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Review

Elicitation of sleep-onset REM periods in normal individuals using the sleep interruption technique (SIT)

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Abstract

Use of the sleep interruption technique (SIT) to elicit sleep onset REM periods (SOREMPs) in normal individuals is introduced along with its theoretical bases, empirical findings, and potential applications. Capitalizing upon the circadian and ultradian nature of REM sleep, the SIT has been developed to examine various psychophysiological characteristics related to REM sleep. The SIT allows us to: (1) obtain SOREMPs at the discretion of the researcher; (2) avoid the contaminating effects of preceding non-REM (NREM)-REM stage ordering on subsequent target sleep episodes; and (3) obtain many REM episodes in a short time by repeating the sleep interruptions. The SIT has been applied in several studies, such as examination of physiological precursors to REM periods, correlates of dream mechanisms, and induction of sleep paralysis in normal individuals. Guidelines for eliciting SOREMP using the SIT, including the parameters to be manipulated, are provided, e.g. NREM duration before sleep interruption, time of night of awakenings, duration of sleep interruption and tasks employed. Directions for further research such as determining optimal type of task to promote SOREMP occurrences, generalization of SOREMP as usual REM periods, and forms of SOREMP occurrences under different conditions in normal individuals and clinical patients are discussed. Finally, possible future uses of the SIT, including combining this technique with new technologies, are also suggested.

Keywords: Sleep; REM; Sleep onset REM; Dream; Sleep paralysis; Sleep cycle; Circadian rhythm; Ultradian rhythm

1. Introduction

In healthy individuals, REM sleep usually occurs after 60–90 min of non-REM (NREM) sleep. This NREM-REM cycle typically repeats four to six times each night. A sleep onset REM period (SOREMP) is an atypical occurrence of REM sleep that is observed at sleep onset and that has been distinguished from typical REM sleep episodes.

In standard clinical terms, SOREMP is defined as REM sleep with a latency of less than 15 min in the Multiple Sleep Latency Test (MSLT; International Classification of Sleep Disorders; ICSD [1]). However, the distribution of SOREMP latencies in normal individuals clearly spans 25 min post-sleep onset when no enforced arousals are made [2,3].

1.1. SOREMP is a symptom observed in clinical settings

SOREMP is perhaps best known as one of the major symptoms of narcolepsy, but it is also observed in depression and schizophrenia. Patients with narcolepsy are likely to show SOREMPs more often than controls during an MSLT [4–6]. Moreover, SOREMPs occur more often during the MSLT in narcolepsy patients who complain of nocturnal sleep disturbances than in those without complaints. It is also known that narcoleptic sleep paralysis appears specifically in SOREMP [7,8].

Depressive patients are also known to frequently exhibit SOREMP episodes [9–11]. Such patients are likely to have negative symptoms more often than those without SOREMPs [12,13]. However, considering differences in REM latency distributions and sleep structures, the mechanisms for SOREMP in depression appear to differ from those in narcolepsy [14] (Table 1). It has been hypothesized that SOREMP occurrences might imply a greater overall severity of symptoms in schizophrenia [12]. An association between schizophrenia and narcolepsy has also been reported [13]: 7% of patients with schizophrenia have some form of psychotic variant of narcolepsy. In addition, schizophrenia patients are nearly four times as likely to

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Table 1
Patterns of SOREMP occurrence in normal individuals and narcoleptic and depressed patients

	Normal	Narcolepsy	Depression
SOREMP during MSLT (daytime)	Rare [30]	Often [1]	Rare [84]
SOREMP in the 1st NREM-REM cycle in nocturnal sleep	None	Bimodal distribution Very short or typical REM latencies [14]	Broad distribution [14,85] Bimodal distribution [9]
SOREMP after sleep interruptions	Bimodal distribution [3,48]	–	Bimodal in the subjects who show SOREMPs in the evening [10]
Nocturnal sleep structure related to SOREMP	Disrupted due to the SIT	Not disrupted [14,87]	Disrupted: decreased SWS [14,86]

carry narcolepsy-associated antigens compared to the normal population [15].

Drawing on the finding that SOREMP often occurs as a secondary symptom in disorders with psychotic symptoms, a common pathophysiological mechanism in the brainstem that underlies abnormal REM sleep regulation and psychosis has been theorized [13].

