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TOPICAL REVIEW

Organic Changes in the Brain, Sleep Loss, and Sleep Modulation With Aging: A Review

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ABSTRACT The sleep loss (SL) are one of the important diseases that endanger the health of aging individuals. This study evaluated SL in aging individuals, and explored the relationship between age and the organic changes that affect brain and sleep. The causes of SL in aging individuals and its harmful effects on them have been outlined. To enable individuals in choosing a suitable way to sleep better, we also reviewed advantages and disadvantages of the existing sleep modulation based on lifestyle habits and drug and physical stimulation. We found the former as more suitable for patients with mild SL, while the latter may fail to achieve the desired effects and may even lead to the onset of new diseases. Therefore, it is proposed to use non-invasive electrical and magnetic stimulations to improve the sleep quality in aging patients.In this review, mechanisms of the two stimulation methods have been summarized. Through analysis, it was found that magnetic stimulation can induce neuronal action potential, which makes patients twitch, and equipment noise causes discomfort in the elderly during treatment. Comparative analysis of stimulation methods revealed that transcranial electrical stimulation (tES) is a considerably safe, convenient, non-invasive, and easy to operate method with few adverse reactions, and it can be considered a potential therapeutic method for SL in aging patients.

INDEX TERMS Aging, SL, non-invasive, tES, transcranial magnetic stimulation (TMS).

I. INTRODUCTION

Studies have proved that animals experienced the need for sleep before they possessed brains [1], [2]. Sleep is an indispensable and important physiological activity across animal kingdom. Humans spend about one-third of their lives sleeping [3]. However, the sleep duration is not evenly distributed during human lifetime and the sleep duration and quality decline with advancing age. As a result, sleep fragmentation and insomnia have become the most common physiological conditions in aging individuals [4], [5]. Sleep loss has become an important disease compromising elderly health.

Aging individuals lack sustained and prolonged sleep, leading to a series of health problems. Some studies have shown that insufficient sleep affects cognitive function, induces memory disorders [6], [7], [8], [9], [10], and increases the probability of dementia and depression [7], [9], [11]. In severe cases, it also causes physical and physiological

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damage, and increases the probability of death [11], [12]. Resolving sleep loss in the elderly can help improve their quality of life.

Sleep loss in the elderly is attributed to multiple factors [13], including medical syndrome, mental illness, primary sleep disorder, social participation, and changes in lifestyle or environment [14], [15], in addition to anatomical and communication changes in the brain due to aging [9], [16]. Although more than 50% of older adults involved in the survey by Foley et al. [12]suffered from sleep disorder, a large proportion of patients attributed their problems to their own poor health and illness [14], [15]. Apart from the impact of diseases, environmental factors, and age, sleep changes are not only closely related to changes in circadian rhythm and steady-state processes (sleep-wake rhythm – activity mode, daytime napping and lethargy, amplitude reduction, and phase shift) but also related to changes in normal brain areas (caudal and hypothalamus) due to aging [13], [16].

The aims of this study are as follows:

- 1) Identify which brain tissues in older persons may undergo organic changes;
- 2) Identify which organic changes in the brain can trigger insomnia in older persons;
- 3) Summarize the Negative effects of insomnia to physical and mental health of older persons;
- 4) Describe how to improve the sleep quality of older persons.

Being a country with the largest population in the world, China has the largest number of aging individuals [17], and is rapidly developing into an "aged society" in the 21st century [18]. Moreover, studies have reported a higher proportion of aging individuals with SL than of any other age groups [19], accounting for about 50% of the surveyed population.

This study focuses on the SL in aging patients, and reviewed the relationship between the brain area, rhythm, and sleep. The main factors that induce SL and existing methods used to promote good sleep in these patients were analyzed and summarized. We propose using non-invasive neural modulation technology to improve sleep in aging individuals with SL to better improve their quality of life.

II. BRAIN AGING AND SL

A. AGE RELATED CHANGES IN THE BRAIN

Human sleep is mainly controlled by the sleep center, which is located at the tail end of the brain stem and hypothalamus [9], [20]. It sends out conduction pulses that act on the cerebral cortex, and are mutually restricted by the ascending reticular activating system of the brain stem that regulates sleep and wakefulness. The hypothalamus is located deep in the brain and its preoptic area is closely related to sleep. Damage to this area can cause severe insomnia in afflicted individuals. The posterior part of the hypothalamus is related to wakefulness and if it is injured, afflicted individuals experience excessive sleep and reduced wakefulness [21], [22], [23]. In contrast, the ascending reticular activating system is located in the thalamus (dorsal thalamus and midbrain), and if a lesion occurs at this site, individuals can experience excessive lethargy, inability to wake up, sleep reversal, and even coma in severe cases. The sleep center also includes the thalamic reticular nucleus (TRN) of the midbrain and the thalamus [24].

With advancing age, the volume of brain tends to decrease (Figure 1 and 2) [25]. In Figure 1, we can see the **(a)** Relationship between brain volume and age.**(b)**Relationship between gray matter volume and age.**(c)**Relationship between white matter volume and age. The solid square represents male individuals and the hollow circle represents the female individuals. It can be seen from the fitting curve that brain volume, white matter, and gray matter decreases with the increase in age. To visualize the age differences in gray matter volumes, the paper divided subjects into two age groups based on age at initial evaluation: 59–69 years (n = 63; mean = 64.6 ± 3.2 years) and 70–85 years (n = 53; mean = 77.3 ± 4.7 years) (Figure 2). Average gray matter maps in stereotaxic space were computed for all 116 subjects, and for each age group separately. The gray matter for all 116 subjects is depicted as an average intensity map in the top row of Figure 2. The average intensities depict the amount of gray matter present in each location. Average gray matter intensity maps for the two age groups are subtracted to show local age differences in gray matter volumes. Age differences in local gray matter volumes are shown for the 59–69 versus 70–85 year olds in the bottom row of Figure 2, with the yellow and bright green regions indicating larger differences. Greater gray matter volumes in younger compared with older subjects are apparent in the hippocampus (H), inferior (IT) and mesial temporal lobes, orbital frontal cortex (OFC), and insula (I). From Figures 1 and 2, we can determine that the weight and blood supply to the hypothalamus gradually declines, connective tissue content gradually increases, and brain structural morphology changes. Simultaneously, the activities of hypothalamic gonadotropin releasing hormone (GnRH) and growth hormone releasing hormone (GHRH) gradually reduce [26], [27], contributing to SL in aging individuals. Therefore, these patients exhibit common SL symptoms, such as going to bed earlier than expected, sleeping less, and daytime sleepiness [28]. In addition, distinct volumetric changes in the cerebral cortex and hippocampus (Fig. 2) [25] directly determine the sleep quality and duration in these patients [29].

The thalamic reticular nucleus (TRN) participates in non-rapid eye movement during sleep, thus stimulating the excitability degree of the spindle, generating spindle waves, and controlling sleep and wakefulness [23]. Some studies have shown that [30], [31], with increasing age, the activity of the spindle gradually weakens, which negatively impacts the amplitude, duration and incidence of the spindle waves, resulting in increased likelihood of SL in the middle-aged and aging individuals (>43 years old) than in the young individuals (20-34 years old) [32], [33], [34].

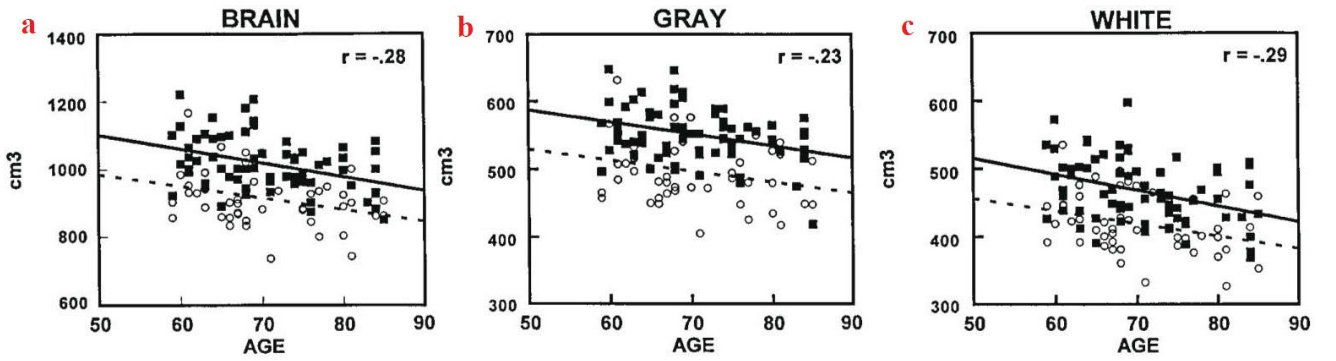

FIGURE 1. Relationship between age and brain parameters [25].

