it. We will then discuss the clinical manifestations, physiopathological mechanisms and management of the excessive sweating in these sleep disorders.

## 2 | METHODS

Obstructive sleep apnea, insomnia, RLS/PLMS and narcolepsy are the focus of this review article because they are sleep disorders that have been associated with nocturnal sweating. We performed a narrative review of the literature including English language articles published between 1980 and 2021 using PubMed/MEDLINE databases. We used the following keywords: "sweating", "hyperhidrosis",

  

"sudomotor", "obstructive sleep apnea", "insomnia", "restless legs syndrome", "periodic limb movements during sleep" and "narcolepsy".

## 3 | NORMAL SUDOMOTOR FUNCTION

In humans the body temperature includes two compartments: (1) the external shell, in which the skin temperature fluctuates along with the environment; and (2) the internal core body temperature (CBT) of the brain, spinal cord and viscera. Due to our homeothermic condition, mechanisms to sustain a stable CBT are needed. Thermal afferent inputs from the skin and core body are processed by circuits at the central nervous system. This control activates the efferent thermal effectors, which allow to maintain the CBT in adequate ranges. CBT as well as circadian rhythms and sleep are controlled by a neural network in the anterior hypothalamus, i.e. preoptic area (POA) and dorsomedial nuclei (Harding et al., 2020). The afferent pathways from sensory skin terminals send information – via spinothalamic tract and parabrachial nuclei projections – to the POA. In this region, which contains warm- and cold-sensitive neurons, the thermal information is integrated to control the efferent thermic responses. When the thermoreceptors in the skin detect a temperature rise, warm-sensitive neurons in the POA trigger responses for heat loss and tonically inhibit cold-sensitive neurons of the hypothalamic dorsomedial nuclei. The central pathways connecting the dorsomedial nuclei with the sympathetic preganglionic neurons in the spinal intermediolateral columns are still not well understood. This response for heat loss results in active vasodilatation and sweating (Benarroch, 2007; Madden & Morrison, 2019; Minota et al., 2019; Tan & Knight, 2018). The active cutaneous vasodilatation depends on acetylcholine and other co-transmitters like calcitonin gene-related polypeptide (Sheng & Zhu, 2018). In the peripheral sympathetic ganglia, the subpopulation of neurons that innervate the eccrine sweat glands synthesize acetylcholine. Sympathetic cholinergic sudomotor activity occurs in a surging pattern; each surge produces a volume of sweat that dilates the sweat ducts and reduces the transdermal resistance, as measured by the electrodermal skin response. Eccrine glands associated with thermoregulation are distributed in the forehead, upper limbs, trunk and lower limbs, while those located in the palms and soles are associated with emotional sweating (Benarroch, 2007; Minota et al., 2019).

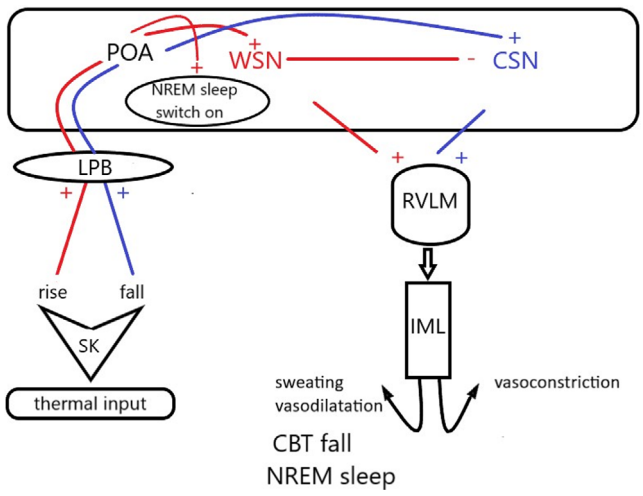


**FIGURE 1** Diagram of the thermal neural circuits involved in thermoregulation. A rise in SK is detected by TRP channels that send information to the LPB in the brainstem, which is transmitted to the POA (red line) with activation of the WSN (tonic inhibition of the CSN). These WSN trigger the sympathetic efferent pathways for heat loss (sweating and skin vasodilatation). Also, these warm afferent pathways can induce NREM sleep and hypothermia (in animal model). A fall in SK activates CSN causing sympathetically mediated skin vasoconstriction. CBT, core body temperature; CSN, cold-sensitive neurons; IML, intermediolateral columns in the spinal cord; LPB, lateral parabraquial nucleus; NREM, non-rapid eye movement; POA, preoptic area; RVLM, rostral ventrolateral medulla; SK, skin temperature; TRP, transient receptor potentials; WSN, warm-sensitive neurons; red lines = warm stimulus pathways; blue lines = cold stimulus pathways

A temperature fall detected by the thermoreceptors in the skin decreases the activity of the warm-sensitive neurons in the POA and this leads to a disinhibition of cold-sensitive neurons in the dorsomedial nuclei that project to the medial preoptic nucleus. Consequently, there is an activation of premotor sympathetic neurons in the nucleus raphe pallidus. Projections from these neurons activate the sympathetic noradrenergic preganglionic neurons in the intermediolateral column that promote cutaneous vasoconstriction (Benarroch, 2007; Tan & Knight, 2018; Figure 1).

## 4 | NORMAL SUDOMOTOR FUNCTION DURING SLEEP

A circadian regulation of the core/shell temperature ratio exists in humans. Distal temperature rises in the evening while CBT decreases; the opposite temperature changes occur in the morning. Interconnections between thermoregulatory and sleep networks are essential for the regulation of CBT during different stages of sleep. A warm microclimate needed for sleep stimulates central hypothalamic mechanisms, and promotes skin vasodilatation in distal limbs, promoting a decline of CBT (Harding et al., 2020). Distal skin temperature increases as compared with proximal skin temperature. This distal-to-proximal temperature gradient is a relevant determinant of sleep latency and sleep consolidation (Kräuchi et al., 2000). In mice, this stimulus increases the activity of preoptic glutamate/nitric oxide synthase neurons, causing hypothermia and non-rapid eye movement (NREM) sleep (Harding et al., 2018). Under circadian control, CBT starts to decrease before falling asleep and reaches a maximal decline during NREM sleep (Harding et al., 2020; Krueger & Takahashi, 1997). The mechanisms of thermoregulation are preserved at this stage, maintaining thermal homeostasis at a lower level of energy dissipation compared with waking hours. During NREM sleep, parasympathetic activity increases, and the sympathetic noradrenergic tone is diminished (Lanfranchi & Somers, 2011), thus, heart rate and blood pressure decrease. A diminished vascular tone leads to peripheral vasodilatation,

which contributes to heat loss (Szymusiak, 2018). Sweat production, which depends on sympathetic cholinergic activation, is normally observed during sleep even in a neutral or warm environment, contributing to the CBT decline process (Parmeggiani, 2003). A study of local sweating rate in humans during nocturnal sleep showed that sweat production was mainly present at NREM stages and that the rate was maximal during deep sleep (Sagot et al., 1987). Accordingly, electrodermal activity (EDA), to be discussed in Section 5, and the sweating rate on the dorsal side of the hand are increased during NREM sleep (Kobayashi et al., 2003).

Rapid eye movement (REM) sleep is characterized by an autonomic instability with marked blood pressure and heart rate fluctuations (Fink et al., 2018). During phasic REM sleep there is a transient increase of sympathetic tone and parasympathetic tone decrease. Direct measurements of muscle sympathetic activity through microneurography show the appearance of bursts of activity during REM sleep. These bursts are also observed during sleep stage transitions, and they are associated with sleep spindles and K-complexes in stage 2 NREM sleep (Miglis, 2016). Behavioural and autonomic thermoregulatory responses during REM sleep are depressed (Parmeggiani, 2003). CBT positively correlates with ambient temperature in this sleep stage, simulating a poikilothermic state (Parmeggiani, 2003; Sagot et al., 1987). Skin vasodilatation and sweating in response to a warm environment are, thus, decreased in REM sleep (Kobayashi et al., 2003; Sagot et al., 1987).