1.2. SOREMP is related to the disruption of sleep-wake cycle in normal individuals

SOREMPs are observed in healthy individuals with non-24-h sleep/wake patterns such as free-running schedules [16–18], shifted sleep-wake schedules [19–21], and/or multiple sleep/wake schedules [22,23], and partial sleep deprivation schedules [24]. Psychological stress attributed to these schedules [22] has been hypothesized to be one of the factors related to SOREMP occurrence. This hypothesis is supported by the finding that SOREMP is a prerequisite for elicitation of isolated sleep paralysis (ISP) in healthy individuals [25], and by the observation of ISP under physical and/or psychological stress and during a disturbed sleep/wake cycle [25,26]. Thus, physiological and/or psychological stresses are thought to be associated with SOREMP in healthy individuals [27,28] although it is difficult to determine whether stress causes SOREMPs under these schedules or vice versa.

SOREMPs are also observed in healthy individuals under everyday circumstances. Just 1 h of sleep interruption (SI) in nocturnal sleep can cause SOREMP episodes as subjects fall back to sleep [3,29]. Bishop et al. [30] have also reported that 17% of normal participants show more than two SOREMP episodes on a standard MSLT procedure.

2. Elicitation of SOREMP using the sleep interruption technique (SIT)

2.1. Benefits of using SOREMP in experimental studies of REM-related phenomena

Many studies have attempted to clarify the mechanisms and functions of REM sleep. Neurophysiological techniques have been used to investigate specific neurons that regulate REM sleep [31]. New technologies such as positron emission tomography and functional magnetic resonant imaging have been deployed to examine neuroanatomical specificity during REM sleep with a focus on measures such as gamma range electroencephalogram (EEG) activity [32] and the decreased activity in the dorsolateral prefrontal cortex [33,34]. It has been hypothesized that during REM sleep, dreams are more likely to appear, visual imagery is more vivid, and some types of memory consolidation are more likely to occur [35–39].

However, when REM sleep-related phenomena are experimentally examined in healthy individuals, it is virtually impossible to obtain REM periods uncontaminated by the influence of previous NREM periods, since each REM period typically appears cyclically after approximately 90 min of NREM sleep (Fig. 1). Similarly, accumulated sleep time or the number and type of sleep stage changes may be confounded with the NREM-REM ordering of stages (Fig. 1a). The sampling of REM periods in a short window following sleep onset 'SOREMP' can overcome these difficulties because specific aspects of REM sleep can be scrutinized while variables such as prior sleep length and depth of NREM and REM sleep are held constant. This

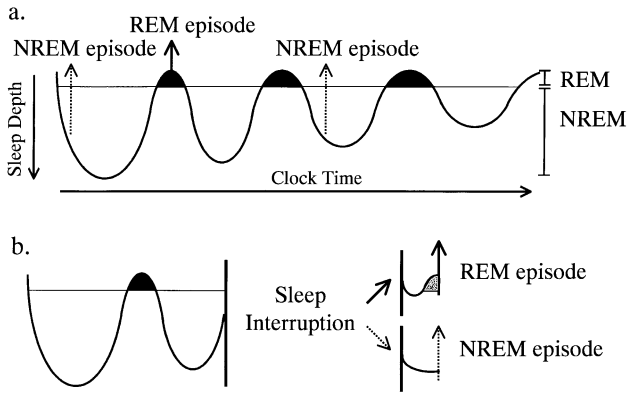

Fig. 1. Schematic representation of data collection timing from REM and NREM episodes during a natural sleep cycle (a); and using the SIT (b). The SIT controls sleep processes preceding target REM and NREM episodes.

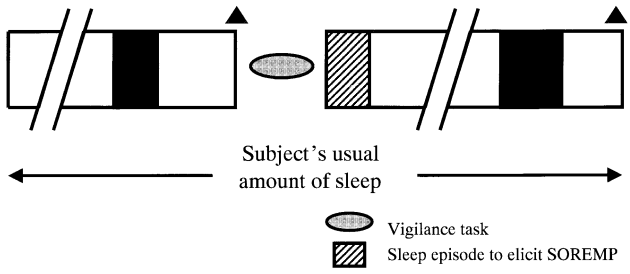

Fig. 2. Schematic representation of the SIT modified from Miyasita et al. [3]. White, NREM sleep; black, REM sleep. Participants are awakened after a specified duration of NREM sleep has elapsed (left triangle). They are then kept awake for approximately 1 h, during which they are assigned some type of task (gray oval). Following the task, participants are allowed to return to sleep. SOREMPs are elicited from the subsequent sleep episode (striped).

type of SOREMP sampling is particularly useful when the goal is to directly compare features of REM and NREM episodes such as physiological measurements or associated mentation (Fig. 1b).

