PSYCHOLOGICAL SLEEP STUDIES: NEW INSIGHTS TO SUPPORT AND INTEGRATE CLINICAL PRACTICE WITHIN THE HEALTHCARE SYSTEM

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PUBLISHED IN: Frontiers in Psychology

frontiers Research Topics

ISSN 1664-8714
ISBN 978-2-88974-659-0
DOI 10.3389/978-2-88974-659-0

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PSYCHOLOGICAL SLEEP STUDIES: NEW INSIGHTS TO SUPPORT AND INTEGRATE CLINICAL PRACTICE WITHIN THE HEALTHCARE SYSTEM

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Citation: Franceschini, C., De Gennaro, L., Baglioni, C., Dimitriou, D., Riemann, D., eds. (2022). Psychological Sleep Studies: New Insights to Support and Integrate Clinical Practice Within the Healthcare System. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-88974-659-0

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frontiers in Psychology

EDITORIAL
published: 16 February 2022
doi: 10.3389/fpsyg.2022.857433

Editorial: Psychological Sleep Studies: New Insights to Support and Integrate Clinical Practice Within the Healthcare System

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Keywords: sleep, sleep disorders, clinical psychology and health, insomnia, dreams, narcolepsy, obstructive sleep apnea

Editorial on the Research Topic

Psychological Sleep Studies: New Insights to Support and Integrate Clinical Practice Within the Healthcare System

OPEN ACCESS

Edited and Reviewed by:
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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *18 January 2022*
Accepted: *24 January 2022*
Published: *16 February 2022*

Citation:
Baglioni C, De Gennaro L, Riemann D, Dimitriou D and Franceschini C (2022) Editorial: Psychological Sleep Studies: New Insights to Support and Integrate Clinical Practice Within the Healthcare System. Front. Psychol. 13:857433. doi: 10.3389/fpsyg.2022.857433

Adequate sleep is essential for good health, physical functioning, cognitive performance, and self-regulatory processes. In contrast, sleep disorders affect multiple aspects of an individual's life, including daytime activity, social interactions, mood, and quality of life, playing a role in the whole healthcare public system. Consistently, sleep disorders, especially insomnia, have been reported to be key risk factors for mental and somatic disorders. The International Classification of Sleep Disorders (ICSD-3rd edition, American Academy of Sleep Medicine, 2014) includes six main clinical divisions: Insomnia, Sleep Related Breathing Disorders, Central Disorders of Hypersomnolence, Circadian Rhythm Sleep-Wake Disorders, Parasomnias, and Sleep Related Movement Disorders. Currently clinical practice is often lacking of systematic consideration of psychological aspects related to sleep disorders. Specifically:

(1) Health primary care does not include standard assessment and consequent treatment of insomnia in both pediatric and adult patients, in the general population or in patients with mental and somatic disorders.
(2) Motivational and psychological aspects of sleep disorders and their treatment are often not assessed and treated adequately.

Potential sleep disorders can interfere with current therapies for a variety of different illnesses, and when treated can improve quality of life and adherence to therapy, as well as severity of psychological symptoms presented by the patient. A complex, likely bidirectional relationship, is documented between sleep and mental health problems, including depression, anxiety, and traumatic stress disorders. Clinically there is an increasing demand for psychologists with expertise in evidence base psychotherapy to join multidisciplinary health teams, providing cognitive-behavioral intervention and support for insomnia, narcolepsy, and adherence to treatment for obstructive sleep apnea.

This Research Topic (RT) brought together heterogeneous cutting-edge research on sleep and its disorders in clinical contexts (e.g., treatments, epidemiology), considering both the general population and clinical patients as well as pediatric and adult samples. Sleep, as a main aspect of physical and mental health, interacts with other processes strictly associated with wellbeing and quality of life. Two studies collected in the present RT deepened the relationship between sleep quality and other indices of health or quality of life, such as physical activity, wellbeing and academic performance (Dubinina et al.; Armand et al.). Both works interestingly pointed out complex interactions between variables, suggesting that multiple factors intervene in defining individual's health patterns. Epidemiological studies are necessary to capture these complex interactions, which may explain individual variability. Specialists should be aware of the different pathways to tailor their intervention to individual's needs, thus, providing more efficacious guide to patients in finding optimal balance for their health and wellbeing. Clinically, sleep should be assessed systematically being fundamental for brain functioning. As Holzinger et al. point out insomnia and nightmares are common experience in patients with psychiatric illness, though often not assessed nor treated. The authors, by reporting an example of a case study of a woman diagnosed with Post-Traumatic Stress Disorder (PTSD), propose a program including psychological treatment for insomnia symptoms and lucid dreams training as clinical module to be offered in psychiatric care.