## 5 | HYPERHIDROSIS: MECHANISMS AND CLINICAL TYPES

Hyperhidrosis corresponds to excessive sweating that surpasses the amount necessary to control CBT. It results from sympathetic cholinergic overactivity in the presence of normal eccrine sweat glands (Nawrocki & Cha, 2019). The activity of skin sympathetic nerves regulates the skin vascular tone and sweat gland responses that mediate heat loss. Individual vasoconstrictor and sudomotor neurons in the sympathetic ganglia normally fire at a low frequency; in patients with hyperhidrosis, these neurons increase their firing rate and, thus, the release of acetylcholine (Macefield & Wallin, 2018). Hyperhidrosis does not refer to a rise of the absolute amount of sweat production, but to an excessive sweating beyond the needs of physiological demands (Schick, 2016). According to its aetiology, hyperhidrosis is classified as a primary disorder or secondary to a specific medical condition or drug. Primary hyperhidrosis is a common condition, a study showed a prevalence of 2.8% in USA population (Strutton et al., 2014), and its cause is not well understood. More than half of the patients report a family history (Hu et al., 2018; Schick, 2016), and the onset is at ≤ 25 years old. Primary hyperhidrosis may occur in response to thermoregulatory demands, but it may also be induced by emotions. An abnormal regulation of cortical and hypothalamic circuits involved in sweating production could be responsible for this condition (Nawrocki & Cha, 2019).

Secondary hyperhidrosis may be generalized or segmentary. Generalized hyperhidrosis can occur during the day and/or at night, and it may be observed in physiological conditions like fever, menopause or when environmental temperature is high. Pathological conditions causing hyperhidrosis include: (1) central and peripheral nervous system disorders that lead to segmental anhidrosis, where compensatory hyperhidrosis occurs in areas of the body with preserved sweat gland innervation; (2) systemic diseases like malignancies, infections, endocrine/metabolic conditions, cardiac and respiratory failure. Nocturnal sweating is frequently observed in conditions such as menopause, tuberculosis, lymphoma, endocarditis, diabetes mellitus, acromegaly, obstructive apnea and Prinzmetal angina; (3) hyperhidrosis may also be an unwanted effect of drugs or their withdrawal (Hu et al., 2018; Nawrocki & Cha, 2019).

Differential diagnosis of nocturnal sweating must consider the following. (1) Primary hyperhidrosis that is mainly located in axilla, palm, soles and the head, and it is rarely present nocturnally, while in sleep disorders the excessive sweating occurs at night and is predominantly located in the trunk and neck. (2) Secondary hyperhidrosis due to systemic diseases shows a generalized body distribution and it is diurnal and/or nocturnal. (3) Secondary hyperhidrosis due to peripheral neuropathies may show segmentary compensatory hyperhidrosis in response to thermoregulatory demands. In central nervous system disorders like stroke and spinal cord injury the excessive sweating is segmentary and distributed according to the level of the lesion. (4) The patient's history allows us to rule out other causes of secondary generalized hyperhidrosis like medication, intoxication, and withdrawal of alcohol or other substances.

## 6 | EVALUATION OF SUDOMOTOR FUNCTION IN SLEEP DISORDERS

Sudomotor function can be assessed subjectively by validated questionnaires, and objectively through different clinical or experimental assessment methods. Both approaches may focus on a basal assessment or may specifically evaluate disturbances occurring during sleep.

### 6.1 | Clinical evaluation of sudomotor function

Specific questionnaires like the Scale for Outcomes in Parkinson' s disease-Autonomic dysfunction (SCOPA-AUT), a 23-question questionnaire divided into six domains (gastrointestinal, urinary, cardiovascular, sudomotor, pupillary and sexual), provide a comprehensive and standardized assessment of autonomic symptoms. Different questions assess separately diurnal and nocturnal hyperhidrosis (Goldstein & Low, 2007; Visser et al., 2004).

Sudomotor function can be assessed by different techniques commonly used in clinical autonomic testing. The thermoregulatory sweat test is a quantitative measurement of central and peripheral sudomotor function. It detects the skin areas with sweat production induced by a rise of CBT, using an indicator powder covering the skin that changes colour with humidity. The sympathetic skin response (SSR) measures changes in electrodermal skin activity evoked by

different types of stimulation (noise, electrical) that activate the central and peripheral sudomotor efferent pathways. The quantitative sudomotor axon reflex sweat test (QSART), induced by iontophoresis of pilocarpine, measures the postganglionic sudomotor nerve activity. Sudoscan is a device that measures the electrochemical skin conduction through reverse iontophoresis in palms and soles, which has also been used in the basal assessment of patients with sleep disorders (Buchmann et al., 2019).

## 6.2 | Measurement of sudomotor function during sleep

Subjective nocturnal hyperhidrosis has been assessed using specific sleep questionnaires such as the Sleep Disorders Questionnaire (Cruz et al., 2012; Douglass et al., 1994) or the Basic Nordic Sleep Questionnaire (Arnardottir et al., 2013; Partinen & Gislason, 1995), which include questions grading the presence of nocturnal excessive sweating, among other sleep disorder symptoms. Both questionnaires grade the perception of nocturnal hyperhidrosis in terms of frequency; "usually" or "always" in the former (Cruz et al., 2012), and ≥ 3 times per week in the latter (Arnardottir et al., 2013).

The ventilated capsule method is the most used method in research settings to directly measure the volume of sweat production in a particular skin area. In short, a small capsule is affixed to the skin and a dry gas (air or nitrogen) is passed through. The local sweat rate can be calculated by determining the humidity difference between the influent and effluent gas streams using a hygrometer and relating this value to the exposed skin area (Kenny & Jay, 2013; Meade et al., 2016). It has been adapted to study the neurotransmitters and mediators controlling the eccrine glands by combining it with the infusion of pharmacological inhibitors through intradermal microdialysis.

The EDA refers to electrical activity of the skin, which readily changes in response to sweating; EDA was formerly labelled galvanic skin response. The activity is assessed by means of voltage measurements obtained by attaching electrodes to the skin. The endosomatic method of measuring EDA does it without externally applied voltage (skin potential), while the exosomatic method – the most used one – applies either AC or DC (Boucsein, 2012). Usually, the palms and fingers are used as sites for attaching the electrodes. It has been shown that EDA correlates highly with the ventilated capsule method and, thus, can be applied as an indirect measure of sweating volume (Kobayashi et al., 2003). In recent years, EDA measurements have been increasingly applied in sleep studies to objectively measure nocturnal hyperhidrosis. Hwang et al. investigated the patterns of the EDA signal during sleep onset and offset, and proposed that EDA can be used to estimate the length of sleep (Hwang et al., 2017). A study with 43 healthy and 48 patients with sleep disorders showed that EDA can be used to robustly distinguish between periods of sleep and periods of being awake (Herlan et al., 2019). Furthermore, several studies have reported that EDA activity is highest during slow-wave sleep, causing a so-called EDA storm (Figure 2), and that EDA activity decreases to very low levels during REM sleep (Arnardottir et al., 2010; R. Liguori et al., 2000; Sano et al., 2014). An EDA storm consists of at least two consecutive 30-s epochs with a minimum of one EDA event (or peak). An EDA event is recorded whenever a change in skin potential of > 50 μV occurs that lasts for at least 1.5 s, where sampling frequency is 32 Hz or more (as reported by most studies) and a low-pass filter with a cutoff frequency between 0.3 Hz and 0.5 Hz is used (Arnardottir et al., 2010). Most of the time, more than 5 events are observed in storms and, occasionally, up to 26 (Sano et al., 2014).