The SIT has been developed to elicit SOREMPs from normal individuals in this experimentally controlled manner. The SIT has proven to be useful in examining various psychophysiological measures of phenomena that are related to REM sleep mechanisms. Experimenters can systematically elicit a desired number of SOREMP episodes or ratio of SOREMP to non-SOREMP episodes depending on the requirements of the study, by manipulating parameters such as elapsed NREM duration before SI, length of SI, task duration, and circadian clock time at which participants are awakened. The following findings provide the theoretical basis guiding manipulation of parameters in the SIT.

2.2. Original SIT to elicit SOREMPs

Miyasita et al. [3] summarized a series of their experiments for eliciting SOREMPs from healthy participants using the SIT. Their procedure is illustrated in Fig. 2.

In these experiments, a total of 44 healthy paid volunteers, aged 18–23 years, were each studied for three or four experimental nights after two adaptation nights and one baseline night. During experimental nights, each participant's sleep was interrupted when 20 min of NREM sleep had elapsed after termination of the 1st REM period. The 20-min duration of NREM period was reported to be enough to clearly determine termination of the 1st REM period [40]. Participants were then kept awake for 7–136 min. During this phase, they were subjected to one of the following conditions: resting on a bed, performing a serial addition task, receiving auditory or photic stimuli, performing an auditory vigilance task, engaging in associative-memory learning, watching TV, or doing physical exercise. Participants were then allowed to return to sleep. SOREMPs were elicited in 22 of 44 participants at this time. Further, out of 129 experimental nights, 35 SOREMPs with REM latencies of less than 25 min and 94 typical REM periods with REM latencies of longer than 25 min (non-SOREMPs) were observed (Fig. 3).

To further examine factors influencing the rate of SOREMP occurrence, parameters preceding SIs were compared between experimental nights with SOREMP (SOREMP nights) and those with non-SOREMP (non-SOREMP nights) among 18 participants who showed both types of nights. Non-SOREMP nights were associated with significantly longer duration of the 2nd or 3rd REM episode compared with either SOREMP nights or baseline nights. Interestingly, total amount of REM sleep in the entire night did not differentiate the groups. Based on these results, Miyasita et al. [3] attempted to assess each of three existing models, i.e. that a REM sleep oscillator: (1) runs only during sleep (sleep-dependent model [41,42]); (2) runs throughout the 24 h period regardless of arousal state (sleep-indepen-

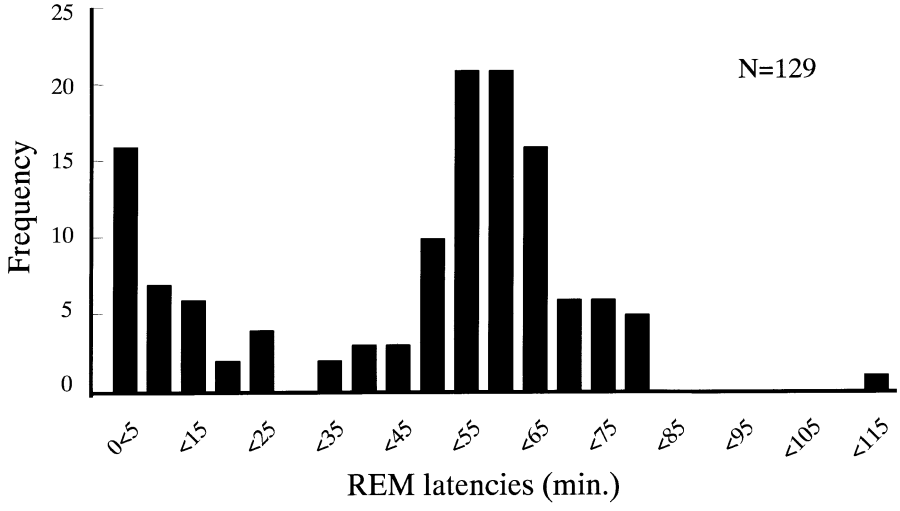

Fig. 3. Bimodal distribution of REM sleep latencies after SI modified from Miyasita et al. [3]. A cluster of REM latencies of less than 25 min is judged to be SOREMP.