Studies dealing with sleep and psychological variables during adolescence are of utmost importance right now. Indeed, sleep goes through dramatic changes during adolescence determined both by biological and social developments. A shift for a more delayed circadian preference is often problematic due to school starting times. The pandemic outbreak and its social consequences particularly affected adolescents' mental health and sleep functioning (e.g., Becker and Gregory, 2020). In the present RT, Haugland et al. provided a contribution to this literature showing extremely high rates of insomnia and sleep difficulties and strict association of sleep problems with psychopathological symptoms in an adolescent sample referred to anxiety treatment. Sleep and circadian preference during adolescence should be systematically assessed and treated in primary care. School preventive programs should be encouraged too.

Several specific clinical populations were considered in the RT. Specifically, two studies focused on treatment for sleep problems directed to parents of children suffering of epilepsy, a population which is highly afflicted by insomnia and difficulties sleeping. While standard protocols exist for behavioral interventions for sleep problems during development, often they do not include adaptation for specific clinical populations. Cook et al. and Wiggs et al. provide data of how protocol adaptations for specific clinical populations may be created with the help of patients (in this case parents of children with epilepsy), thus, offering modules which satisfy individual's wishes and may promote better motivation and adherence to prescriptions. Considering adults, two studies contributed to the understanding of the relationship between sleep quality and pain. Zambelli et al. reported on a large sample of 1,234 participants with chronic pain that better sleep quality was associated to a reduced link between depression and pain. Blytt et al. nevertheless, found in patients with dementia that those reporting more pain had actually longer sleep times within the time the spent in bed as registered with actigraphy. Again, complex interactions between variables are suggested by results of empirical studies. While sleep patterns should be more carefully assessed and considered clinically, research should be strengthened to deepen different individual pathways.

Psychological interest in sleep research is often directed to the disorder of insomnia and to the link between sleep and mental health. Nevertheless, another area of great interest is how psychological variables associate to sleep disorders and how motivational and psychological interventions can contribute to medical treatment of sleep disorders. As two studies in the RT point out Narcolepsy type 1 (NT1), a neurological chronic disease associated with altered sleep structure and behavior, is characterized by cognitive and emotional dysfunctions. The works by Filardi et al. and Scarpelli et al. deepened sleep, psychological, and psychopathological variables in this disorder through, respectively, the example of a case of an adolescent girl and a study comparing patients and controls during the pandemic period. Psychological interest in sleep research is growing and expanding to all areas of interest. This should correspond to a more standardized inclusion of clinical psychologists/psychotherapists in sleep medicine teams, as well as a regular interest in sleep variables in psychotherapy.

Continuous positive airway pressure (CPAP) therapy is the standard treatment for obstructive sleep apnea (OSA) syndrome. However, optimizing adherence to CPAP therapy of individuals remains very challenging for clinicians because of the role played by the psychological components. Two studies considered this issue. Scarpina et al. found that a psychological training assessing risks and benefits of CPAP therapy improved adherence to treatment. Consistently a review of Rapelli et al. about motivational intervention for CPAP therapy support their integration in care for OSA patients. A final paper in the RT by Galbiati et al. deepened the mechanisms underlying psychological treatment for insomnia. Cognitive Behavior Treatment for Insomnia (CBT-I) is recognized as first line intervention for patients with insomnia comorbid and non-comorbid with other disorders (e.g., Riemann et al., 2017). Though, there is a need to explore more in details what are the mechanisms explaining its efficacy. The authors reported results from group therapy showing that the intervention reduced nighttime symptoms of insomnia and dysfunctional beliefs about sleep in patients. However, patients did not change the way they reacted on their own thoughts about sleep loss and its consequences. These secondary cognitions, often exacerbating the disorder, are indeed not systematically considered in standard CBT-I protocols. Emergent protocols, as the Mindfulness Based Treatment for Insomnia (MBTI) proposed by Ong et al. (2012), direct their attention to aspects associated with secondary arousal and cognitions, and it has been suggested to improve CBT-I efficacy by

