

Thermo-parasomnia. Prediction of a possible sleep disorder or entity

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ABSTRACT

Parasomnias are a group of sleep disorders that are characterized by the presence of undesirable behavioral, experiential, or autonomic nervous system events during sleep initiation, within sleep, or during arousals from any stage of non-rapid eye movement (NREM) or rapid eye movement (REM) sleep. During wakefulness and NREM sleep, the hypothalamus plays a central role in thermoregulation. REM sleep has a very distinct thermoregulatory response that is characterized by an inhibition of hypothalamic control over body temperature, with resulting poikilothermia. The role of the thermoregulatory features of REM sleep is currently unknown. Drawing conclusions from other parasomnias one can assume that a disorder could exist in which the thermoregulatory features of REM sleep are impaired. The existence of this condition may have eluded current research because most of the research on thermoregulation has been completed using animal models or healthy volunteers. If this disorder were to exist, it could be associated with metabolic disorders, or with neurodegenerative conditions, and perhaps it could be an early biomarker for alpha-synucleinopathies in idiopathic REM sleep behavior disorder. New and evolving wearable technologies offer the promise of facilitating the monitoring of core body temperature and the testing of this hypothesized thermoregulatory autonomic disorder and its clinical correlates.

Keywords: Parasomnias; Sleep, REM; Sleep Wake Disorders; Body Temperature Regulation.

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INTRODUCTION

Parasomnias are a group of sleep disorders that are characterized by the presence of undesirable behavioral, experiential, or autonomic nervous system events during sleep initiation, within sleep, or during arousals from any stage of NREM or REM sleep. Some parasomnias, such as somnambulism, were described centuries ago while other conditions, such as sexsomnia, have been described more recently (*viz.* beginning in 1986). For most parasomnias, it is possible to identify how elements from a given state of consciousness (NREM sleep, REM sleep, wakefulness) intrude into another state to result in a spectrum of dissociated states.

Sleepwalking, sleep talking, sleep related eating, and sexsomnia are all related to NREM sleep and in all of these entities we can see how elements that are characteristic of wakefulness coexist with NREM sleep. Recurrent sleep paralysis, another parasomnia, is characterized by persistence of muscle atonia, an element of REM sleep, during wakefulness.¹

REM sleep behavior disorder (RBD) is the best-described and studied REM sleep parasomnia and it is characterized by disruptions of the muscular atonia that is typical of REM sleep.² The specific role of REM atonia has been an ongoing mystery but the impact of its disruption is very evident in the form of dream-enacting behaviors with injuries, negative psychosocial impact, and legal consequences.³ Idiopathic RBD has special relevance because it has been identified as an early sign, or precursor, of alpha-synuclein neurodegenerative disorders such as Parkinson's disease, Dementia with Lewy bodies, and Multiple System Atrophy.^{3,4}

THERMOREGULATION DURING REM SLEEP

While the primary function(s) of REM sleep remains unknown, some of its cardinal features are well studied. REM sleep is associated with a distinct thermoregulatory pattern. It is established that thermoregulation responses are inhibited during REM sleep. Parmeggiani and Rabini⁵ were the first to describe the suppression of shivering and panting during REM sleep. During wakefulness, the hypothalamus occupies a central position in the control of body temperature; REM sleep is characterized by an inhibition in hypothalamic control of body temperature.^{6,7} It has been proposed that REM sleep is a poikilothermic state, while wakefulness and NREM sleep are homeothermic.⁸

Looking at other parasomnias, one can come to the logical and theoretical conclusion that there could be a disease or entity that would be mainly characterized by a disruption in the thermoregulatory features of REM sleep, in other words a predominantly or exclusively autonomic nervous system parasomnia (analogous to pure autonomic epileptic seizures, a rare but well-documented phenomenon).

PREDICTED DISORDER/ HYPOTHESIS

- REM sleep with preserved thermoregulation

This would be a condition in which the usual thermoregulatory features of REM sleep are lost or at least impaired.