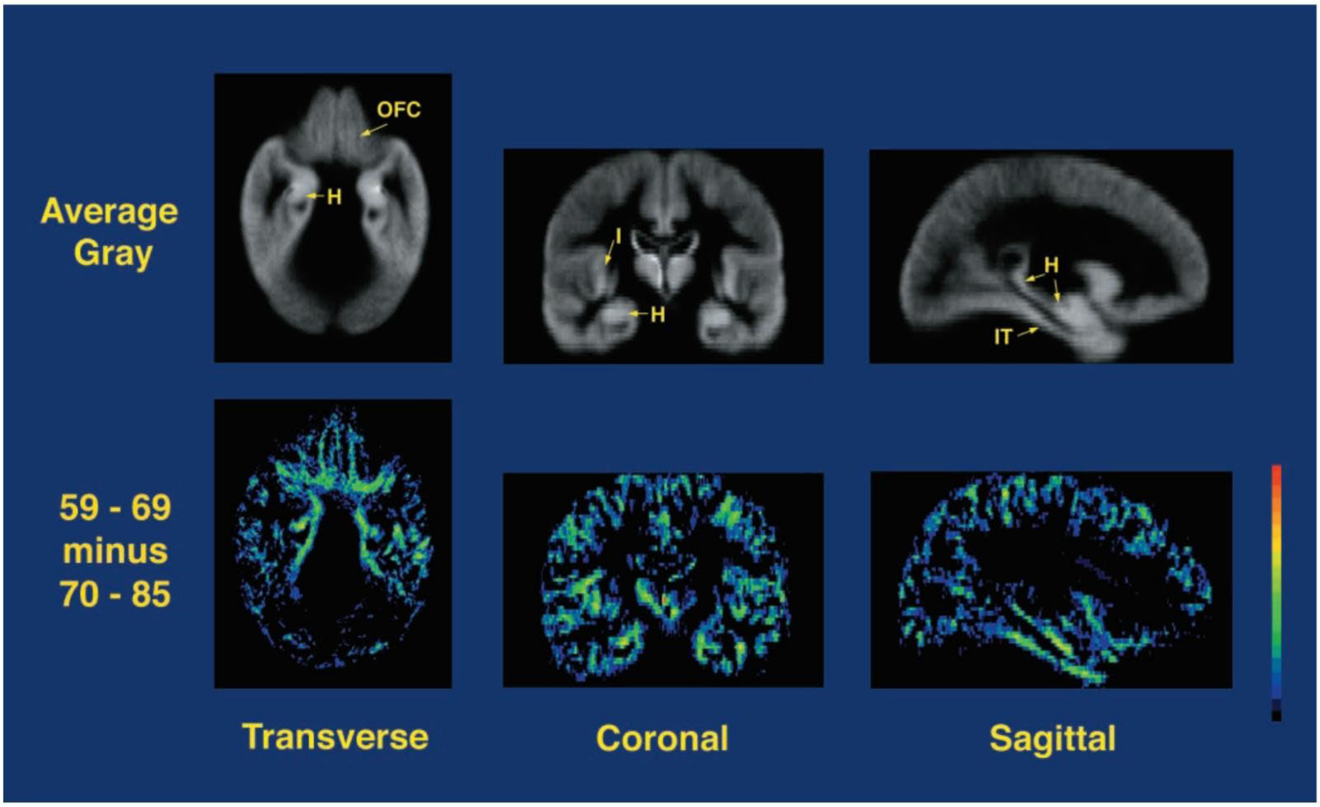

FIGURE 2. The age differences in gray matter volumes [25].

B. RELATIONSHIP BETWEEN SL AND AGING RELATED ORGANIC CHANGES IN BRAIN

Aging individuals are more likely to sleep early and wake up early as compared to young individuals [35], [36], [37], indicating a shift in the amplitude of the circadian rhythm in the aging population. However, other studies have reported contrasting results [37], [38], [39]. With aging, sleep becomes more dispersed and shows gradual increase in the number of awakenings and wakefulness episodes. In a study conducted on 149 male volunteers aged 16-83, the sleep duration of middle-aged (>40) to aging people was reduced by 27 minutes for every increase of 10 years in age [40].

In the young (>18) to middle-aged (<60) individuals, slow wave sleep (SWS) gradually decreased (18.8±3.4% of the total sleep time) and rapid eye movement (REM) sleep decreased by about 50% [36], [40], [41]. In aging individuals, the amplitude of wave activity, which is directly related to sleep, significantly decreased; this was caused by age-related cortical tissue loss and hypothalamic degeneration, especially changes in the modulation process of frontal lobe region and thalamic cortex [41]. Simultaneously, number, density, and duration of sleep-related spindles was also further lowered [42], [43].

Electroencephalogram (EEG) monitoring and analysis of aging individuals revealed that the bands of delta, theta, and sigma frequencies decreased significantly during sleep as manifested by observations that during non-REM sleep, bands of frequency lower than 14 Hz decreased, whereas during REM sleep, bands of frequency lower than 10 Hz decreased [44], [45], [46]. In aging individuals, slow wave activity shows very minor sleep-dependent attenuation during night sleep and the frequency of the nocturnal spindle activity is decreased compared to that in young individuals, which confirms the homeostasis process by which sleep is related to age [44], [45].

In addition to hypothalamus and spindle, hypocretin/orexin(Hcrt/OX) neuron activity directly affects sleep. Research shows that aging mice show sleep fragmentation and significant loss (up to 38%) of Hcrt neurons. Moreover, wakefulness and non-rapid eye movement sleep are reportedly more frequent in aging mice [47] because Hcrt neurons show more frequent discharge patterns, which leads to wakefulness seizures and disrupted sleep. In addition, with increased age, individuals experience increased autoimmune activity, and age-related encephalitis can also cause SL [48].

C. HARMFUL EFFECTS OF AGING-RELATED SL

Sleep deficiency and SL are very common in aging individuals and long-term sleep deprivation can damage the brain [49]. Moreover, SL and sleep deficiency are directly related to dementia and risk of all-cause mortality [11]. In a study conducted on patients who slept less than 5 hours a day, the risk of dementia was 45% higher and that of all-cause mortality was more than 2-fold than that in individuals who had normal sleep [11]. Insufficient sleep also accelerates memory decline in aging individuals [10], [50], impacting their cognitive ability [6], [7], [9], thus increasing their probability of dementia and depression [7], [9], [11]. Moreover, long-term sleep deprivation can cause a series of complex diseases, such as Post-Concussion Syndrome (PCS) [51], severely deteriorate mental and physical health [52], accelerate aging [53], and affect ability to exercise [54] and increase the risk of falls.

III. SLEEP MODULATION IN THE ELDERLY

A. SLEEP MODULATION THROUGH LIFESTYLE HABITS

Exercise is an important way to improve sleep quality [55]. Strenuous exercise can cause physical discomfort in aging individuals. Therefore, low-intensity exercise, such as shadowboxing and walking, can have an easing effect on patients with mild SL [56]. They can also improve their sleep quality through regulation of diet and sleep environment, among other factors. Studies have shown that the tryptophan in milk can promote sleep quality [57]; therefore, aging patients may benefit from drinking a cup of hot milk before going to bed. Changes such as reducing the light intensity in the sleep environment [58], sleeping with a partner or placing some clothes with the partner's smell besides themselves [59], and appropriately increasing the quilt weight in winter [60], relieve mild SL in aging individuals.

TABLE 1. Analysis of the advantages and disadvantages of sleep modulation methods.

Order number	Methods	Advantages	Disadvantages
1	Habits and customs [55–60]	Convenient, no side effects	Slow effectiveness and weak anti-interference ability
2	Drug intervention [61,62]	Convenient, highly effective, and strong anti-interference ability	Significant side effects, resulting in drug resistance and multi-drug combination syndrome
3	Physical stimulation [63–86]	Highly effective, strong anti-interference ability, and fewer side effects	Not convenient to carry and operate

B. SLEEP MODULATION BY DRUGS AND PHYSICAL STIMULATION

Drug assisted sleep is the commonly used method by aging individuals to improve sleep [61]. Aging patients experience a more severe neurocognitive impairment and may use a variety of drugs to alleviate their effects. The half-life of hypnotic drugs may be longer in aging individuals due to slower metabolism than that in young people, and the combination of multiple drugs can further increase the risk of falls and multi-drug syndrome (American College of Physicians (ACP) Internal Medicine Meeting, 2021) [62]; moreover, long-term use of drugs can cause drug dependency in patients. Melatonin is recommended to use for supplementary treatment to improve sleep. Similarly, to ensure better sleep, aging individuals should try not to use the mobile phones within an hour before going to bed. Studies have shown that the blue light generated by the screen of mobile phones or electronic products affect sleep [63], and worsen the sleep quality because of exposure to prolonged electromagnetic radiation (EMR) of mobile phone signals [64] In addition, listening to music during sleep should also be avoided, including berceuse, because music causes a lingering ''earworm effect'' that can affect sleep, which leads to individuals waking up more often at night, and result in a longer period of shallow sleep [65].the advantages and disadvantages of existing sleep modulation methods show in Table 1.