The EDA measurements in the above-cited publications were all obtained with elaborate medical or clinical devices. Recent advances in wearable technology allow the possibility of measuring EDA through a so-called wearable device (often, a smartwatch; Kim et al., 2021; Majumder et al., 2017). When stressed or aroused, humans frequently react through increased sweating (Chen

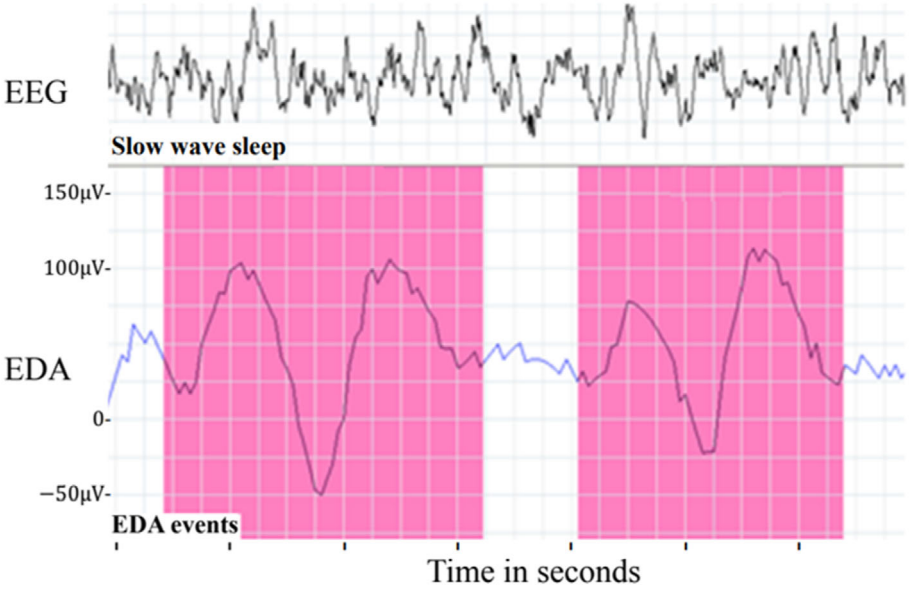


**FIGURE 2** Electrodermal activity (EDA) recording in a patient in slow-wave sleep showing bursts of increased EDA as measured by the skin potential method, highlighted by the pink squares as compared with basal activity in between

et al., 2015). This has led to various applications of wearables measuring EDA, for example, to assess engagement, immersion and enjoyment, satisfaction during presentations (Gashi et al., 2019), or how active students are in the classroom (Pijeira-Díaz et al., 2018). Only very recently, the set of applications has been extended to include assessment of sleep through EDA measurements. It has been found that the EDA magnitude during the night was a predictor for self-reported sleep efficiency (Romine et al., 2019). These studies using non-intrusive devices for EDA and sleep quality evaluation, in general, open a plethora of research possibilities.

## 7 | HYPERHIDROSIS IN SLEEP DISORDERS

### 7.1 | Hyperhidrosis in OSA

Excessive sweating is frequent in OSA (Guilleminault & Bassiri, 2005). Nocturnal hyperhidrosis can be troublesome, but few patients report this symptom spontaneously, albeit about 30%–40% of adult OSA patients experience it, based on subjective reports (Arnardottir et al., 2013; Cruz et al., 2012; Mold et al., 2012). It is most prominent around the neck and upper thorax (Guilleminault & Bassiri, 2005), and can be significantly reduced through treatment (Arnardottir et al., 2013; Kiely et al., 1999). Routine use of sleep-related symptoms questionnaires that include the assessment of sweating complaints, as previously mentioned, may be useful for its detection. Reports of frequent nocturnal hyperhidrosis in patients with OSA are associated with younger age, insomnia, excessive daytime sleepiness, and gastrointestinal reflux (Arnardottir et al., 2013). However, the reported frequency of nocturnal hyperhidrosis does not associate with the severity of OSA, as measured by the apnea–hypopnea index (Arnardottir et al., 2013). Among untreated patients with OSA, those who reported frequent nocturnal hyperhidrosis showed a higher EDA index, an objective measure of increased night sweating. However, in treated patients, even though both decreased, the association between these two variables was lost, possibly reflecting the fact that sleeping more soundly through the night made the patients less aware of this symptom (Arnardottir et al., 2010). The risk of sleepiness-related accidents in patients with OSA is better predicted by self-reported daytime sleepiness than by the apnea–hypopnea index, and is also independently associated with nocturnal sweating (Philip et al., 2020).

The percentage of REM sleep among total sleep time is reduced in patients with OSA with measured nocturnal hyperhidrosis, as compared with other patients with OSA, and it increases with treatment (Arnardottir et al., 2010). One potential cause for this inverse relationship is that REM sleep may be inhibited by high sympathetic activity, as suggested by pharmacological experimental studies (Pal & Mallick, 2006; Ross et al., 1995). Studies have shown that patients with untreated OSA have an increased sympathetic drive during sleep and wakefulness, and that a higher EDA during the night tends to correlate with higher diurnal blood pressure Arnardottir et al., 2010). A non-invasive measurement of skin sympathetic activity that shows sweat gland production is increased in patients with OSA during sleep (He et al., 2020). These findings support the hypothesis that high sympathetic activation may explain nocturnal hyperhidrosis and affect sleep quality. Further studies are needed, however, to clarify the pathophysiology of hyperhidrosis in OSA.

It is not known whether nocturnal hyperhidrosis in OSA may represent a biomarker of a phenotype with different prognostic profile or whether it only constitutes a sign of individual variability without relationship to clinically relevant phenotypes. Unsupervised cluster analyses of clinical parameters in untreated patients with OSA with moderate-to-severe disease do support the former notion, as reported nocturnal sweating was one of the symptoms clustered together into a "disturbed sleep" group. This cluster included symptoms of insomnia, restlessness and RLS, while the other two clusters were those with "excessive diurnal sleepiness" and "minimally symptomatic" (Ye et al., 2014). These findings were validated in a bigger international sample, where a report of nocturnal hyperhidrosis was more likely to cluster with "disturbed sleep" and "upper airway symptoms with sleepiness" (Keenan et al., 2018).

### 7.2 | Hyperhidrosis in insomnia

A study using specific questionnaires for sweating symptoms in a general population cohort has shown an association between nocturnal hyperhidrosis and insomnia symptoms (Arnardottir et al., 2013). Several psychiatric conditions, such as anxiety and depression (Oh et al., 2019), and medical comorbidities (Taylor et al., 2007) can contribute to the presence of hyperhidrosis in insomniacs.

Insomnia and nocturnal hyperhidrosis are frequent symptoms in the perimenopausal period. Self-report of vasomotor symptoms (nocturnal hyperhidrosis and/or hot flushing) during the perimenopause period has shown an association with insomnia. However, it has been suggested that the presence of insomnia may be a factor that leads patients to be more aware of their symptoms (Baker et al., 2018). Data from a study by the Woman Health Initiative (WHI) among a large number of postmenopausal women showed a significant independent association between nocturnal hyperhidrosis and insomnia, with a stronger partial correlation with maintenance of sleep (Hartz et al., 2013). The presence of nocturnal hyperhidrosis and insomnia during the perimenopause period may also be a manifestation of underdiagnosed OSA (Baker et al., 2018). Thus, the presence of OSA should be considered.