Since REM sleep is characterized by a lack of hypothalamic control of central body temperature, this hypothetical condition would be characterized by periods of hypothalamic control over thermoregulation, *i.e.* a renormalization of thermoregulation in REM sleep. Since most parasomnias are characterized by “intermittent” intrusions into another state, one can extrapolate that this entity may manifest as a phasic or intermittent phenomenon during REM sleep.

PERSPECTIVES AND POTENTIAL CLINICAL SIGNIFICANCE OF THESE ENTITIES

There is limited research in field of thermoregulation during sleep. Most of the research regarding temperature control during REM sleep has been conducted using animal models or healthy individuals. Most studies on thermoregulation involve very small sample sizes. Knowledge about autonomic function and autonomic disorders tends to be limited in the clinical sleep medicine community. Collection and analysis of core body temperature during sleep is not routinely done during clinical polysomnograms.

It is difficult to predict the full clinical significance of an entity that has not been identified yet but we could draw some hypothesis based on the information that is available from other parasomnias and other neurological conditions.

If our hypothetical condition were to be identified, the interruptions in thermoregulation during REM would behave in a similar way as the interruptions in muscle atonia that are observed in RBD. Extrapolating from the relationship between REM sleep behavior disorder and neurodegenerative disorders, one can hypothesize that “REM sleep with preserved thermoregulation” could be associated with the same group of neurodegenerative diseases. Alpha-synucleinopathies are also associated with autonomic dysfunction but the research to date has not focused on temperature control during specific sleep stages.

Nevertheless, given the current intense interest in identifying early biomarkers for future alpha-synuclein neurodegeneration in middle aged and older patients with idiopathic (>80% of whom will eventually convert to overt neurodegeneration)⁹, monitoring the status of thermoregulation during REM sleep is a promising new area worthy of investigation, especially since new and evolving wearable technologies¹⁰ can facilitate the gathering of the data.

Zhong et al.¹¹ have described an anomaly in thermoregulation in individuals with Parkinson's disease and RBD. In this study, patients with Parkinson's disease and RBD had decreased amplitude in core body temperature profiles when compared to healthy age-matched controls. Unfortunately, this study did not look at whether the anomaly in core body temperature was specifically related to REM sleep or not. It is very possible that “REM sleep with preserved thermoregulation” could be associated with RBD but it would have to present alone in some individuals in order to be considered a parasomnia by itself.

At this point, there is limited evidence to support the idea that having some thermoregulatory features during the “wrong” stage of sleep could have a clinical impact by itself but

these features could represent early signs of other conditions, notably alpha-synuclein neurodegenerative disorders.

POTENTIAL IDENTIFICATION OF THIS DISORDER

In order to prove our hypothesis, and identify this condition, one must study the thermoregulatory pattern of a large cohort of individuals. Studying a population with other disorders that are known to affect the autonomic nervous system could increase the chances of finding our proposed entity. Studying patients with advanced Parkinson's disease or Multiple Systems Atrophy could be particularly helpful since both conditions are associated with another REM sleep parasomnia (i.e. RBD) and with autonomic dysfunction.

LIMITATIONS

There has been some theoretical and experimental progress but the main role of REM sleep is unclear and the potential of role of the poikilothermic state during REM sleep is even less clear. The sleep research community would have to identify the main role of REM sleep and its thermoregulatory functions before the full scope of this potential condition could be well understood.

The logistics of large studies involving body, temperature could be very challenging but this could be mitigated with the introduction of newer technologies. Wearable devices that measure body temperature and other autonomic markers are becoming very popular and could be easy to analyze.

SUMMARY

It is well known that REM sleep and wakefulness exhibit distinctive thermoregulatory "signatures" and an entity or disorder could exist in which thermoregulatory characteristics of REM sleep are impaired. This entity has not been described

to this day. While a more solid understanding of this potential condition could take decades, bringing attention to this area of sleep research remains at least interesting.

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