including more attention to daytime symptoms and emotional variables. Nevertheless, empirical data are not yet stable enough (e.g., Baglioni et al., 2020).

Though heterogeneous, and covering several different topics, all papers included in the RT support the relevance of sleep assessment and treatment in primary and secondary care. Future research should deepen further the complex interaction between health variables in specific clinical population to guide protocols which can be tailored to individual's needs. All together the papers of this RT give support and suggestion to improve clinical and healthcare attention to sleep.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

ACKNOWLEDGMENTS

We would like to thank all the authors who agreed to participate in this Topic with their original contributions, and to all the reviewers who promoted the quality of research and manuscripts with their comments.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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CASE REPORT
published: 12 March 2021
doi: 10.3389/fpsyg.2021.634941

Case Report: Burden of Illness in Narcolepsy Type 1: Hikikomori in a Teenage Girl

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Narcolepsy type 1 (NT1) deeply impacts on quality of life, especially during adolescence, with NT1 children and adolescents that frequently report difficulties in integration with peers and decreased participation in after-school activities. Here we describe the case of NT1 teenager girl presenting with severe physical and social withdrawal, fulfilling the proposed diagnostic criteria for hikikomori, together with the classic NT1 symptoms. Social withdrawal is an overlooked phenomenon among NT1 children and adolescents that, if present, require a multidisciplinary approach and personalized interventions, but patients can benefit from NT1 pharmacological treatment.

Keywords: narcolepsy, hikikomori (social withdrawal), actigraphy, delayed sleep phase, adolescent, sodium oxybate

OPEN ACCESS

Edited by:
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Reviewed by:
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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *29 November 2020*
Accepted: *12 February 2021*
Published: *12 March 2021*

Citation:
Filardi M, Blunda V, Vandi S, Musetti A, Posar A, Visconti P, Pizza F, Plazzi G and Franceschini C (2021) Case Report: Burden of Illness in Narcolepsy Type 1: Hikikomori in a Teenage Girl. Front. Psychol. 12:634941. doi: 10.3389/fpsyg.2021.634941

INTRODUCTION

Narcolepsy type 1 (NT1) is a rare neurological disorder characterized by excessive daytime sleepiness (EDS), untimely REM sleep manifestations, and nocturnal sleep disruption (Plazzi et al., 2018). NT1 mostly arises during childhood/early adolescence and is frequently accompanied by a rapid weight gain up to obesity (Ponziani et al., 2016). Moreover, in addition to the classic symptoms, pediatric NT1 patients are at increased risk of impairment in several cognitive domains and frequently exhibit emotional and externalizing problems (Plazzi et al., 2018).

Since the late 90s, a severe condition of prolonged social withdrawal, also known by the Japanese term "hikikomori," has been described among Japanese teenagers and young adults (Teo, 2010). The term hikikomori describes a phenomenon characterized by a severe form of physical and social withdrawal: individuals with hikikomori isolate themselves in their own home, stop going to school or the workplace, and refuse interactions with peers and people outside the family unit (Kato et al., 2019). Initially considered a Japanese culture-bound phenomenon, hikikomori cases have been described in several countries (Malagón-Amor et al., 2015; Teo et al., 2015).