Thermoregulatory changes have been shown to occur in primary chronic insomnia: in patients with sleep-onset insomnia, the CBT circadian decline during sleep is delayed, whereas in patients with early morning awakenings it is advanced (Lack et al., 2008). In a group of elderly insomniacs, CBT manipulation with a hot bath before bedtime allowed to improve sleep continuity (Dorsey et al., 1999). In patients with chronic insomnia, increased diurnal EDA was reported (Broman & Hetta, 1994). This along with other evidence of diurnal sympathetic overactivity, such as changes in heart rate variability and increased circulating catecholamines, are possibly the manifestation of a maintained hyperarousal state (Vargas et al., 2020). Thermoregulatory and non-thermoregulatory factors may therefore contribute to

abnormal sudomotor activity in primary chronic insomnia. Further studies are required to disclose the mechanism of hyperhidrosis in different sub-groups of insomnia patients and its relationship with other clinical manifestations.

## 7.3 | Hyperhidrosis in RLS/PLMS

Restless legs syndrome is characterized by an unpleasant urge to move the legs associated with sensory symptoms. Most patients show PLMS. PLMS is a condition where periodic limb movement occurs during sleep, in the absence of other sleep disturbances. RLS and PLMS are two different phenotypes of the same disease and respond to the same treatment (Figorilli et al., 2017). Studies that have explored the presence of nocturnal hyperhidrosis in patients with RLS have used different inclusion criteria and different questionnaires for addressing sweating symptoms. A study of self-reported symptoms in adults and geriatric patients showed that hyperhidrosis was associated with RLS (Mold et al., 2004; Mold et al., 2006). This was confirmed in another study on a general population cohort subjected to the Nordic Sleep Questionnaire in which diagnosis followed the International RLS Study Group diagnostic criteria (Arnardottir et al., 2013). Women with

**TABLE 1** Thermoregulatory symptoms and tests in OSA, insomnia, RLS/PLMS and narcolepsy

| Sweating studies | *n*/ Controls | Study characteristics | Methods | Main findings |
|---|---|---|---|---|
| **OSA** | | | | |
| **symptoms** | | | **questionnaire** | thermoregulation |
| Cruz et al. (2012) | 98 | PSG, prospective | Sleep disorder | night sweating |
| Arnardottir et al. (2013) | 822/703 | PM, prospective | Nordic sleep | night sweating: 30.6%/9.3% male, 33%/12.8% women |
| **Tests** | | | **technique** | Activity |
| Arnardottir et al. (2010) | 24 | PSG, prospective | EDA (sleep) | increased |
| Korkmaz et al. (2016) | 31/18 | PSG, prospective | SSR | decreased (neck) |
| He et al. (2020) | 18/8 | PSG, prospective | Skin sympathetic activity (sleep) | increased |
| **Insomnia** | | | | |
| **symptoms** | | | **questionnaire** | thermoregulation |
| Arnardottir et al. (2013) | 822/703 | PM, prospective | Nordic sleep | night sweating: fall asleep 37.3% stay asleep 52% |
| Hartz et al. (2013) | 148.938 | Cross-sectional | WHI-IRS | night sweating |
| **Tests** | | | **technique** | activity |
| Broman and Hetta (1994) | 40/20 | prospective | EDA | increased |
| **RLS/ PLMS** | | | | |
| **Symptoms** | | | **questionnaire** | thermoregulation |
| Mold et al. (2004) | 795 | cross-sectional | QWB-SA | diurnal sweating |
| Shneyder et al. (2013) | 49/291 | Retrospective | SCOPA-Aut | heat intolerance |
| **Tests** | | | **technique** | activity |
| Lim (2012) | 56/36 | prospective | QSART | normal: arm, leg |
| **Narcolepsy** | | | | |
| **symptoms** | | | **questionnaire** | thermoregulation |
| Sturzenneger and Bassetti (2004) | 57/40 | MSLT prospective | Sleep questions | night sweating 29% |
| Klein et al. (2014) | 15/15 | MSLT prospective | SCOPA-Aut | night sweating |
| Barateau et al. (2019) | 92/109 | MSLT prospective | SCOPA-Aut | diurnal sweating heat intolerance |
| Rocchi et al. (2020) | 12/14 | MSLT prospective | SCOPA-Aut | increased score |
| **Tests** | | | **technique** | |
| Rocchi et al. (2020) | 12/14 | MSLT prospective | Sudoscan | Low amplitude (hands) |

*Note*: EDA, electrodermal activity; MSLT, Multiple Sleep Latency Test; OSA, obstructive sleep apnea; PLMS, periodic limb movements in sleep; PM, portable monitor (Embletta, T3 device); PSG, polysomnography; QSART, quantitative sudomotor axon reflex sweat test; QWB-SA, Quality of Well Being Scale Self-Administered; RLS, restless legs syndrome; SCOPA-Aut, Scales for Outcomes in Parkinson's Autonomic Tests; SSR, sympathetic skin response; WHI-IRS, Women Health Initiative Insomnia Rating Scale.

**TABLE 2** Possible mechanisms of hyperhidrosis in OSA, insomnia, RLS/PLMS and narcolepsy

| Disorder | Possible mechanism of hyperhidrosis | Supporting findings | Authors |
|---|---|---|---|
| OSA | sympathetic activation | increased nocturnal EDA with higher systolic BP | Arnardottir et al. (2010) |
| | high sympathetic drive | increased burst of skin sympathetic activity during sleep | He et al. (2020) |
| Insomnia | sympathetic activation | increased diurnal EDA higher arousal level | Broman and Hetta (1994) |
| RLS/PLMS | sympathetic activation | dopaminergic inhibitory neurons deficiency | Miglis (2016) |
| | sympathetic activation compensatory sweat | cortical arousal in PLMS in response to distal vaso and sudomotor dysfunction | C. Liguori et al. (2020) |
| Narcolepsy | diminished distal sympathetic function | abnormal skin temperature gradient (distal-proximal) | Fronczek et al. (2006) |
| | increased temperature at night | core body temperature profile higher than controls | Van Der Heide et al. (2016)) |

*Note*: BP, blood pressure; EDA, electrodermal activity; OSA, obstructive sleep apnea; PLMS, periodic leg movements in sleep; RLS, restless legs syndrome.

RLS more frequently report nocturnal hyperhidrosis during the menopausal period (Wesström et al., 2008). Worsening of RLS symptoms has been reported during the summer, and this was associated with nocturnal hyperhidrosis in men (C. Liguori et al., 2020). On the other hand, two studies with a small number of patients with RLS did not find significant hyperhidrosis in these patients using a questionnaire designed to assess autonomic symptoms (Erdal et al., 2020; Shneyder et al., 2013).

Due to the association between small-fibre neuropathy and RLS (Trenkwalder et al., 2016), sudomotor fibres have been investigated in respective patients. Most electrophysiological studies have shown normal sweat gland function (Erdal et al., 2020; Isak et al., 2011; Lim et al., 2012; Tyvaert et al., 2009). Interestingly, a study that used laser-Doppler flowmetry and thermography found a defective skin vasodilation in the feet of idiopathic RLS patients when responding to a warm ambient temperature (Anderson et al., 2013). This diminished thermoregulatory vasomotor and sudomotor response in the feet may account for a compensatory hyperhidrosis in the trunk of patients with RLS (C. Liguori et al., 2020).

Dopamine deficiency is among the proposed mechanisms involved in RLS. As dopaminergic inhibitory neurons project to the preganglionic sympathetic neurons in the intermediolateral columns, dopamine deficiency may lead to peripheral sympathetic overactivity (Miglis, 2016). PLMS may also be associated with cortical arousal and enhanced sympathetic activity (Figorilli et al., 2017). The possible association between cardiovascular comorbidity and the presence of hyperhidrosis in patients with PLMS has not been reported. Assessment of drug treatment efficacy in patients with RLS has been mainly focused on reduction of sensory symptoms and its impact on sleep and quality of life (Allen et al., 2018). The response of sweating symptoms to pharmacological treatments has not been reported.