IV. PROMOTING SLEEP VIA NON-INVASIVE NEURAL MODULATION

Using routine sleep modulation is difficult for patients with severe SL, and most of them rely on drugs. In the 1970s, transcranial electrical stimulation was attempted in the aging individuals to improve their sleep [66], [67]. Following such stimulations, the sleep latency of insomniacs was shortened, the awake time in bed was reduced, duration of the first stage of non-rapid eye movement (NREM) sleep was shortened, and percentage of slow wave activity in the fourth stage of NREM sleep was increased, with the effect potentially

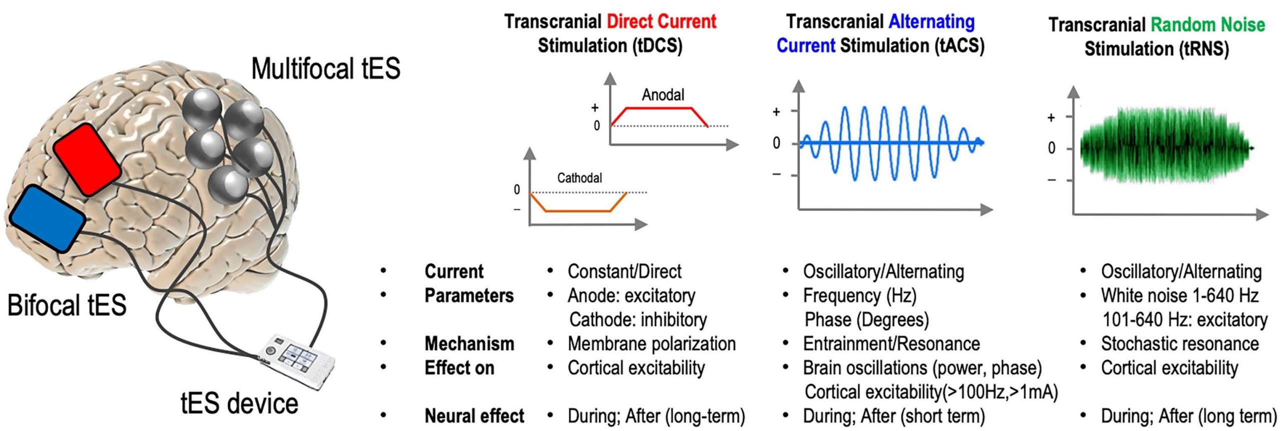

FIGURE 3. Noninvasive transcranial electrical stimulation (tES) technique [70].

lasting approximately two years [68].Transcranial electrical stimulation (tES) requires two electrodes (red=anode, blue=cathode), with at least one placed directly on the scalp (up, left). More channels can be added to record EEG extensively and perform high-resolution ''multifocal'' tES. Available protocols include transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), and transcranial random noise stimulation (tRNS). Different stimulation protocols allow induction of changes in cortical excitability, as well as more specific effects on brain oscillations, e.g.,the α or γ rhythms (Figure 3). In this technique, transcranial direct current stimulation (tDCS) was first applied to modulate the neural activity. A 0.5 2.0 mA DC current was applied using the electrode and single continuous stimulation did not exceed 30 minutes. Sleep modulation was achieved by changing the resting membrane potential of neurons to regulate neural activity with electrical stimulation of 5 days per week for 1 4 continuous weeks [69], [70], [71], [72], [73], [74], (Figure 3). In the system, the anode stimulation of tDCS had an excitatory effect, while the cathode stimulation had an inhibitory effect. Studies showed that the anode stimulation of tDCS can increase the amplitude of motor evoked potential, thus enhancing neuron excitability; in contrast, cathode stimulation can reduce its amplitude, thus inhibiting neuron excitability [75]. The tDCS stimulation can modulate sleep by regulating glutamate concentration, which acts as an neuroglia in glial cells and affects sleep [76]. Studies have proved the efficacy of tDCS treatment for all patients with SL [71], [72], [77], [78]. Transcranial alternating current stimulation (tACS) aims at regulating sleep by adjusting the DC electrical signals in tDCS to an AC electrical signal with a waveform similar to the wave observed during sleep [69], [70], [79], [80].

In addition to transcranial electrical stimulation, transcranial magnetic stimulation (TMS) can also regulate sleep. Transcranial magnetic stimulation (TMS) relies on passing electrical current through a conductive coil and inducing a time-varying focal high magnetic field (~2 T) that generates a strong electric field (>100 V/m). This directly causes neuronal spiking with a high spatial resolution (~0.53 cm of activated brain tissue) (down, left). Different TMS protocols can be implemented by delivering trains of TMS pulses (repetitive TMS, rTMS) or by pairing pulses, which induces various effects such as increased/decreased corticospinal excitability, increased/decreased cortical plasticity, modulation of brain excitatory/inhibitory balance, and changes in local connectivity and blood flow/perfusion (Figure 4). The system is applied tangent to the scalp layer through the regulating coil to stimulate the bilateral dorsolateral prefrontal cortex (DLPFC) wherein the stimulation emission frequency is 1 Hz, the resting motion threshold (RMT) is 80-85%, stimulation duration is 2 s, and the intermittent duration is 1 s. Stimulation is performed 300-400 times for each treatment, for about 20 minutes, once a day, for 14 consecutive days. This treatment has been clinically proven to significantly improve sleep [81], [82], [83], [84], [85], [86]. Its mechanism of action uses the principle of electromagnetic induction to make the patient's brain produce an electric field that can interact with the external electromagnetic field and improve the cerebral blood circulation, affect the metabolism of catecholamine, promote the release of endogenous dopamine, significantly increase the patient's dopamine around the ipsilateral caudate nucleus, inhibit the decomposition of dopamine in the brain nervous system, and regulate the excitability of the direct and indirect circuits of striatum pallidum at the affected side. Meanwhile, low-frequency repetitive transcranial magnetic stimulation (rTMS) treatment can promote the release of inhibitory neurotransmitters γ-aminobutyric acid and 5-hydroxytryptamine, slow down the nerve conduction velocity and reduce the activity of neurons, restrain the function of the upward reticular excitatory system of the brain stem of patients, and increase the non-rapid eye movement sleep; thus greatly improving the sleep quality of patients [81], [82], [83], [84], [85], [86].

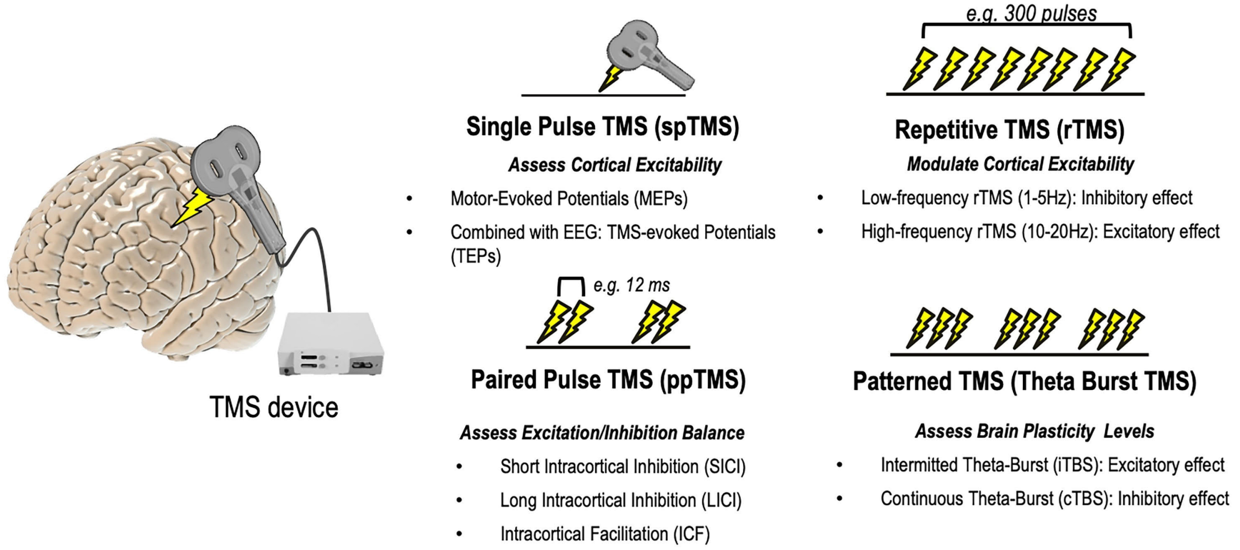

FIGURE 4. Noninvasive transcranial Magnetic Stimulation (TMS) technique [70].