Although not included in the current DSM, a set of diagnostic criteria for hikikomori have been proposed (Teo and Gaw, 2010). To meet these criteria, the subject must (1) stay at home or in their room for most of the day, almost all days; (2) avoid social participation (stopping going to school or the workplace) and social relationships with peers and family members; (3) experience significant functional impairment or distress associated with social isolation; and (4) continuous social isolation has to last 6 months or more. Hikikomori syndrome has a high

comorbidity with anxiety, mood disorders (Koyama et al., 2010) and Internet addiction (Kato et al., 2020) and has been associated with wet beriberi (Tanabe et al., 2018) and elephantiasis nostras verrucosa (Moriuchi et al., 2015). Here we present a case of NT1 associated with pathological social withdrawal. The case report has been conducted according to the CARE guidelines (Riley et al., 2017).

CASE DESCRIPTION

A 15-year-old girl, adopted at the age of 3 after spending 1 year in community, at the age of 11 started to present severe EDS during the school hours and resumed the habit of napping in the afternoon. Nocturnal sleep became interrupted by frequent awakenings; she also experienced episodes of sudden muscular weakness triggered by laughter/anger and an abrupt weight gain. At the age of 12, she was diagnosed with a specific learning disorder.

At the age of 13, she was admitted to our Narcolepsy Center (December 2018).

Clinical, neurological examination and brain MRI were normal, but the patient was overweight (BMI: 25.7) and markedly sleepy (Epworth Sleepiness Scale for Children and Adolescents, ESS-CHAD = 18/24). Psychiatric evaluation performed by a psychiatrist with vast experience in child and adolescent psychiatry (A.P.) did not disclose personality disorders or depressive mood (Children's Depression Inventory 2, CDI 2: 1/54). Twenty-four-hour video-polysomnography (v-PSG) documented two sleep episodes (one in the early morning and one in the afternoon) characterized by direct transition into REM sleep (sleep onset REM periods, SOREMP) (**Figure 1A**) and the multiple sleep latency test documented pathological sleep latency (3.12 min with 4/5 SOREMP). She denied hypnagogic/hypnopompic hallucinations and sleep paralysis; cataplexy was video-documented through a standardized procedure. The patient carried the HLA DQB1*06:02 allele and had reduced cerebrospinal fluid hypocretin-1 level (82.47 pg/mL).

Accordingly, NT1 was diagnosed and a treatment with Pitolisant up to 36 mg daily started with a remarkable improvement of EDS and cataplexy.

After 7 months of physical and mental well-being, during which the patient regularly attended school and sport activity, she reported loss of efficacy of the treatment with Pitolisant (June 2019).

Subsequently (July 2019), she quit sport activity and voluntarily withdrew from social life, rarely leaving her parents' home (less than once a month) and spending most of the day on the Internet and playing video games. At the start of the new school year (September 2019), she sporadically attended school for about a month and definitely dropped out of school in October.

Shortly thereafter, she further isolated herself rarely leaving her room and refusing to communicate even with her parents and to leave the room for having lunch/dinner (her mother left the meals outside the door). Moreover, she started to delay the onset of the sleep phase.

In December 2019, she underwent a second hospitalization, preceded by actigraphy (**Figure 2A**). Clinical and neurological examinations were unremarkable, subjective sleepiness decreased (ESS-CHAD: 12/24) but her weight did not change (BMI: 26.18).

Psychiatric evaluation disclosed social withdrawal behavior, attentional deficits, impaired cognitive flexibility (NEPSY-II test battery), and a low emotional quotient (emotional quotient inventory–youth version score: 60, normal range 90–110) with relevant difficulties in several emotional domains including adaptability, general mood, and positive impression.

Abbreviations: NT1, narcolepsy type 1; EDS, excessive daytime sleepiness; ESS-CHAD, Epworth Sleepiness Scale for Children and Adolescents; SOREMP, sleep onset REM period; BMI, body mass index; v-PSG, video-polysomnography; CDI 2, Children's Depression Inventory 2; DSM, Diagnostic and Statistical Manual of Mental Disorders.