### 7.4 | Hyperhidrosis in narcolepsy

The presence of nocturnal hyperhidrosis in narcoleptic patients was reported decades ago (Clark et al., 1980; Sturzenneger & Bassetti, 2004). Further studies with NT1 patients using a questionnaire for autonomic symptoms have reported hyperhidrosis in, both, untreated (Barateau et al., 2019; Rocchi et al., 2020) and treated individuals (Klein et al., 2014). A study of electrochemical skin conductance, using the Sudoscan device, showed sudomotor dysfunction in the upper but not in the lower limbs (Rocchi et al., 2020). No other studies of sudomotor function in NT1 have been reported.

Patients with NT1 show abnormal circadian regulation of skin temperature with a high distal-to-proximal skin temperature gradient during the day that, normally, is observed in healthy subjects only during sleep (Fronczek et al., 2006). An increase in skin temperature gradient also preceded the onset of sleep attacks during the day (van der Heide et al. 2016). However, continuous temperature monitoring in a laboratory setting did not show a difference in CBT circadian values or patterns between NT1 patients and controls (Grimaldi et al., 2010). Another study, in ambulatory NT1 patients, showed a trend towards a higher CBT and a lower distal skin temperature during the night compared with controls (van der Heide et al. 2016), this elevated CBT during sleep may contribute to night sweating.

Hyperhidrosis in NT1 may be in part explained by an abnormal autonomic regulation. The orexin neurons constitute a main part of the central autonomic network and, thus, the deficiency of orexin in NT1 could be associated with autonomic dysfunction in these patients (Plazzi et al., 2011). Autonomic function studies in animals with orexin deficiency and in NT1 patients have yielded conflicting results (Fronzeck & Thijs, 2013). The elevated distal skin temperature (Fronczek et al., 2006) and decreased electrochemical skin conductance in the hands (Rocchi et al., 2020) during the day may reflect a distal decreased sympathetic vasomotor and sudomotor tone, respectively. Use of psychostimulants and the frequent association of NT1 with OSA and cardiovascular comorbidities may be factors that partly explain the finding of an increased sympathetic activity and cardiovascular risk (Silvani, 2020). Table 1 summarizes symptoms and tests, and Table 2 shows possible mechanisms responsible for hyperhidrosis.

## 8 | DISCUSSION

Hyperhidrosis is associated with several sleep disorders. In patients with OSA, insomnia, RLS/PLMS and NT1, studies using different questionnaires have shown excessive sweating (Arnardottir

et al., 2013; Barateau et al., 2019; Cruz et al., 2012; Mold et al., 2004; Mold et al., 2006; Mold et al., 2012; Rocchi et al., 2020). The sensitivity and specificity of sweating symptoms have not been reported in OSA, insomnia, RLS and NT1. An international study with a large number of patients with OSA showed that the presence of excessive night sweating was useful to identify clinical clusters of patients (Keenan et al., 2018). For patients with OSA, skin conductance changes have been evaluated through EDA measurements during sleep, which has allowed us to study sudomotor function and its relationship with clinical and polysomnographic features (Arnardottir et al., 2010). No studies of sudomotor function during sleep have been reported for insomnia, RLS and NT1. There are few studies on sweating during waking hours using sudomotor function tests. In patients with OSA and NT1, a decreased response was reported (Korkmaz et al., 2016; Rocchi et al., 2020), while normal function was found in patients with RLS (Erdal et al., 2020; Isak et al., 2011; Tyvaert et al., 2009). These tests only provide a single measurement of sudomotor function, while EDA measurements continuously assess function for longer periods of time.

There are several factors that may contribute to increased sympathetic sudomotor activity in sleep disorders. Some of them, such as frequent arousals, sleep fragmentation and short sleep duration, are common in OSA, insomnia and RLS. (Figorilli et al., 2017; Miglis, 2016). Abnormal central sympathetic regulation associated with orexin deficiency in NT1 may also contribute to increase of sympathetic sudomotor activity (Miglis, 2016). There is some evidence of abnormal thermoregulation in insomnia, RLS and NT1 patients (C. Liguori et al., 2020; Van Der Heide et al., 2016), but its possible contribution to sweating dysfunction has not been determined. A study on patients with OSA showed that excessive night sweating was not associated with an abnormal thermoregulatory drive (Arnardottir et al., 2010). Other factors like the presence of comorbidities, drugs and hormonal changes in women must be also considered and addressed.

Successful treatment of OSA has been shown to reduce nocturnal hyperhidrosis (Arnardottir et al., 2010; Arnardottir et al., 2013; Cruz et al., 2012). There is a lack of information regarding the treatment of hyperhidrosis in other sleep disorders. For the assessment of potential therapies, it is important to consider that subjective report of symptoms may be influenced by sleep fragmentation and insomnia. Studying the relationship between self-reported symptoms and objective measurements of sweating could be useful to identify different patients' phenotypes, and improve treatment outcomes and their quality of life.

## 9 | SUMMARY

Hyperhidrosis, mainly manifested as night sweating, is a relevant complaint in OSA, insomnia, RLS and NT1. Questionnaires and the evaluation of sudomotor activity during sleep with continuous recordings are both useful tools to study hyperhidrosis in sleep disorders. While most of the studies have been carried out in patients with OSA, it is conceivable that in all the previously mentioned conditions, the presence of sympathetic overactivity may be a common factor contributing to sudomotor dysfunction. Future research may enhance our understanding of the pathophysiology and possible therapies of hyperhidrosis in sleep in the mentioned sleep disorders.

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JI and ESA wrote the paper with important contributions from JCC, EA, JS and RI. All authors participated in the revision of the manuscript and have approved the final manuscript to be published.

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## CONFLICT OF INTEREST

None of the authors has any conflicts of interest to declare.

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## ORCID

*Juan Idiaquez* https://orcid.org/0000-0001-6253-2289
*Erna S. Arnardottir* https://orcid.org/0000-0003-0877-3529

## REFERENCES

Allen, R. P., Picchietti, D. L., Auerbach, M., Cho, Y. W., Connor, J. R., Earley, C. J., & Winkelman, J. W. (2018). Evidence-based and consensus clinical practice guidelines for the iron treatment of restless legs syndrome/Willis-Ekbom disease in adults and children: An IRLSSG task force report. *Sleep Medicine*, *41*, 27–44. https://doi.org/10.1016/j.sleep.2017.11.1126

Anderson, K. N., Di Maria, C., & Allen, J. (2013). Novel assessment of microvascular changes in idiopathic restless legs syndrome (Willis-Ekbom disease). *Journal of Sleep Research*, *22*(3), 315–321. https://doi.org/10.1111/jsr.12025

Arnardottir, E. S., Janson, C., Bjornsdottir, E., Benediktsdottir, B., Juliusson, S., Kuna, S. T., & Gislason, T. (2013). Nocturnal sweating - A common symptom of obstructive sleep apnoea: The Icelandic sleep apnoea cohort. *BMJ Open*, *3*(5), 1–10. https://doi.org/10.1136/bmjopen-2013-002795

Arnardottir, E. S., Thorleifsdottir, B., Svanborg, E., Olafsson, I., & Gislason, T. (2010). Sleep-related sweating in obstructive sleep apnoea: Association with sleep stages and blood pressure. *Journal of Sleep Research*, *19*(1 PART. 2), 122–130. https://doi.org/10.1111/j.1365-2869.2009.00743.x