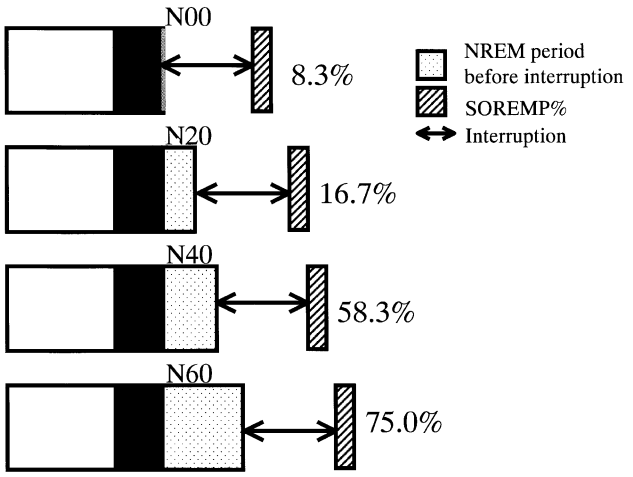

Fig. 4. Ultradian influence on SOREMP occurrence rates. White, NREM sleep; black, REM sleep; striped, SOREMP episodes. N00, N20, N40, N60/ durations of preceding NREM sleep elapsed before sleep interruption, i.e. 0, 20, 40, and 60 min, respectively.

dent model [43]); or (3) is reset to its initial state by awakenings (reset model [44]). Taking these models and their own findings into account, Miyasita et al. [3] proposed a 'modified reset-model' to explain SOREMP occurrences. In this model, intervening wakefulness functions to reset the REM rhythm, and produces a potential for SOREMP. For example, they hypothesized that narcoleptic patients have a low reset threshold and thus a high potential for SOREMP occurrences. They further examined factors that would influence SOREMP occurrence rates, such as ultradian rhythm, circadian rhythm, and individual factors as described below, which provide a theoretical basis for the application of the SIT in practical use.

2.3. What influences the probability of SOREMP occurrences in the SIT

2.3.1. Ultradian factors

One of the ultradian factors likely to influence SOREMP occurrences after SI is duration of the NREM period preceding the SI. Miyasita et al. [45] manipulated NREM length in the 2nd NREM-REM sleep cycle before SI to be either 0, 20, 40, or 60 min (N00, N20, N40, and N60; Fig. 4). Following a 60-min SI, SOREMPs occurred in 8.3, 16.7, 58.3, and 75.0%, respectively. They concluded that longer pre-SI NREM periods predict a higher post-SI SOREMP occurrence rate.

A second ultradian factor is SI duration. In the 2nd cycle, when SI is shorter than 40 min or longer than 120 min, subsequent SOREMP occurrence rates are virtually zero. Within the range of 40–120 min, SOREMP occurrence rates are nearly equal (20–33.4%). Therefore, it was suggested that a SI within the range of 40–120 min is crucial for eliciting SOREMP occurrences [3].

The third ultradian factor is duration of the task during SI. Fukuda et al. [46] manipulated the duration of an auditory vigilance task to be 0 min (resting without task), 30 or 60 min during a constant 90-min SI. They found that SOREMP occurs more often and with shorter REM latencies after the 60-min task. In sum, ultradian factors such as duration of pre-SI NREM periods, SI length, and task duration during the SI seem to systematically influence the probability of SOREMP occurrences.

2.3.2. Circadian factors

Drawing on the close relationship between REM sleep and body temperature rhythm previously reported [16,17,47], Sasaki et al. [48] examined whether SOREMP occurrence reflects REM propensity in the natural course of nocturnal sleep in normal individuals. They manipulated circadian factors by interrupting nocturnal sleep either in the 2nd or the 4th NREM-REM cycle and determined the probability of SOREMP occurrences. SOREMPs occurred significantly more often in the 4th cycle (87.5%) than in the 2nd cycle (58.1%; Fig. 5).