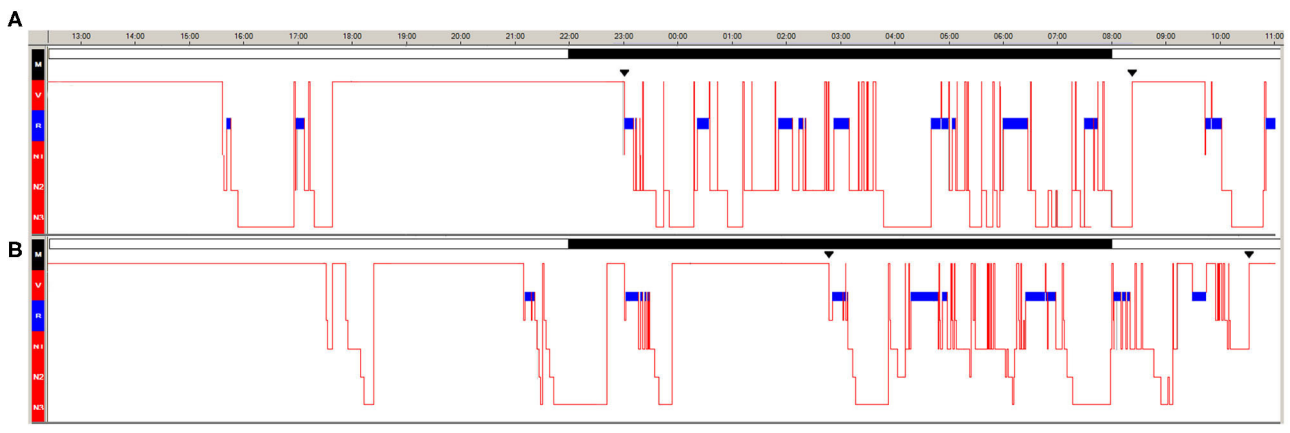

FIGURE 1 | Twenty-four hours v-PSG during the first **(A)** and second **(B)** hospitalization. The blue bar indicates REM sleep. Continuous black bars indicate the ward's lights-off and lights-on times.

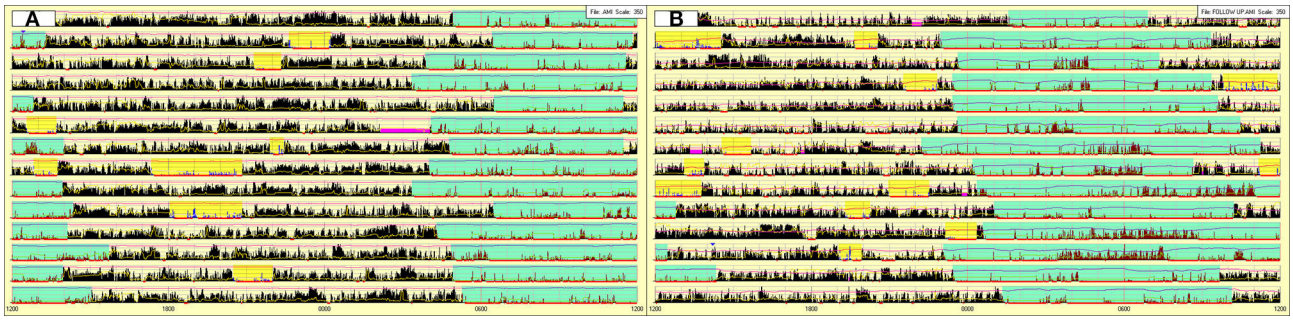

FIGURE 2 | Actigraphy prior to the second hospitalization **(A)** and after 3 months of stable treatment with sodium oxybate **(B)**. Sky-blue highlight = nocturnal sleep period. Yellow highlight = diurnal sleep episodes. Fuchsia highlight = periods of device removal.