Baker, F., Lampio, L., Saaresranta, T., & Polo-Kantola, P. (2018). Sleep and sleep disorders in the menopausal transition. *Physiology & Behavior*, *176*(3), 139–148. https://doi.org/10.1016/j.jsmc.2018.04.011

Barateau, L., Chenini, S., Evangelista, E., Jaussent, I., Lopez, R., & Dauvilliers, Y. (2019). Clinical autonomic dysfunction in narcolepsy type 1. *Sleep*, *42*(12), 1–9. https://doi.org/10.1093/sleep/zsz187

Benarroch, E. E. (2007). Thermoregulation: Recent concepts and remaining questions. *Neurology*, *69*(12), 1293–1297. https://doi.org/10.1212/01.wnl.0000275537.71623.8e

Boucsein, W. (2012). *Electrodermal activity. Springer science & business media* (2nd ed.). Springer. https://doi.org/10.1007/978-1-4614-1126-0

Broman, J.-E., & Hetta, J. (1994). Electrodermal activity in patients with persistent insomnia. *Journal of Sleep Research*, *3*(3), 165–170. https://doi.org/10.1111/j1365-2869.1994.tb00124.x

Buchmann, S. J., Penzlin, A. I., Kubasch, M. L., Illigens, B. M. W., & Siepmann, T. (2019). Assessment of sudomotor function. *Clinical Autonomic Research*, *29*(1), 41–53. https://doi.org/10.1007/s10286-018-0530-2

Chen, W., Jaques, N., Taylor, S., Sano, A., Fedor, S., & Picard, R. W. (2015). Wavelet-based motion artifact removal for electrodermal activity. In *2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)* (pp. 6223–6226). IEEE. https://doi.org/10.1109/EMBC.2015.7319814

Clark, R. W., Boudoulas, H., Schaal, S. F., & Schmidt, H. S. (1980). Adrenergic hyperactivity and cardiac abnormality in primary disorders of sleep. *Neurology*, *30*(2), 113–119. https://doi.org/10.1212/wnl.30.2.113

Cruz, I. A. C., Drummond, M., & Winck, J. C. (2012). Obstructive sleep apnea symptoms beyond sleepiness and snoring: Effects of nasal APAP therapy. *Sleep and Breathing*, *16*(2), 361–366. https://doi.org/10.1007/s11325-011-0502-4

Dorsey, C. M., Teicher, M. H., Cohen-Zion, M., Stefanovic, L., Satlin, A., Tartarini, W., Harper, D., & Lukas, S. (1999 Nov). Core body temperature and sleep of older female insomniacs before and after passive body heating. *Sleep*, *22*(7), 891–898. https://doi.org/10.1093/sleep/22.7.891

Douglass, A. B., Bomstein, R., Nino-Murcia, G., Keenan, S., Miles, L., Zarcone, V. P., Jr., & Dement, W. C. (1994). The sleep disorders questionnaire I: Creation and multivariate structure of SDQ. *Sleep*, *17*(2), 160–167. https://doi.org/10.1093/sleep/17.2.160

Erdal, Y., Akdogan, O., Nalbantoglu, M., Kavasoglu, G., & Emre, U. (2020). Autonomic dysfunction in restless legs syndrome. *Sleep and Breathing*, *24*(3), 995–999. https://doi.org/10.1007/s11325-019-01939-8

Figorilli, M., Puligheddu, M., Congiu, P., & Ferri, R. (2017). The clinical importance of periodic leg movements in sleep. *Current Treatment Options in Neurology*, *19*(3), 10. https://doi.org/10.1007/s11940-017-0446-5

Fink, A. M., Bronas, U. G., & Calik, M. W. (2018). Autonomic regulation during sleep and wakefulness: A review with implications for defining the pathophysiology of neurological disorders. *Clinical Autonomic Research*, *28*(6), 509–518. https://doi.org/10.1007/s10286-018-0560-9

Fronczek, R., Overeem, S., Lammers, G. J., Van Dijk, J. G., & Van Someren, E. J. W. (2006). Altered skin-temperature regulation in narcolepsy relates to sleep propensity. *Sleep*, *29*(11), 1444–1449. https://doi.org/10.1093/sleep/29.11.1444

Fronzeck, R., & Thijs, R. D. (2013). Autonomic alterations in narcolepsy. Contrasting results in mice and men. *Sleep*, *36*(1), 9. https://doi.org/10.5665/sleep.2286

Gashi, S., Di Lascio, E., & Santini, S. (2019). Using unobtrusive wearable sensors to measure the physiological synchrony between presenters and audience members. *Proceedings of the ACM on Interactive, Mobile, Wearable and Ubiquitous Technologies*, *3*(1), 1–19. https://doi.org/10.1145/3314400

Goldstein, D., & Low, P. (2007). Clinical evaluation of the autonomic nervous system. *CONTINUUM: Lifelong Learning in Neurology*, *13*(6), 33. https://doi.org/10.1212/01.CON.0000299965.28266.ec

Grimaldi, D., Agati, P., Pierangeli, G., Franceschini, C., Guaraldi, P., Barletta, G., & Cortelli, P. (2010). Hypocretin deficiency in narcolepsy with cataplexy is associated with a normal body core temperature modulation. *Chronobiology International*, *27*(8), 1596–1608. https://doi.org/10.3109/07420528.2010.504907

Guilleminault, C., & Bassiri, A. (2005). Clinical Features and Evaluation of Obstructive Sleep Apnea-Hypopnea Syndrome and Upper Airway Resistance Syndrome. In *Principles and Practice of Sleep Medicine (4th Ed)*. Elsevier/Saunders. https://doi.org/10.1016/B0-72-160797-7/50094-X

Harding, E. C., Franks, N. P., & Wisden, W. (2020). Sleep and thermoregulation. *Current Opinion in Physiology*, *15*, 7–13. https://doi.org/10.1016/j.cophys.2019.11.008

Harding, E. C., Yu, X., Miao, A., Andrews, N., Ma, Y., Ye, Z., & Franks, N. P. (2018). A neuronal hub binding sleep initiation and body cooling in response to a warm external stimulus. *Current Biology*, *28*(14), 2263–2273.e4. https://doi.org/10.1016/j.cub.2018.05.054

Hartz, A., Ross, J. J., Noyes, R., & Williams, P. (2013). Somatic symptoms and psychological characteristics associated with insomnia in postmenopausal women. *Sleep Medicine*, *14*(1), 71–78. https://doi.org/10.1016/j.sleep.2012.08.003

He, W., Tang, Y., Meng, G., Wang, D., Wong, J., Mitscher, G. A., Adams, D., Everett, T. H., 4th, Chen, P. S., & Manchanda, S. (2020). (2020). Skin sympathetic nerve activity in patients with obstructive sleep apnea. *Heart Rhythm*, *17*(11), 1936–1943. https://doi.org/10.1016/j.hrthm.2020.06.018

Herlan, A., Ottenbacher, J., Schneider, J., Riemann, D., & Feige, B. (2019). Electrodermal activity patterns in sleep stages and their utility for sleep versus wake classification. *Journal of Sleep Research*, *28*(2), 1–8. https://doi.org/10.1111/jsr.12694

Hu, Y., Converse, C., Lyons, M. C., & Hsu, W. H. (2018). Neural control of sweat secretion: A review. *British Journal of Dermatology*, *178*(6), 1246–1256. https://doi.org/10.1111/bjd.15808

Hwang, S. H., Seo, S., Yoon, H. N., Jung, D. W., Baek, H. J., Cho, J., & Park, K. S. (2017). Sleep period time estimation based on Electrodermal activity. *IEEE Journal of Biomedical and Health Informatics*, *21*(1), 115–122. https://doi.org/10.1109/JBHI.2015.2490480