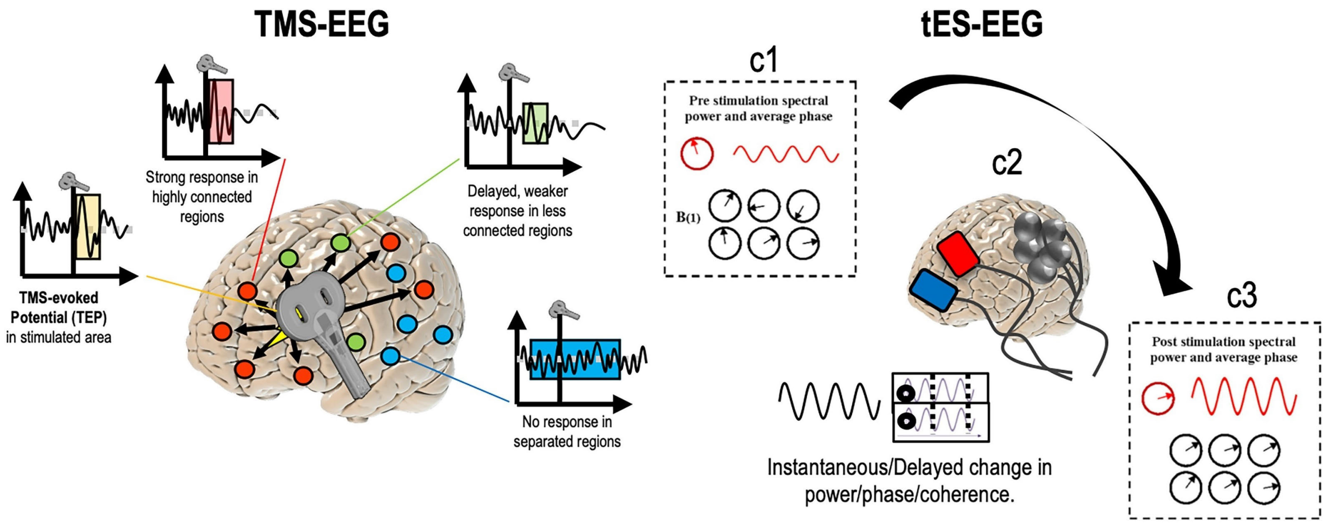

FIGURE 5. Stimulation techniques combined with electrophysiological techniques [70].

In addition, stimulation techniques can be combined with electrophysiological techniques such as in simultaneous TMS-EEG and tES-EEG recordings. In the case of TMS, a focal magnetic pulse is delivered to a specific region of the brain using a neuronavigational system (based on the individual's MRI), which allows precise anatomical targeting of cortical areas at 1-mm resolution. The activity elicited by the pulse is mostly local, with distant effects usually observed for regions structurally or functionally connected to the stimulation site. Both local reactivity and short-long range connectivity can be evaluated, either in terms of TEPs or time-frequency analysis. Distant or out-of-network regions might show delayed or no responses. While TMS provides higher spatial resolution, tES allows frequency-specific modulation of brain electrical activity by steering neuronal populations towards an externally induced oscillatory pattern using alternating current. The response to tACS can be expressed in terms of spectral power changes investigated prior to (c1), during (c2), and/or after (c3) stimulation, phase-coherence, and other connectivity metrics, with the effects being measurable at the stimulated area as well as distant or resonant regions(Figure 5) [70], [87], [88], [89].

V. DISCUSSION

SL are caused by a combination of psychological, physiological, social, and other factors. Aging individuals experience several degenerative changes in body including the brain [4], [5]. Moreover, aging patients present with several diseases

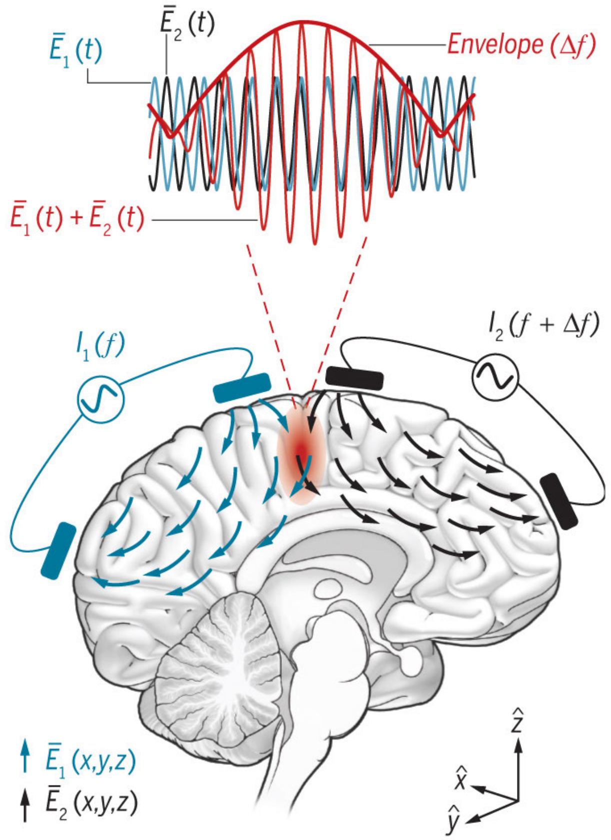

FIGURE 6. Non-invasive deep brain stimulation. Electric field vectors$\overline{E_1}(x, y, x)$ and $\overline{E_2}(x, y, x)$ (gray and blue arrows, respectively) resulting from alternating currents I_1 and I_2 simultaneously applied to the scalp of a head model.I_1 and I_2 were applied at kHz frequencies f_1 (here, 1mA at 1kHz applied across the gray electrodes) and f_2 (1mA at 1.04kHz, across the blue electrodes) that were higher than the range of frequencies of normal neural operation; thus, neurons were driven only at the difference frequency. Field amplitudes were normalized to maximum. The field vectors were recorded at a time point in which the two currents were applied in-phase from top to bottom electrodes [91].

and complex drug usage history. Drug usage for promoting sleep may change drug sensitivity and tolerance and increase the risk of adverse drug reactions (American College of Physicians (ACP) Internal Medicine Meeting, 2021) [62]. Therefore, physiotherapy, psychotherapy, exercise, and other non-drug therapies are recommended as an alternative for clinical management of SL in these individuals.

tES (tDCS and tACS) and transcranial magnetic stimulation (TMS) are widely used in clinical treatment. However, since tES does not induce neuronal action potential and the current intensity is weak, its therapeutic effect on SL is often not as effective as that of TMS [90]. As the signal characteristics change in tES, the depth of stimulation gradually increases (Figure 6), and the targeted modulation also affects other neuronal function [91]. Evidence-based medicine has confirmed the clinical therapeutic efficacy of tES in SL [92].Because the driving voltage required by tES is lower, the device is safer; further, this low voltage device does not need a voltage raising module, allowing simpler design and easier miniaturization of the device, making it convenient to carry. Meanwhile, EEG monitoring of aging patient receiving tES therapy would assist to design optimal stimulation combinations. The targeted area is regulated by selecting the stimulation point and changing the signal characteristics (intensity, frequency, delay) with simple operation. The tES is expected to become one of the key methods of physical therapy for SL in aging individuals due to its higher safety, convenience, non-invasive property, easy operability, and few adverse reactions compared to that of TMS.

Although both non-invasive current stimulation methods (tDCS and tACS) improve the sleep quality of insomnia patients to similar extent, there are significant differences in the affected brain area and acting depth of the two stimulation techniques. In tDCS, DC electrical signal is used as the stimulation signal, and the cerebral cortex is the main functional area of current signal, and regulation of the associated brain regions is realized through electrical feedback of the cerebral cortex. During the regulation process, only the amplitude and duration of signal can be changed, and the program control mode is relatively onefold [93], [94], [95], [96]. In tACS, AC signal is used as the stimulation signal. Because the AC signal has a certain penetrability, deeper parts of the brain in addition to the cerebral cortex are the functional areas of the current signal. The signal can not only regulate the associated brain regions through electrical feedback of the cerebral cortex, but also deep target areas of the brain by changing multi-factor parameters such as amplitude, frequency, and phase of the signal, stimulation delay, and stimulation electrode combination; moreover, the regulatory effect is more persistent and targeted [91], [97], [98].