2.3.3. Individual differences

Long sleepers and short sleepers were subjected to the SIT to examine the effects of individual differences on SOREMP occurrences [29]. Five long and six short sleepers, screened with questionnaires, slept six consecutive nights in the sleep lab. The SIT was used on the 4th, 5th, and 6th nights. Three types of tasks (associative-memory learning, serial addition, physical exercise on a stationary bicycle) were counterbalanced across these three nights. As predicted, SOREMPs appeared only in short sleepers. Short sleepers also showed a significant increase in the amount of REM sleep from the 1st to the 2nd NREM-REM cycle in the baseline night compared to long sleepers. Fukuda et al. [29] construed these findings to imply that enhanced REM sleep pressure or propensity affected SOREMP occurrence rates at the second sleep onset following SI only in short sleepers. However, further studies are required to determine what kind of individual differences influence SOREMP, including well-known sleep typologies such as regular-irregular [49], morningness-eveningness [50], or poor-good [51] sleepers.

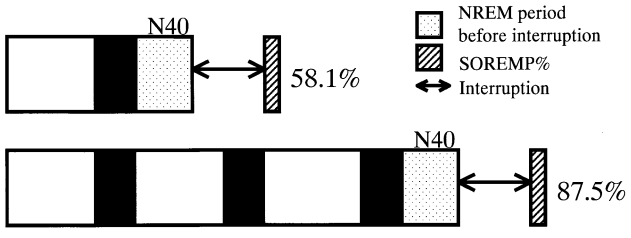

Fig. 5. Circadian phases influence on SOREMP occurrence rates in which participants were awakened from 2nd and 4th NREM-REM cycles and subjected to the SIT. White, NREM sleep; black, REM sleep; striped, SOREMP episodes. More SOREMP appeared in the 4th cycle (lower) than in the 2nd cycle (upper), modified from Sasaki et al. [48].

3. Application of the SIT

The previous work demonstrates that by manipulating parameters of the SIT, the predictability of SOREMP occurrences can be improved. Hence, the SIT is a potentially powerful tool for empirically studying basic sleep processes, e.g. REM sleep correlates (physiological activity, dreaming), regulation of NREM-REM cycle, and simulation of clinical symptoms related to SOREMP. Below, some studies that applied the SIT are reviewed.

3.1. Physiological predecessors of SOREMP occurrence

According to the standardized sleep scoring system [52], stage REM is defined as a state accompanied by three fundamental physiological markers; desynchronized EEG, phasic rapid eye movements, and tonic suppression of muscle activity. In addition, several physiological markers are observed in advance of the initial appearance of these three markers, e.g. increased heart rate variability [53], suppression of sweating effector activity [54], and attenuation of N300 activity [55]. The latter can appear up to 15 min prior to REM sleep as defined by the standard criteria [52]. These findings allow us to hypothesize that similar physiological antecedents may predict SOREMP occurrences. Yamamoto et al. [56] examined several physiological markers every 3 s preceding SOREMPs elicited using the SIT. Alpha EEG activity, eye movement activity, and muscle tension were compared from lights-off up to the onset of SOREMP and NREMP. Results indicated that reduced tonic muscle activity, fluctuations in alpha EEG activity, and consistent slow eye movements predicted SOREMP occurrences.

Hypothesizing that REM pressure affects SOREMP occurrences, Fukuda et al. [57] compared SOREMP and non-SOREMP for REM density and REM duration in the 1st REM period prior to SI. No differences were found, leading them to further hypothesize that some physiological antecedents in the sleep onset period are more closely related than others to subsequent SOREMP occurrences. Fukuda et al. [57] found that respiration activity was more highly activated during the sleep onset periods preceding SOREMP compared to those preceding non-SOREMP. In addition, shorter sleep latencies were observed before SOREMP episodes than those before non-SOREMP episodes. Ishii et al. [58] have also found that the levels of subjective sleepiness before SOREMP episodes were higher than those before NREMP episodes.

In sum, some of the physiological states observed to precede SOREMP – consistent muscle atonia, slow eye movement activity, highly activated respiration – are antecedents highly suggestive of those in typical REM sleep. Increased sleepiness observed preceding SOREMP coincides with the finding that participants who showed more than two SOREMPs on the MSLT were sleepier than those with less than two SOREMPs [30]. Considering that REM mechanisms typically start at the end of a NREM period, it could be speculated that this sleepiness before SOREMP may reflect a minimum arousal level that allows REM mechanisms to begin even though participants are not yet in an explicit sleep state.