Isak, B., Uluc, K., Salcini, C., Agan, K., Tanridag, T., & Us, O. (2011). A neurophysiological approach to the complex organisation of the spine: F-wave duration and the cutaneous silent period in restless legs syndrome. *Clinical Neurophysiology*, *122*(2), 383–390. https://doi.org/10.1016/j.clinph.2010.07.005

Keenan, B. T., Kim, J., Singh, B., Bittencourt, L., Chen, N. H., Cistulli, P. A., & Pack, A. I. (2018). Recognizable clinical subtypes of obstructive sleep apnea across international sleep centers: A cluster analysis. *Sleep*, *41*(3), 1–14. https://doi.org/10.1093/sleep/zsx214

Kenny, G. P., & Jay, O. (2013). Thermometry, calorimetry, and mean body temperature during heat stress. *Comprehensive Physiology*, *3*(4), 1689–1719. https://doi.org/10.1002/cphy.c130011

Kiely, J. L., Murphy, M., & McNicholas, W. T. (1999). Subjective efficacy of nasal CPAP therapy in obstructive sleep apnoea syndrome: A prospective controlled study. *European Respiratory Journal*, *13*(5), 1086–1090. https://doi.org/10.1034/j.1399-3003.1999.13e24.x

Kim, H., Kwon, S., Kwon, Y. T., & Yeo, W. H. (2021). Soft wireless bioelectronics and differential electrodermal activity for home sleep monitoring. *Sensors (Switzerland)*, *21*(2), 1–10. https://doi.org/10.3390/s21020354

Klein, G., Burghaus, L., Vaillant, M., Pieri, V., Fink, G. R., & Diederich, N. (2014). Dysautonomia in narcolepsy: Evidence by questionnaire assessment. *Journal of Clinical Neurology (Korea)*, *10*(4), 314–319. https://doi.org/10.3988/jcn.2014.10.4.314

Kobayashi, R., Koike, Y., Hirayama, M., Ito, H., & Sobue, G. (2003). Skin sympathetic nerve function during sleep - a study with effector responses. *Autonomic Neuroscience: Basic and Clinical*, *103*(1–2), 121–126. https://doi.org/10.1016/S1566-0702(02)00261-8

Korkmaz, B., Benbir Şenel, G., Kızıltan, M. E., & Karadeniz, D. (2016). Demonstration of sympathetic dysfunction in patients with obstructive sleep apnea syndrome by measuring sympathetic skin responses from the neck. *Sleep Medicine*, *25*, 13–15. https://doi.org/10.1016/j.sleep.2016.06.030

Kräuchi, K., Cajochen, C., Werth, E., & Wirz-Justice, A. (2000). Functional link between distal vasodilation and sleep-onset latency? *American Journal of Physiology - Regulatory Integrative and Comparative Physiology*, *278*(3 47–3), 741–748. https://doi.org/10.1152/ajpregu.2000.278.3.r741

Krueger, J. M., & Takahashi, S. (1997). Thermoregulation and sleep. Closely linked but separable. *Annals of the New York Academy of Sciences*, *813* (901), 281–286. https://doi.org/10.1111/j.1749-6632.1997.tb51706.x

Lack, L. C., Gradisar, M., Van Someren, E. J. W., Wright, H. R., & Lushington, K. (2008). The relationship between insomnia and body temperatures. *Sleep Medicine Reviews*, *12*(4), 307–317. https://doi.org/10.1016/j.smrv.2008.02.003

Lanfranchi, P. A., & Somers, V. K. (2011). Cardiovascular physiology: Autonomic control in health and in sleep disorders. In *Principles and Practice of Sleep Medicine: Fifth Edition (Fifth Edit)*. Elsevier Inc. https://doi.org/10.1016/B978-1-4160-6645-3.00020-7

Liguori, C., Holzknecht, E., Placidi, F., Izzi, F., Mercuri, N. B., Högl, B., & Stefani, A. (2020). Seasonality of restless legs syndrome: Symptom variability in winter and summer times. *Sleep Medicine*, *66*, 10–14. https://doi.org/10.1016/j.sleep.2019.07.026

Liguori, R., Donadio, V., Foschini, E., Di Stasi, V., Plazzi, G., Lugaresi, E., & Montagna, P. (2000). Sleep stage-related changes in sympathetic sudomotor and vasomotor skin responses in man. *Clinical Neurophysiology*, *111*(3), 434–439. https://doi.org/10.1016/S1388-2457(99)00294-1

Lim, Y. M., Chang, S. E., Chung, S., Kang, B. H., & Kim, K. K. (2012). Small fiber function in drug naïve patients with idiopathic restless legs syndrome. *Journal of Clinical Neuroscience*, *19*(5), 702–705. https://doi.org/10.1016/j.jocn.2011.07.043

Macefield, V. G., & Wallin, B. G. (2018). Physiological and pathophysiological firing properties of single postganglionic sympathetic neurons in humans. *Journal of Neurophysiology*, *119*(3), 944–956. https://doi.org/10.1152/jn.00004.2017

Madden, C. J., & Morrison, S. F. (2019). Central nervous system circuits that control body temperature. *Neuroscience Letters*, *23*(696), 225–232. https://doi.org/10.1016/j.neulet.2018.11.027

Majumder, S., Mondal, T., & Deen, M. J. (2017). Wearable sensors for remote health monitoring. *Sensors (Switzerland)*, *17*(1), 1-45. https://doi.org/10.3390/s17010130

Meade, R. D., Louie, J. C., Poirier, M. P., Mcginn, R., Fujii, N., & Kenny, G. P. (2016). Exploring the mechanisms underpinning sweating: The development of a specialized ventilated capsule for use with intradermal microdialysis. *Physiological Reports*, *4*(6), 1–11. https://doi.org/10.14814/phy2.12738

Miglis, M. G. (2016). Autonomic dysfunction in primary sleep disorders. *Sleep Medicine*, *19*, 40–49. https://doi.org/10.1016/j.sleep.2015.10.001

Minota, K., Coon, E. A., & Benarroch, E. E. (2019). Neurologic aspects of sweating and its disorders. *Neurology*, *92*(21), 999–1005. https://doi.org/10.1212/WNL.0000000000007540

Mold, J. W., Holtzclaw, B. J., & McCarthy, L. (2012). Night sweats: A systematic review of the literature. *Journal of the American Board of Family Medicine*, *25*(6), 878–893. https://doi.org/10.3122/jabfm.2012.06.120033

Mold, J. W., Roberts, M., & Aboshady, H. M. (2004). Prevalence and predictors of night sweats, day sweats, and hot flashes in older primary care patients: An OKPRN study. *Annals of Family Medicine*, *2*(5), 391–397. https://doi.org/10.1370/afm.72

Mold, J. W., Woolley, J. H., & Nagykaldi, Z. (2006). Associations between night sweats and other sleep disturbances: An OKPRN study. *Annals of Family Medicine*, *4*(5), 423–426. https://doi.org/10.1370/afm.554

Nawrocki, S., & Cha, J. (2019). The etiology, diagnosis, and management of hyperhidrosis: A comprehensive review: Therapeutic options. *Journal of the American Academy of Dermatology*, *81*(3), 669–680. https://doi.org/10.1016/j.jaad.2018.11.066

Oh, C. M., Kim, H. Y., Na, H. K., Cho, K. H., & Chu, M. K. (2019). The effect of anxiety and depression on sleep quality of individuals with high risk for insomnia: A population-based study. *Frontiers in Neurology*, *10* (JUL), 1–8. https://doi.org/10.3389/fneur.2019.00849

Pal, D., & Mallick, B. N. (2006). Role of noradrenergic and GABA-ergic inputs in pedunculopontine tegmentum for regulation of rapid eye movement sleep in rats. *Neuropharmacology*, *51*(1), 1–11.10.1016/j.neuropharm.2006.02.006.