VI. FUTURE WORK

From existing references, we find that the obvious organic changes in older, middle-aged, and younger people have been analyzed in many studies, but the problem of insufficient sleep is a neurological problem. In addition to the impact of organic changes, neuropathy induced by organic changes is an important cause of sleep deprivation. Accurately analyzing patients' neural electrical signals can help us more accurately understand insomnia syndrome caused by organic changes. To date, there has been little research on this topic and it is worthy of attention in future research.

Insufficient sleep can lead to various diseases in the elderly, but the relationship between insufficient sleep and disease induction is currently unclear and involves many interdisciplinary challenges. Therefore, interdisciplinary research on sleep deprivation is an important direction for future sleep research.

In this study, we found through the study of non-invasive neural regulation techniques that tES and TMS technologies promote sleep and improve sleep quality in older persons. In future insomnia treatment, doctors can regulate patients' sleep by stimulating the target area. Similarly, in existing achievements, the neural regulatory mechanisms of electrical and magnetic stimulation signals on the target area are not yet explicit. In future research, we will also focus on combining electrophysiological signals such as patients' electroencephalogram(EEG) [99] and electrocardiogram(ECG) [100] to study the neural regulatory mechanisms.

VII. CONCLUSION

This study focused on the issue of insomnia in the elderly. To explore the relationship between insomnia in the elderly and organic changes of the brain, we reviewed the relationship between age and changes in the brain. Through summarizing the findings, the following conclusions are drawn: (1) As a person grows older, the volume (weight) of the brain significantly decreases, which due to aging and is inevitable. (2) Insufficient sleep in the elderly can lead to many diseases, so improving the quality of sleep in the elderly is very important. (3) For elderly insomnia patients with mild symptoms, it is recommended to adjust their lifestyle habits; for patients with severe insomnia, medication and physical therapy are needed to promote sleep in the elderly. (4) For patients with severe insomnia, we need to consider the poor effectiveness of medication and physical stimulation as sleep regulation methods and the risk of inducing new diseases. This study focuses on analyzing the mechanism and application effects of non-invasive electrical and magnetic stimulation methods proposed in clinical practice to improve sleep habits in the elderly. Through analysis, it is found that magnetic stimulation can induce neuronal action potential, which will make patients twitch, and equipment noise will cause discomfort to the elderly during treatment. In contrast, tES is more suitable for the treatment of insomnia. (5) In response to the problems of shallow stimulation depth and poor programmable control ability in tDCS, a case study of deep brain stimulation using AC electrical stimulation was summarized and analyzed, providing new treatment ideas for clinical practice.

VIII. ABBREVIATIONS

The following abbreviations are used in this manuscript:

TABLE 2. Abbreviations and abbreviation comprehension.

Abbreviation	Abbreviation comprehension
SL	sleep loss
tES	transcranial electrical stimulation
TMS	transcranial magnetic stimulation
OFC	orbital frontal cortex
TRN	thalamic reticular nucleus
GnRH	gonadotropin releasing hormone
GHRH	growth hormone releasing hormone
SWS	slow wave sleep
REM	rapid eye movement
EEG	Electroencephalogram
Hcrt/OX	hypocretin/orexin
PCS	Post-Concussion Syndrome
ACP	American College of Physicians
EMR	electromagnetic radiation
NREM	non-rapid eye movement
tDCS	transcranial direct current stimulation
DC	direct current
tACS	transcranial alternating current stimulation
AC	alternating current
tRNS	transcranial random noise stimulation
MRI	Magnetic Resonance Imaging
TEPs	TMS-evoked potentials
DLPFC	dorsolateral prefrontal cortex
RMT	resting motion threshold
rTMS	repetitive transcranial magnetic stimulation
ECG	electrocardiogram

REFERENCES

[1] H. J. Kanaya, S. Park, J.-H. Kim, J. Kusumi, S. Krenenou, E. Sawatari, A. Sato, J. Lee, H. Bang, Y. Kobayakawa, C. Lim, and T. Q. Itoh, "A sleep-like state in hydra unravels conserved sleep mechanisms during the evolutionary development of the central nervous system," *Sci. Adv.*, vol. 6, no. 41, Oct. 2020, Art. no. eabb9415.

[2] T. V. Vaidyanathan, M. Collard, S. Yokoyama, M. E. Reitman, and K. E. Poskanzer, "Cortical astrocytes independently regulate sleep depth and duration via separate GPCR pathways," *eLife*, vol. 10, p. e63329, Mar. 2021.

[3] L. H. Jacobson and D. Hoyer, "Losing sleep with age," *Science*, vol. 375, no. 6583, pp. 816–817, Feb. 2022.

[4] D. Kocevska et al., "Sleep characteristics across the lifespan in 1.1 million people from The Netherlands, United Kingdom and United States: A systematic review and meta-analysis," *Nature Hum. Behav.*, vol. 5, pp. 113–122, Nov. 2021.

[5] B. A. Mander, J. R. Winer, and M. P. Walker, "Sleep and human aging," *Neuron*, vol. 94, no. 1, pp. 19–36, Apr. 2017.

[6] C. J. Lowe, A. Safati, and P. A. Hall, "The neurocognitive consequences of sleep restriction: A meta-analytic review," *Neurosci. Biobehav. Rev.*, vol. 80, pp. 586–604, Sep. 2017.

[7] M. R. Irwin, "Sleep and inflammation: Partners in sickness and in health," *Nature Rev. Immunol.*, vol. 19, no. 11, pp. 702–715, Nov. 2019.

[8] S. J. Brooks, E. S. Katz, and C. Stamoulis, "Shorter duration and lower quality sleep have widespread detrimental effects on developing functional brain networks in early adolescence," *Cerebral Cortex Commun.*, vol. 3, no. 1, p. tgab062, Jan. 2022.

[9] L. Besedovsky, T. Lange, and M. Haack, "The sleep-immune crosstalk in health and disease," *Physiol. Rev.*, vol. 99, no. 3, pp. 1325–1380, Jul. 2019.

[10] T. Schreiner, M. Petzka, T. Staudigl, and B. P. Staresina, "Endogenous memory reactivation during sleep in humans is clocked by slow oscillation-spindle complexes," *Nature Commun.*, vol. 12, no. 1, p. 3112, May 2021.

[11] R. Robbins, S. F. Quan, M. D. Weaver, G. Bormes, L. K. Barger, and C. A. Czeisler, "Examining sleep deficiency and disturbance and their risk for incident dementia and all-cause mortality in older adults across 5 years in the United States," *Aging*, vol. 13, no. 3, pp. 3254–3268, Feb. 2021.

[12] D. J. Foley, A. A. Monjan, S. L. Brown, E. M. Simonsick, R. B. Wallace, and D. G. Blazer, "Sleep complaints among elderly persons: An epidemiologic study of three communities," *Sleep*, vol. 18, no. 6, pp. 425–432, Aug. 1995.

[13] J. X. Li, M. V. Vitiello, and N. S. Gooneratne, "Sleep in normal aging," *Sleep Med. Clinics*, vol. 17, no. 2, pp. 161–171, 2022.

[14] M. V. Vitiello, L. H. Larsen, and K. E. Moe, "Age-related sleep change: Gender and estrogen effects on the subjective–objective sleep quality relationships of healthy, noncomplaining older men and women," *J. Psychosomatic Res.*, vol. 56, no. 5, pp. 503–510, 2004.

[15] J. Luo, G. Zhu, Q. Zhao, Q. Guo, H. Meng, Z. Hong, and D. Ding, ''Prevalence and risk factors of poor sleep quality among Chinese elderly in an urban community: Results from the Shanghai aging study,'' *PLoS ONE*, vol. 8, no. 11, Nov. 2013, Art. no. e81261.

[16] J. Mattis and A. Sehgal, ''Circadian rhythms, sleep, and disorders of aging,'' *Trends Endocrinol. Metabolism*, vol. 27, no. 4, pp. 192–203, 2016.

[17] D. X. Zhao, Z. L. Han, and L. Wang, ''The spatial pattern of aging population distribution and its generating mechanism in China,'' (in Chinese), *Acta Geographica Sinica*, vol. 72, no. 10, pp. 1762–1775, 2017.