3.2. The effect of sleep interruption on temperature rhythm

To investigate relationships between body temperature and sleep structures, the effects of SI on body temperature were compared among baseline, SOREMP and non-SOREMP nights [59]. In this study, body temperature from post-SI lights out to sleep onset decreased more markedly in SOREMP than in non-SOREMP episodes. The authors concluded that SI causes a decrease in body temperature and an increase in REM propensity. Furthermore, Sasaki et al. [60] looked at the relationship between body temperature and SI length using the SIT. The temperature drop was significantly larger when SI was longer than 60 min. Furthermore, no relationship between amount of slow wave sleep and temperature was observed. Accordingly, the authors cast doubt on the popular theory [61–66] that one function of slow wave sleep is to lower temperature and rather supported an indirect relationship between body temperature and slow wave sleep activity shown by Dijk et al. [67]. Hence, they concluded that the long SI itself causes a decrease in body temperature at the re-entry into sleep, regardless of the amount of slow wave sleep in the experimental condition.

Although the number of studies comparing physiological variables during SOREMPs with those during NREM states in normal individuals is still limited, the SIT provides unique and informative findings about physiological mechanisms of the various sleep states.

3.3. Examination of REM-related mentation

Since various forms of mentation are obtained when people are awakened from different states, such as sleep onset, NREM sleep, and REM sleep, it has been controversial whether REM sleep is a specific precondition for dreaming (see reviews, refs. [31,39,68]). It is problematic to compare NREM and REM because different orders and depths of sleep preceding these two types of sleep may confound mentation measures. Therefore, Takeuchi et al. [69,70] conducted two studies applying the SIT to collect SOREMP and NREM mentation at sleep onset with minimal influence of preceding sleep processes. Using two different lab settings and subjects (Japanese and Canadian) but a single constant set of SIT procedures, consistent results were obtained. Through the analyzes of sleep stages [70] and EEG power spectra [69], they were able to demonstrate relationships between: (1) preceding REM states and increased probability of SOREMP dreams; and (2) preceding arousal events and increased probability of NREM dreams. Therefore, they theorized that REM mechanisms promote dreaming during SOREMP while arousal processes

promote dreaming during sleep onset NREM periods. This is one example of a powerful use of the SIT to give new perspective to existing theories or findings related to REM sleep.

The SIT could be useful to evoke and examine correlates of multiple REM episodes within a short period of time. For example, in the studies examined above, dream experiences were assessed using rating scales constructed and normed in Japan [71], and translated into English [72]. These scales were intended to address methodological difficulties common to psychophysiological dream studies, such as the reliability of subjects' verbal reports, the reliability of experimenters when coding dreams [73], and the validity of questions used to examine psychophysiological activity underlying dreaming [74,75]. The SIT was used to obtain large numbers of dream reports from various sleep stages including SOREMP, in relatively few nights.

3.4. Examination of sleep paralysis

The SIT can be beneficial in clinical research related to REM-related symptoms or disorders because it can simulate clinical conditions that implicate SOREMPs, e.g. narcolepsy, depression, schizophrenia.

The SIT enabled Takeuchi et al. to elicit sleep paralysis experimentally in normal participants (ISP) [25,26]. Several survey studies have shown a high prevalence of ISP in the normal population [26,76,77], but their physiological mechanisms were unclear. Polysomnography that they recorded during ISPs provided physiological evidence of simultaneous appearances of REM sleep and wakefulness, e.g. participants reported a clear awareness of surroundings and simultaneous hallucinations with intense anxiety/terror [25]. Moreover, analysis of performance data preceding ISPs elicited from SOREMP in a multi-phasic SIT schedule [26], provided evidence that ISP is likely to appear as a phenotype of REM dissociation during SOREMP when participants with low tolerance for disrupted sleep-wake rhythms are placed in the SIT schedule.

4. Suggested SIT protocol

Based upon the findings described for this series of SIT studies, we suggest the following basic guidelines for eliciting SOREMPs.