Parmeggiani, P. L. (2003). Thermoregulation and sleep. *Frontiers in Bioscience*, *8*, s557–s567.

Partinen, M., & Gislason, T. (1995). Basic Nordic sleep questionnaire (BNSQ): A quantitated measure of subjective sleep complaints. *Journal of Sleep Research.*, *4*, 150–155. https://doi.org/10.1111/j.1365-2869.1995.tb00205.x

Philip, P., Bailly, S., Benmerad, M., Micoulaud-Franchi, J. A., Grillet, Y., Sapene, M., Jullian -Desayes, I., Joyeux-Faure, M., Tamisier, R., & Pepin, J. L. (2020). Self-reported sleepiness and not the apnoea hypopnoea index is the best predictor of sleepiness-related accidents in obstructive sleep apnoea. *Scientific Reports*, *10*, 16267. https://doi.org/10.1038/s41598-020-72430-8

Pijeira-Díaz, H. J., Drachsler, H., Kirschner, P. A., & Järvelä, S. (2018). Profiling sympathetic arousal in a physics course: How active are students? *Journal of Computer Assisted Learning*, *34*(4), 397–408. https://doi.org/10.1111/jcal.12271

Plazzi, G., Moghadam, K. K., Maggi, L. S., Donadio, V., Vetrugno, R., Liguori, R., & Ferri, R. (2011). Autonomic disturbances in narcolepsy. *Sleep Medicine Reviews*, *15*(3), 187–196. https://doi.org/10.1016/j.smrv.2010.05.002

Rocchi, C., Placidi, F., Del Bianco, C., Liguori, C., Pisani, A., Mercuri, N. B., & Izzi, F. (2020). Autonomic symptoms, cardiovascular and sudomotor evaluation in de novo type 1 narcolepsy. *Clinical Autonomic Research*, *30*(6), 557–562. https://doi.org/10.1007/s10286-020-00718-w

Romine, W., Banerjee, T., & Goodman, G. (2019). Toward sensor-based sleep monitoring with electrodermal activity measures. *Sensors (Switzerland)*, *19*(6), 1–9. https://doi.org/10.3390/s19061417

Ross, R. J., Gresch, P. J., Ball, W. A., Sanford, L. D., & Morrison, A. R. (1995). REM sleep inhibition by desipramine: Evidence for an α-1 adrenergic mechanism. *Brain Research*, *701*(1–2), 129–134. https://doi.org/10.1016/0006-8993(95)00984-X

Sagot, J. C., Amoros, C., Candas, V., & Libert, J. P. (1987). Sweating responses and body temperatures during nocturnal sleep in humans. *American Journal of Physiology - Regulatory Integrative and Comparative Physiology*, *252*(3 [21/3]), R462–R470. https://doi.org/10.1152/ajpregu.1987.252.3.r462

Sano, A., Picard, R. W., & Stickgold, R. (2014). Quantitative analysis of wrist electrodermal activity during sleep. *International Journal of Psychophysiology*, *94*(3), 382–389. https://doi.org/10.1016/j.ijpsycho.2014.09.011

Schick, C. H. (2016). Pathophysiology of hyperhidrosis. *Thoracic Surgery Clinics*, *26*(4), 389–393. https://doi.org/10.1016/j.thorsurg.2016.06.002

Sheng, Y., & Zhu, L. (2018). The crosstalk between autonomic nervous system and blood vessels. *International Journal of Physiology, Pathophysiology and Pharmacology*, *10*(1), 17–28 Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/29593847%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC5871626

Shneyder, N., Adler, C. H., Hentz, J. G., Shill, H., Caviness, J. N., Sabbagh, M. N., & Driver-Dunckley, E. (2013). Autonomic complaints in patients with restless legs syndrome. *Sleep Medicine*, *14*(12), 1413–1416. https://doi.org/10.1016/j.sleep.2013.08.781

Silvani, A. (2020). Autonomic nervous system dysfunction in narcolepsy type 1: Time to move forward to the next level? *Clin Auton Research*, *30*, 501–502. https://doi.org/10.1007/s10286-020-00742-e

Strutton, D. R., Kowalski, J. W., Glaser, D. A., & Stang, P. E. (2014). US prevalence of hyperhidrosis and impact on individuals with axillary hyperhidrosis: Results from a national survey. *Journal of the American Academy of Dermatology*, *51*(2), 241–248. https://doi.org/10.1016/j.jaad.2003.12.040

Sturzenneger, C., & Bassetti, C. L. (2004). The clinical spectrum of narcolepsy with cataplexy: A reappraisal. *Journal of Sleep Research*, *13*(4), 395–406 10.111/j.1365-2869.x.

Szymusiak, R. (2018). *Body temperature and sleep. Handbook of clinical neurology* (1st ed.). Elsevier B.V. https://doi.org/10.1016/B978-0-444-63912-7.00020-5

Tan, C. L., & Knight, Z. A. (2018). Regulation of body temperature by the nervous system. *Neuron*, *98*(1), 31–48. https://doi.org/10.1016/j.neuron.2018.02.022

Taylor, D. J., Mallory, L. J., Lichstein, K. L., Durrence, H. H., Riedel, B. W., & Bush, A. J. (2007). Comorbidity of chronic insomnia with medical problems. *Sleep*, *30*(2), 213–218. https://doi.org/10.1093/sleep/30.2.213

Trenkwalder, C., Allen, R., Högl, B., Paulus, W., & Winkelmann, J. (2016). Restless legs syndrome associated with major diseases. *Neurology*, *86*(14), 1336–1343. https://doi.org/10.1212/WNL.0000000000002542

Tyvaert, L., Laureau, E., Hurtevent, J. P., Hurtevent, J. F., Derambure, P., & Monaca, C. (2009). A-delta and C-fibres function in primary restless legs syndrome. *Neurophysiologie Clinique*, *39*(6), 267–274. https://doi.org/10.1016/j.neucli.2009.06.003

Van Der Heide, A., Werth, E., Donjacour, C. E. H. M., Reijntjes, R. H. A. M., Lammers, G. J., Van Someren, E. J. W., & Fronczek, R. (2016). Core body and skin temperature in type 1 narcolepsy in daily life; effects of sodium oxybate and prediction of sleep attacks. *Sleep*, *39*(11), 1941–1949. https://doi.org/10.5665/sleep.6220

Vargas, I., Nguyen, A. M., Muench, A., Bastien, C. H., Ellis, J. G., & Perlis, M. L. (2020). Acute and chronic insomnia: What has time and/or hyperarousal got to do with it? *Brain Sciences*, *10*(2), 1–11. https://doi.org/10.3390/brainsci10020071

Visser, M., Marinus, J., Stiggelbout, A. M., & van Hilten, J. J. (2004). Assessment of autonomic dysfunction in Parkinson's disease: The SCOPA-AUT. *Movement Disorders*, *19*(11), 1306–1312. https://doi.org/10.1002/mds.20153

Wesström, J., Nilsson, S., Sundström-Poromaa, I., & Ulfberg, J. (2008). Restless legs syndrome among women: Prevalence, co-morbidity and possible relationship to menopause. *Climacteric*, *11*(5), 422–428. https://doi.org/10.1080/13697130802359683

Ye, L., Pien, G. W., Ratcliffe, S. J., Björnsdottir, E., Arnardottir, E. S., Pack, A. I., & Gislason, T. (2014). The different clinical faces of obstructive sleep apnoea: A cluster analysis. *European Respiratory Journal*, *44*(6), 1600–1607. https://doi.org/10.1183/09031936.00032314

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