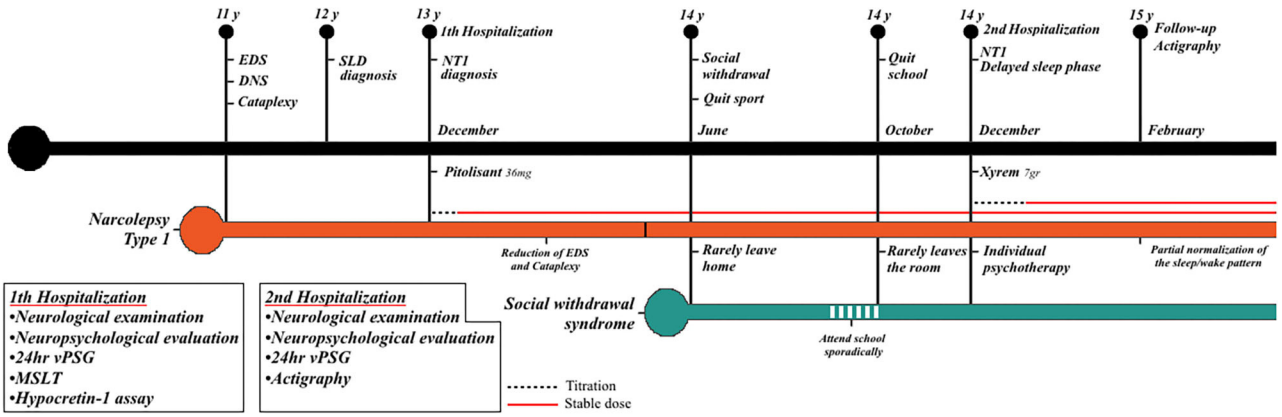

FIGURE 3 | Timeline with relevant data from the episode of care and evaluations performed. Black bar = lifetime events. Orange bar = NT1 disease course. Cyan bar = social withdrawal. NT1, narcolepsy type 1; EDS, excessive daytime sleepiness; DNS, disrupted nighttime sleep; SLD, specific learning disorder; v-PSG, video-polysomnography; MSLT, multiple sleep latency test.

Actigraphy (**Figure 2A**) documented the typical profile of NT1 children (nocturnal hyperactivity and frequent diurnal naps) coupled with a delayed sleep phase (bedtime 4:48 ± 1:04, wake-up time: 13:15 ± 1:24) (Filardi et al., 2016).

The 24-h v-PSG documented several diurnal sleep episodes in the late afternoon and early evening ($n = 5$, 3/5 with SOREMP), delayed sleep onset (bedtime at 1:14), and reduced nocturnal total sleep time (**Figure 1B**).

Based on the presence of delayed sleep–wake phase and socially withdrawn behavior, a treatment with sodium oxybate up to 7 g daily (3.5 grams at about 23:30 and a second equal dose after 3.5 h) associated with individual psychotherapy was started.

After 3 months of stable pharmacological treatment (February 2020), the follow-up actigraphy (**Figure 2B**) documented a partial normalization of the sleep/wake schedules but also highlighted the presence of periods, concurrent with the second sodium oxybate intake, characterized by sudden increase of light and intense motor activity, indicating that during several nights the patient remained awake for prolonged time, most likely to play video games.

As expected, the treatment with sodium oxybate induced a major weight loss (Filardi et al., 2018) and the patient's BMI returned within the normality range (BMI: 20.44).

On the other hand, the psychotherapeutic intervention (delivered "in person") has proven beneficial with the patient who was slowly starting to resume relations with the closest peer.

DISCUSSION

This is the first report of hikikomori in a patient with NT1.

Our patient fulfilled the proposed diagnostic criteria for hikikomori, presenting with severe physical and social withdrawal that lasted for more than 6 months and significantly interfered with her functional life (school dropout) (Teo and Gaw, 2010). Nonetheless, the patient did not complain of distress associated with the social isolation; at the psychiatric evaluation, when asked about the reasons for her withdrawal behavior, she did not provide an explanation but firmly reaffirmed her intention of not wanting to go to school anymore and stay home all day. A timeline with relevant data and evaluations carried out are reported in **Figure 3**.

Although the etiology of hikikomori is still unknown, we speculate that several NT1 features may have facilitated the social withdrawal of our patient.

First, disrupted nighttime sleep is a common feature in NT1 children and adolescents who present numerous brief awakenings, often with difficulties returning asleep (Roth et al., 2013).

These long-lasting periods of wakefulness, when parents are asleep, represent a window of opportunity for online gaming and excessive Internet use, which in turn might have prompted the patient to delay the sleep phase in order to align it with the online gaming schedule.