[18] X. Xu, Y. Zhao, X. Zhang, and S. Xia, ''Identifying the impacts of social, economic, and environmental factors on population aging in the Yangtze river delta using the geographical detector technique,'' *Sustainability*, vol. 10, no. 5, p. 1528, May 2018.

[19] E. O. Bixler, A. N. Vgontzas, H.-M. Lin, S. L. Calhoun, A. Vela-Bueno, and A. Kales, ''Excessive daytime sleepiness in a general population sample: The role of sleep apnea, age, obesity, diabetes, and depression,'' *J. Clin. Endocrinol. Metabolism*, vol. 90, no. 8, pp. 4510–4515, Aug. 2005.

[20] A. Manceau and M. Jorda, ''Les centres mésodiencéphaliques du sommeil,'' *Sem Hop*, vol. 24, pp. 3193–3202, Dec. 1948.

[21] J. Jiang, G. Zou, J. Liu, S. Zhou, J. Xu, H. Sun, Q. Zou, and J. Gao, ''Functional connectivity of the human hypothalamus during wakefulness and nonrapid eye movement sleep,'' *Hum. Brain Mapping*, vol. 42, no. 11, pp. 3667–3679, Aug. 2021.

[22] M. E. Carter, ''Neuroethology: Regulation of pre-sleep behaviors,'' *Current Biol.*, vol. 32, no. 4, pp. 806–822, 2022.

[23] S. Ding, L. Gao, H. Kukun, K. Ai, W. Zhao, C. Xie, and Y. Wang, ''Novel neuroimaging biomarker for sleep quality in insomnia disorder: A hypothalamus resting state study,'' *Frontiers Neurosci.*, vol. 15, Feb. 2021, Art. no. 634984.

[24] O. A. Moody, E. R. Zhang, K. F. Vincent, R. Kato, E. D. Melonakos, C. J. Nehs, and K. Solt, ''The neural circuits underlying general anesthesia and sleep,'' *Anesthesia Analgesia*, vol. 132, no. 5, pp. 1254–1264, 2021.

[25] S. M. Resnick, A. F. Goldszal, and C. Davatzikos, ''One-year age changes in MRI brain volumes in older adults,'' *Cerebral Cortex*, vol. 10, no. 5, pp. 464–472, May 2000.

[26] K. H. Hajdarovic, D. Yu, L.-A. Hassell, S. A. Evans, S. Packer, N. Neretti, and A. E. Webb, ''Single-cell analysis of the aging female mouse hypothalamus,'' *Nature Aging*, vol. 2, no. 7, pp. 662–678, Jul. 2022.

[27] Y. Suda, T. Nakashima, H. Matsumoto, D. Sato, S. Nagano, H. Mikata, S. Yoshida, K. Tanaka, Y. Hamada, N. Kuzumaki, and M. Narita, ''Normal aging induces PD-1-enriched exhausted microglia and A1-like reactive astrocytes in the hypothalamus,'' *Biochem. Biophys. Res. Commun.*, vol. 541, pp. 22–29, Feb. 2021.

[28] H. L. Müller, M. Tauber, E. A. Lawson, J. Özyurt, B. Bison, J.-P. Martinez-Barbera, S. Puget, T. E. Merchant, and H. M. van Santen, ''Hypothalamic syndrome,'' *Nature Rev. Disease Primers*, vol. 8, Apr. 2022, Art. no. 24.

[29] L. B. Krone, T. Yamagata, C. Blanco-Duque, M. C. C. Guillaumin, M. C. Kahn, V. van der Vinne, L. E. McKillop, S. K. E. Tam, S. N. Peirson, C. J. Akerman, A. Hoerder-Suabedissen, Z. Molnár, and V. V. Vyazovskiy, ''A role for the cortex in sleep–wake regulation,'' *Nature Neurosci.*, vol. 24, pp. 1210–1215, Aug. 2021.

[30] S. S. Bowersox, K. I. Kaitin, and W. C. Dement, ''EEG spindle activity as a function of age: Relationship to sleep continuity,'' *Brain Res.*, vol. 334, no. 2, pp. 303–308, May 1985.

[31] M. C. Nicolau, M. Akaârir, A. Gamundí, J. González, and R. V. Rial, ''Why we sleep: The evolutionary pathway to the mammalian sleep,'' *Prog. Neurobiol.*, vol. 62, no. 4, pp. 379–406, Nov. 2000.

[32] R. Di Perri, M. Meduri, A. E. Di Rosa, R. Musolino, and F. Simone, ''Sleep spindles in healthy people. III) an automatic, quantitative and topographical analysis in aged subjects. (preliminary report),'' *Boll. Soc. It. Biol. Sper.*, vol. 53, no. 12, pp. 997–1003, 1977.

[33] R. T. Pivik and F. W. Bylsma, ''Spinal reflex modulation during sleep spindles in man,'' *Sleep Res.*, vol. 11, no. 1, p. 37, 1982.

[34] C. P. Jose and R. S. Jack, ''Sleep spindle characteristics as a function of age,'' *Sleep*, vol. 5, no. 1, pp. 73–84, Sep. 1982.

[35] J. Carrier, T. H. Monk, D. J. Buysse, and D. J. Kupfer, ''Sleep and morningness-eveningness in the 'middle' years of life (20-59y),'' *J. Sleep Res.*, vol. 6, no. 4, pp. 230–237, Dec. 1997.

[36] B. Phillips and S. Ancoli-Israel, ''Sleep disorders in the elderly,'' *Sleep Med.*, vol. 2, no. 2, pp. 99–114, Mar. 2001.

[37] S. Ancoli-Israel, ''Sleep disorders in older adults. A primary care guide to assessing 4 common sleep problems in geriatric patients,'' *Geriatrics*, vol. 59, no. 1, pp. 37–41, 2004.

[38] J. Martin, T. Shochat, and S. Ancoli-Israel, ''Assessment and treatment of sleep disturbances in older adults,'' *Clin. Psychol. Rev.*, vol. 20, no. 6, pp. 783–805, Aug. 2000.

[39] E. van Cauter, L. Plat, R. Leproult, and G. Copinschi, ''Alterations of circadian rhythmicity and sleep in aging: Endocrine consequences,'' *Hormone Res. Paediatrics*, vol. 49, nos. 3–4, pp. 147–152, 1998.

[40] E. Van Cauter, R. Leproult, and L. Plat, ''Age-related changes in slow wave sleep and REM sleep and relationship with growth hormone and cortisol levels in healthy men,'' *J. Amer. Med. Assoc.*, vol. 284, no. 7, pp. 861–868, 2000.

[41] K. Crowley, J. Trinder, and I. M. Colrain, ''An examination of evoked K-complex amplitude and frequency of occurrence in the elderly,'' *J. Sleep Res.*, vol. 11, no. 2, pp. 129–140, Jun. 2002.

[42] K. Crowley, J. Trinder, Y. Kim, M. Carrington, and I. M. Colrain, ''The effects of normal aging on sleep spindle and K-complex production,'' *Clin. Neurophysiol.*, vol. 113, no. 10, pp. 1615–1622, Oct. 2002.

[43] A. Nicolas, D. Petit, S. Rompré, and J. Montplaisir, ''Sleep spindle characteristics in healthy subjects of different age groups,'' *Clin. Neurophysiol.*, vol. 112, no. 3, pp. 521–527, Mar. 2001.

[44] J. Carrier, S. Land, D. J. Buysse, D. J. Kupfer, and T. H. Monk, ''The effects of age and gender on sleep EEG power spectral density in the middle years of life (ages 20–60 years old)'' *Psychophysiology*, vol. 38, no. 2, pp. 232–242, Mar. 2001.

[45] H.-P. Landolt, D.-J. Dijk, P. Achermann, and A. A. Borbély, ''Effect of age on the sleep EEG: Slow-wave activity and spindle frequency activity in young and middle-aged men,'' *Brain Res.*, vol. 738, no. 2, pp. 205–212, Nov. 1996.

[46] H.-P. Landolt and A. A. Borbély, ''Age-dependent changes in sleep EEG topography,'' *Clin. Neurophysiol.*, vol. 112, no. 2, pp. 369–377, Feb. 2001.

[47] S. B. Li, V. M. Damonte, C. Chen, G. X. Wang, J. M. Kebschull, H. Yamaguchi, W. J. Bian, C. Purmann, R. Pattni, A. E. Urban, and P. Mourrain, ''Hyperexcitable arousal circuits drive sleep instability during aging,'' *Science*, vol. 375, p. eabh3021, Feb. 2022.

[48] A. Muñoz-Lopetegi, F. Graus, J. Dalmau, and J. Santamaria, ''Sleep disorders in autoimmune encephalitis,'' *Lancet Neurol.*, vol. 19, no. 12, pp. 1010–1022, Dec. 2020.