4.1. Participants

Participants should be carefully screened to determine if they have narcolepsy-related symptoms such as cataplexy and sleep attacks (for details on narcolepsy criteria, see ICSD [1]). It is a logical assumption that SOREMP would be expressed differently in individuals with a potential predisposition to narcolepsy.

Due to circadian specificity in SOREMP [48], participants' sleep cycles should be regularly maintained before the study. They should be provided with sleep logs for at least 1 week before the study to track their wake-sleep cycles as well as to determine probable sleep length in the lab. Participants should refrain from alcohol, unusual amounts of caffeine, any type of medication with a sedative effect, and atypical naps before and during the study. Note that anything that could influence sleep patterns may also change SOREMP occurrence patterns.

4.2. Adaptation and baseline nights

Whether participants are accustomed to their sleep environment is crucial for regulation of sleep. Unfamiliarity with the sleep environment in the earlier nights is known as 'the first night effect', which is likely to be reflected in a missed 1st REM period or a fragmented sleep pattern [78–80]. When sleep patterns change due to the 1st night effect, it may also influence sleep structure in the 2nd night (e.g. increases of REM sleep or slow wave sleep as a rebound). This may cause difficulties in interpretation of the sleep pattern in the both 1st and 2nd nights. Hence, adaptation night(s) help to avoid the possibility that sleep patterns are disrupted during experimental nights. Further, a baseline night is necessary when interruption nights are to be compared to baseline. Therefore, a minimum of two nights before starting the SIT is necessary for subjects to fully adjust to the laboratory. Whether a 3rd night is needed will depend upon whether the baseline night is required for the study. If a baseline is necessary, the recording of two adaptation and one baseline nights is recommended.

4.3. Experimental nights

The basic protocol for eliciting SOREMPs is:

1. awaken participant when 40–60 min of NREM sleep has elapsed since the end of a REM episode;
2. keep participant awake for 60–80 min. During this SI, administer a vigilance task or a comparable task that maintains arousal above a minimum level;
3. allow participant to return to sleep and wait for the onset of a SOREMP. Note that at present there is no a priori way to determine if a particular sleep onset will produce a SOREMP, only to predict the overall ratio of SOREMP/NREM across several trials.

4.4. Parameters to be manipulated

SOREMP occurrence rates can be manipulated by changing the parameters preceding SI as indicated below.

4.4.1. Pre-SI NREM duration

The longer the prior NREM period, the more likely SOREMPs are to occur [45] (see Fig. 4). It should be noted that using a NREM period longer than 60 min would entail a potential risk of a REM episode appearing

before the SI awakening. Depending on the individual NREM durations observed on adaptation and baseline nights, some participants may need slight adjustments to their suggested pre-SI NREM durations.

4.4.2. Time of night

SOREMPs occur more frequently in the later part of the night as Sasaki et al. [48] demonstrated (Fig. 5). In our experience, detection of the termination of 1st REM period is sometimes more difficult than later cycles due to weak REM propensities in the early part of the night. On the other hand, SI after the 5th cycle might not result in a SOREMP because some participants show only four or five NREM-REM cycles in one night or may not be able to return to sleep. Hence, awakening between the 2nd and 4th NREM-REM cycles seems most practical.

4.4.3. Duration of SI

A total SI duration of 60–80 min including time taken to fall asleep seems to be most feasible based upon: (1) relationship between longer tasks and increased SOREMPs [46]; (2) substantially consistent SOREMP % after SIs longer than 40 min [3]; and (3) possible fatigue caused by the long task.

4.4.4. Duration and type of task

As seen in the findings of Fukuda et al. [46], the longer the task the more likely SOREMPs are to occur. Whether type of task critically influences SOREMP occurrence is not yet known [29] (see below 'issues to be examined further'). However, at least an auditory vigilance task, which has been used in several studies [25,26,48,70], appears to be effective at eliciting SOREMPs.

5. Issues to be examined further

5.1. What is the best SI task for promoting SOREMP occurrences?

The optimal task for eliciting SOREMP is yet to be determined. Fukuda et al. [29] found that four SOREMPs occurred after physical exercises, two after a serial addition task, and none after an associative-memory learning task [Cochran's Q test; $P < 0.005$, chi square $= 6.0$, df $= 2$] and cautiously proposed that physical or psychological stress may influence SOREMP. However, their sample size is not large enough to be conclusive. In another similar study [81], after exercise REM duration and density decreased but not REM latency. Therefore, it is possible that physical exercise may not be critical for onset of REM sleep itself, but may affect REM structure. Further studies will be needed to conclude whether the type of task(s) influence SOREMP occurrences.