[49] S. J. Brooks, E. S. Katz, and C. Stamoulis, ''Shorter duration and lower quality sleep have widespread detrimental effects on developing functional brain networks in early adolescence,'' *Cerebral Cortex Commun.*, vol. 3, no. 1, p. tgab062, Jan. 2022.

[50] A. Baril, A. S. Beiser, E. Sanchez, V. Mysliwiec, S. Redline, D. J. Gottlieb, G. T. O'Connor, M. M. Gonzales, D. Himali, S. Seshadri, J. J. Himali, and M. P. Pase, ''Insomnia symptom severity and cognitive performance: Moderating role of APOE genotype,'' *Alzheimer's Dementia*, vol. 18, no. 3, pp. 408–421, Mar. 2022.

[51] J. B. Caccese, G. L. Iverson, K. J. Hunzinger, B. M. Asken, J. R. Clugston, K. L. Cameron, M. N. Houston, S. J. Svoboda, J. C. Jackson, G. T. McGinty, C. A. Estevez, A. J. Susmarski, A. Enrique, K. N. Bryk, S. P. Broglio, T. W. McAllister, M. McCrea, P. F. Pasquina, and T. A. Buckley, ''Factors associated with symptom reporting in U.S. service academy cadets and NCAA Student athletes without concussion: Findings from the CARE consortium,'' *Sports Med.*, vol. 51, no. 5, pp. 1087–1105, May 2021.

[52] S. Lee, ''Naturally occurring consecutive sleep loss and day-to-day trajectories of affective and physical well-being,'' *Ann. Behav. Med.*, vol. 56, no. 4, pp. 393–404, 2022.

[53] J. E. Carroll, K. M. Ross, S. Horvath, M. Okun, C. Hobel, K. E. Rentscher, M. Coussons-Read, and C. D. Schetter, ''Postpartum sleep loss and accelerated epigenetic aging,'' *Sleep Health*, vol. 7, no. 3, pp. 362–367, Jun. 2021.

[54] G. S. Umemura, J. P. Pinho, J. Duysens, H. I. Krebs, and A. Forner-Cordero, ''Sleep deprivation affects gait control,'' *Sci. Rep.*, vol. 11, no. 1, p. 21104, Oct. 2021.

[55] Y. Liu, L. Yang, M. J. Stampfer, S. Redline, S. S. Tworoger, and T. Huang, ''Physical activity, sedentary behaviour and incidence of obstructive sleep apnoea in three prospective U.S. cohorts,'' *Eur. Respiratory J.*, vol. 59, no. 2, Feb. 2022, Art. no. 2100606.

[56] M. S. Parco, P. Y. Angus, B. T. Tam, E. C. Chin, S. Y. Doris, K.-F. Chung, S. S. Hui, J. Woo, D. Y. Fong, P. H. Lee, and G. X. Wei, ''Effects of tai chi or exercise on sleep in older adults with insomnia: A randomized clinical trial,'' *JAMA Netw. Open*, vol. 4, Feb. 2021, Art. no. e2037199.

[57] J. Qian, L. Zheng, G. Su, M. Huang, D. Luo, and M. Zhao, ''Identification and screening of potential bioactive peptides with sleep-enhancing effects in bovine milk casein hydrolysate,'' *J. Agricult. Food Chem.*, vol. 69, no. 38, pp. 11246–11258, Sep. 2021.

[58] L. Amdisen, S. Daugaard, J. M. Vestergaard, A. Vested, J. P. Bonde, H. T. Vistisen, J. Christoffersen, A. H. Garde, Å. M. Hansen, J. Markvart, V. Schlünssen, and H. A. Kolstad, ''A longitudinal study of morning, evening, and night light intensities and nocturnal sleep quality in a working population,'' *Chronobiol. Int.*, vol. 39, no. 4, pp. 579–589, Apr. 2022.

[59] M. K. Hofer and F. S. Chen, ''The scent of a good night's sleep: Olfactory cues of a romantic partner improve sleep efficiency,'' *Psychol. Sci.*, vol. 31, no. 4, pp. 449–459, Apr. 2020.

[60] E. M. S. Meth, L. E. M. Brandão, L. T. van Egmond, P. Xue, A. Grip, J. Wu, A. Adan, F. Andersson, A. P. Pacheco, K. Uvnäs-Moberg, J. Cedernaes, and C. Benedict, ''A weighted blanket increases pre-sleep salivary concentrations of melatonin in young, healthy adults,'' *J. Sleep Res.*, vol. 32, no. 2, p. e13743, Apr. 2023.

[61] S. K. Roepke and S. Ancoli-Israel, ''Sleep disorders in the elderly,'' *Indian J. Med. Res.*, vol. 131, pp. 302–310, Feb. 2010.

[62] *Pearls for the Management of Insomnia Not to Miss*, Lettieri, Amer. College Physicians (ACP) Internal Med. Meeting, Orlando, FL, USA, Apr. 2021.

[63] K. M. Duraccio, K. K. Zaugg, R. C. Blackburn, and C. D. Jensen, ''Does iPhone night shift mitigate negative effects of smartphone use on sleep outcomes in emerging adults?'' *Sleep Health*, vol. 7, no. 4, pp. 478–484, Aug. 2021.

[64] L. Liu, H. Deng, X. Tang, Y. Lu, J. Zhou, X. Wang, Y. Zhao, B. Huang, and Y. Shi, ''Specific electromagnetic radiation in the wireless signal range increases wakefulness in mice,'' *Proc. Nat. Acad. Sci. USA*, vol. 118, no. 31, Aug. 2021, Art. no. e2105838118.

[65] M. K. Scullin, C. Gao, and P. Fillmore, ''Bedtime music, involuntary musical imagery, and sleep,'' *Psychol. Sci.*, vol. 32, no. 7, pp. 985–997, Jul. 2021.

[66] J. P. Feighner, S. L. Brown, and J. E. Olivier, ''Electrosleep therapy: A controlled double blind study,'' *J. Nervous Mental Disease*, vol. 157, no. 2, pp. 121–128, Aug. 1973.

[67] D. K. Nias, ''Therapeutic effects of low-level direct electrical currents,'' *Psychol. Bull.*, vol. 83, no. 5, pp. 766–773, 1976.

[68] R. D. Cartwright and M. F. Weiss, ''The effects of electrosleep on insomnia revisited,'' *J. Nervous Mental Disease*, vol. 161, no. 2, pp. 134–137, Aug. 1975.

[69] C. Dondé, J. Brunelin, J.-A. Micoulaud-Franchi, J. Maruani, M. Lejoyeux, M. Polosan, and P. A. Geoffroy, ''The effects of transcranial electrical stimulation of the brain on sleep: A systematic review,'' *Frontiers Psychiatry*, vol. 12, Jun. 2021, Art. no. 646569.

[70] S. M. Romanella, D. Roe, R. Paciorek, D. Cappon, G. Ruffini, A. Menardi, A. Rossi, S. Rossi, and E. Santarnecchi, ''Sleep, noninvasive brain stimulation, and the aging brain: Challenges and opportunities,'' *Ageing Res. Rev.*, vol. 61, Aug. 2020, Art. no. 101067.

[71] J. Sheng, C. Xie, D.-Q. Fan, X. Lei, and J. Yu, ''High definition-transcranial direct current stimulation changes older adults' subjective sleep and corresponding resting-state functional connectivity,'' *Int. J. Psychophysiol.*, vol. 129, pp. 1–8, Jul. 2018.

[72] M. Acler, T. Bocci, D. Valenti, M. Turri, A. Priori, and L. Bertolasi, ''Transcranial direct current stimulation (tDCS) for sleep disturbances and fatigue in patients with post-polio syndrome,'' *Restor Neurol. Neurosci.*, vol. 31, no. 5, pp. 661–668, 2013.

[73] A. Minichino, F. S. Bersani, F. Spagnoli, A. Corrado, F. De Michele, W. K. Calò, M. Primavera, B. Yang, L. Bernabei, F. Macrì, L. Vergnani, M. Biondi, and R. D. Chiaie, ''Prefronto-cerebellar transcranial direct current stimulation improves sleep quality in euthymic bipolar patients: A brief report,'' *Behav. Neurol.*, vol. 2014, Dec. 2014, Art. no. 876521.

[74] M.-P. Harvey, D. Lorrain, M. Martel, K. Bergeron-Vezina, F. Houde, M. Seguin, and G. Leonard, ''Can we improve pain and sleep in elderly individuals with transcranial direct current stimulation?—Results from a randomized controlled pilot study,'' *Clin. Interventions Aging*, vol. 12, pp. 937–947, Jun. 2017.

[75] A. L. de Lima, F. M. A. Braga, R. M. M. da Costa, E. P. Gomes, A. R. Brunoni, and R. Pegado, ''Transcranial direct current stimulation for the treatment of generalized anxiety disorder: A randomized clinical trial,'' *J. Affect. Disorders*, vol. 259, pp. 31–37, Dec. 2019.

[76] J. Ruohonen and J. Karhu, ''TDCS possibly stimulates glial cells,'' *Clin. Neurophysiol.*, vol. 123, no. 10, p. 121, Oct. 2012.

[77] M. R. Saebipour, M. T. Joghataei, A. Yoonessi, K. Sadeghniiat-Haghighi, N. Khalighinejad, and S. Khademi, ''Slow oscillating transcranial direct current stimulation during sleep has a sleep-stabilizing effect in chronic insomnia: A pilot study,'' *J. Sleep Res.*, vol. 24, no. 5, pp. 518–525, Oct. 2015.

[78] P. M. B. Rocha, F. S. Neves, and H. Corrêa, ''Significant sleep disturbances in euthymic bipolar patients,'' *Comprehensive Psychiatry*, vol. 54, no. 7, pp. 1003–1008, Oct. 2013.

[79] C. S. Herrmann, S. Rach, T. Neuling, and D. Strüber, ''Transcranial alternating current stimulation: A review of the underlying mechanisms and modulation of cognitive processes,'' *Frontiers Hum. Neurosci.*, vol. 7, p. 279, Jun. 2013.

[80] B. Rasch and J. Born, ''About sleep's role in memory,'' *Physiol. Rev.*, vol. 93, no. 2, pp. 681–766, 2013.

[81] R. Nardone, Y. Höller, F. Brigo, F. Tezzon, S. Golaszewski, and E. Trinka, ''Transcranial magnetic stimulation and sleep disorders: Pathophysiologic insights,'' *Sleep Med.*, vol. 14, no. 11, pp. 1047–1058, Nov. 2013.

[82] A. Leung, P. Shirvalkar, R. Chen, J. Kuluva, M. Vaninetti, R. Bermudes, L. Poree, E. M. Wassermann, B. Kopell, and R. Levy, ''Transcranial magnetic stimulation for pain, headache, and comorbid depression: INS-NANS expert consensus panel review and recommendation,'' *Neuromodulation*, vol. 23, no. 3, pp. 267–290, Apr. 2020.

[83] Y.-P. Zhang, W.-J. Liao, and W.-G. Xia, ''Effect of acupuncture cooperated with low-frequency repetitive transcranial magnetic stimulation on chronic insomnia: A randomized clinical trial,'' *Current Med. Sci.*, vol. 38, no. 3, pp. 491–498, Jun. 2018.

[84] J. Feng, Q. Zhang, C. Zhang, Z. Wen, and X. Zhou, ''The effect of sequential bilateral low-frequency rTMS over dorsolateral prefrontal cortex on serum level of BDNF and GABA in patients with primary insomnia,'' *Brain Behav.*, vol. 9, no. 2, Feb. 2019, Art. no. e01206.

[85] P. Song, H. Lin, S. Li, L. Wang, J. Liu, N. Li, and Y. Wang, ''Repetitive transcranial magnetic stimulation (rTMS) modulates time-varying electroencephalography (EEG) network in primary insomnia patients: A TMS-EEG study,'' *Sleep Med.*, vol. 56, pp. 157–163, Apr. 2019.

[86] C. A. Melo-Silva, S. Gakwaya, E. Rousseau, and F. Sériès, ''Consecutive transcranial magnetic stimulation twitches reduce flow limitation during sleep in apnoeic patients,'' *Exp. Physiol.*, vol. 98, no. 9, pp. 1366–1375, Sep. 2013.

[87] K. J. Friston, C. D. Frith, and R. S. J. Frackowiak, ''Time-dependent changes in effective connectivity measured with PET,'' *Hum. Brain Mapping*, vol. 1, no. 1, pp. 69–79, 1993.

[88] M. Massimini, F. Ferrarelli, S. Sarasso, and G. Tononi, ''Cortical mechanisms of loss of consciousness: insight from TMS/EEG studies,'' *Arch. Italiennes Biol.*, vol. 150, pp. 44–55, Jun. 2012.

[89] M. Castellano, D. Ibanez-Soria, E. Kroupi, J. Acedo, M. Campolo, X. Martinez, A. Soria-Frisch, J. Valls-Sole, A. Verma, and G. Ruffini, ''Occipital tACS bursts during a visual task impact ongoing neural oscillationpower, coherence and LZW complexity,'' *bioRxiv*, Oct. 2017, Art. no. 198788.

[90] G. S. Richardson, G. Zammit, S. Wang-Weigand, and J. Zhang, ''Safety and subjective sleep effects of ramelteon administration in adults and older adults with chronic primary insomnia: A 1-year, open-label study,'' *J. Clin. Psychiatry*, vol. 70, no. 4, pp. 467–476, Apr. 2009, doi: 10.4088/jcp.07m03834.

[91] N. Grossman, D. Bono, N. Dedic, S. B. Kodandaramaiah, A. Rudenko, H. J. Suk, A. M. Cassara, E. Neufeld, N. Kuster, L. H. Tsai, and A. Pascual-Leone, ''Noninvasive deep brain stimulation via temporally interfering electric fields,'' *Cell*, vol. 169, no. 6, pp. 1029–1041, 2017.

[92] A. R. Brunoni, A. H. Moffa, B. Sampaio-Junior, L. Borrione, M. L. Moreno, R. A. Fernandes, B. P. Veronezi, B. S. Nogueira, L. V. M. Aparicio, L. B. Razza, R. Chamorro, L. C. Tort, R. Fraguas, P. A. Lotufo, W. F. Gattaz, F. Fregni, and I. M. Benseñor, ''Trial of electrical direct-current therapy versus escitalopram for depression,'' *New England J. Med.*, vol. 376, no. 26, pp. 2523–2533, Jun. 2017.

[93] A. Liu, M. Vöröslakos, G. Kronberg, S. Henin, M. R. Krause, Y. Huang, A. Opitz, A. Mehta, C. C. Pack, B. Krekelberg, A. Berényi, L. C. Parra, L. Melloni, O. Devinsky, and G. Buzsáki, "Immediate neurophysiological effects of transcranial electrical stimulation," *Nature Commun.*, vol. 9, no. 1, p. 5092, Nov. 2018.

[94] C. T. Moritz, S. I. Perlmutter, and E. E. Fetz, "Direct control of paralysed muscles by cortical neurons," *Nature*, vol. 456, 639–642, Dec. 2008.

[95] G. M. Noetscher, J. Yanamadala, S. N. Makarov, and A. Pascual-Leone, "Comparison of cephalic and extracephalic montages for transcranial direct current stimulation—A numerical study," *IEEE Trans. Biomed. Eng.*, vol. 61, no. 9, pp. 2488–2498, Sep. 2014.

[96] L. Angius, A. R. Mauger, J. Hopker, A. Pascual-Leone, E. Santarnecchi, and S. M. Marcora, "Bilateral extracephalic transcranial direct current stimulation improves endurance performance in healthy individuals," *Brain Stimulation*, vol. 11, no. 1, pp. 108–117, Jan. 2018.

[97] B. Asamoah, A. Khatoun, and M. McLaughlin, "tACS motor system effects can be caused by transcutaneous stimulation of peripheral nerves," *Nature Commun.*, vol. 10, p. 266, Jan. 2019.

[98] A. D'Atri, C. Romano, M. Gorgoni, S. Scarpelli, V. Alfonsi, M. Ferrara, F. Ferlazzo, P. M. Rossini, and L. De Gennaro, "Bilateral 5 Hz transcranial alternating current stimulation on fronto-temporal areas modulates resting-state EEG," *Sci. Rep.*, vol. 7, no. 1, p. 15672, Nov. 2017.

[99] S. T. Aung, M. Hassan, M. Brady, Z. I. Mannan, S. Azam, A. Karim, S. Zaman, and Y. Wongsawat, "Entropy-based emotion recognition from multichannel EEG signals using artificial neural network," *Comput. Intell. Neurosci.*, vol. 2022, Oct. 2022, Art. no. 6000989.

[100] K. Kido, T. Tamura, N. Ono, M. Altaf-Ul-Amin, M. Sekine, S. Kanaya, and M. Huang, "A novel CNN-based framework for classification of signal quality and sleep position from a capacitive ECG measurement," *Sensors*, vol. 19, no. 7, p. 1731, Apr. 2019.

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