5.2. Can SOREMP be generalized as usual REM periods?

Although physiological correlates of SOREMPs are interpreted to be comparable to those of typical REM sleep episodes, whether SOREMP can be regarded as the same type of entity as a typical REM period remains an important issue. SOREMPs are different from typical REM periods in at least four phenotypic aspects. (1) Greater probability of occurrence of non-24-h sleep/wake schedules [16,17,21,22,29]; (2) related to enhanced REM sleep pressure or REM propensity [48]; (3) likely to occur at the trough of the body temperature rhythm [16,17,47]; and (4) a necessary but insufficient condition for sleep paralysis and/or hypnagogic hallucination to occur [25,26,82]. However, SOREMP still possesses all the typical components known to reflect specific patterns of neural activity during REM sleep [31], i.e. rapid eye movements, muscle atonia, and desynchronized EEG. Therefore, the functional aspects of REM sleep seem to remain during SOREMP.

Recently, dream properties were compared between SOREMPs and usual REM periods during a multi-phasic sleep schedule and SOREMP dreams were found to be less impressive and more negative in the later part of the protocol than typical REM dreams [83]. It was hypothesized that SOREMP dreams, due to their temporal proximity to wakefulness, reflect previous arousal states more than do typical REM dreams. In light of this result and the finding that sleep paralysis with awareness of surroundings occurs during SOREMP, it is likely that arousal level during SOREMP is higher than in typical REM sleep periods. SOREMP seems to be functionally the same as a typical REM period, yet its arousal level may be different. Therefore, caution is still advised when interpreting results obtained from SOREMP recordings as representative of typical REM sleep. More normative studies of SOREMP processes need to be conducted.

5.3. Are mechanisms of SOREMP in healthy individuals the same as those observed in clinical patients?

As mentioned earlier in this paper, SOREMPs are often observed in patients with narcolepsy or depression. Furthermore, the pattern of SOREMP occurrences differs depending on the conditions (Table 1).

In patients, SOREMPs are usually observed as one clinical manifestation, not as an independent disorder itself. For instance, cataplexy, a central symptom in narcolepsy patients, has been suggested to be triggered by mechanisms independent from REM sleep-related symptoms, e.g. SOREMP or sleep paralysis [88]. Thus, it is likely that SOREMPs occur as 'a side effect' or symptom of disorders that implicate similar mechanisms. It has been reported that temperature phase is advanced in narcoleptic patients with SOREMP [89,90]. Mayer et al. [90] proposed dysfunction of the mechanism to lock REM and temperature rhythms in narcoleptic patients as a contributor to SOREMP occur-

rence. In healthy individuals, SOREMPs occur under a disrupted sleep cycle, which also often disrupts temperature rhythm. Therefore, considering these findings together, differences in SOREMP occurrence likely reflect the level of dysfunction of REM-regulation mechanisms more than some primary pathology per se, and it may be that the mechanisms of SOREMP occurrence are similar in healthy individuals and clinical patients. In other words, SOREMP occurrence itself is an 'abnormal' state caused by disruption or dysfunction of REM-regulation mechanisms regardless of whether it occurs in normal individuals or clinical patients. If there are intrinsic differences closely related to the pathology of the primary disorder, they may involve whether the threshold for triggering REM is lower or higher, and whether the dysfunction is consistent or recuperative. Therefore elicitation of SOREMP could be regarded as creating a temporary, albeit artificial, dysfunction of REM-regulation mechanisms and a lowering of the REM threshold. Further findings comparing SOREMPs observed from individuals with various disorders as well as those obtained from normal individuals in the SIT protocol can address these questions more completely.

6. Conclusion

The SIT, developed utilizing the ultradian and circadian features of REM sleep, was introduced as a useful tool for examining various REM sleep-related phenomena. By manipulating parameters that precede interruptions, the probability of eliciting SOREMPs in the SIT can be manipulated. It's continued and expanded use with other techniques (e.g. neuro-imaging) and it's careful interpretation holds out promise for further findings in both clinical and basic research areas.

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