Indeed, delayed sleep phase is rare in pediatric NT1 patients (Filardi et al., 2016), while social withdrawal syndrome has been associated with irregular sleep–wake pattern (Chauliac et al., 2017) and sleep–wake rhythm inversion has been described in hikikomori cases (Gondim et al., 2017).

Second, the rapid weight gain that frequently accompanies NT1 onset (Ponziani et al., 2016), as in our patient, drastically modifies physical appearance and consequently perceived body image.

Third, NT1 negatively impacts on quality of life, especially during adolescence, with several studies that have reported poor school performance with difficulties in integration, frequent absenteeism, and decreased participation in after-school activities (Plazzi et al., 2018).

Basing on studies that highlighted an association between peer-related loneliness and maladjustment, we can speculate that the patient's difficulties hamper the establishment of stable social relationships with peers and may have contributed to social withdrawal (Musetti et al., 2020).

Fourth, hikikomori subjects have a higher lifetime prevalence of anxiety disorders (Koyama et al., 2010) and depression (Teo, 2013) and are more likely to have autistic tendencies (Katsuki et al., 2020).

Similarly, NT1 children and adolescents have an increased susceptibility to psychiatric disorders (Blackwell et al., 2017) and cases of NT1 with comorbid autism spectrum disorder have been recently described (Prihodova et al., 2018).

In our case, the concomitant presence of NT1 symptoms and social withdrawal behavior significantly complicated the patient's pharmacological and behavioral management.

Indeed, in a relatively short period of time we had to modify the pharmacological therapy twice and refer the patient to psychotherapeutic treatment. Family support, home visit by social workers or psychologists, and individual psychotherapy are recommended and considered effective for hikikomori subjects (Kato et al., 2019) and similarly could prove beneficial for NT1 patients with concomitant hikikomori syndrome. A possible limitation of the present report is that the child and adolescent psychiatrist did not conduct a structured clinical interview to rule out the presence of psychiatric comorbidity. Social withdrawal may be an overlooked phenomenon among NT1 children and adolescents that, if present, requires multidisciplinary management. Actigraphy may prove useful to track the disease course over time and ecologically monitor treatment response and adherence.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the minor(s)' legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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Conflict of Interest: GP participated in the advisory board for UCB Pharma, Jazz Pharmaceuticals, Idorsia, and Bioprojet, outside the submitted work.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychology

ORIGINAL RESEARCH
published: 24 March 2021
doi: 10.3389/fpsyg.2021.638879

Sleep Duration and Insomnia in Adolescents Seeking Treatment for Anxiety in Primary Health Care

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Edited by:
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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *07 December 2020*
Accepted: *04 March 2021*
Published: *24 March 2021*

Citation:
Haugland BSM, Hysing M, Baste V, Wergeland GJ, Rapee RM, Hoffart A, Haaland ÅT and Bjaastad JF (2021) Sleep Duration and Insomnia in Adolescents Seeking Treatment for Anxiety in Primary Health Care. Front. Psychol. 12:638879. doi: 10.3389/fpsyg.2021.638879

There is limited knowledge about sleep in adolescents with elevated levels of anxiety treated within primary health care settings, potentially resulting in sleep problems not being sufficiently addressed by primary health care workers. In the current study self-reported anxiety, insomnia, sleep onset latency, sleep duration, and depressive symptoms were assessed in 313 adolescents (12–16 years; mean age 14.0, *SD* = 0.84, 84.0% girls) referred to treatment for anxiety within primary health care. Results showed that 38.1% of the adolescents met criteria for insomnia, 34.8% reported short sleep duration (<7 h), and 83.1% reported long sleep onset latency (≥30 min). Total anxiety symptoms were related to all sleep variables after controlling for age and sex. Furthermore, all anxiety symptom sub-types were associated with insomnia and sleep onset latency, whereas most anxiety subtypes were associated with sleep duration. Adolescents' depressive symptoms accounted for most of the anxiety-sleep associations, emphasizing the importance of depressive symptoms for sleep. However, anxiety was associated with insomnia and sleep onset latency also among youth with low levels of depressive symptoms. The findings suggests that primary health care workers should assess sleep duration, sleep onset latency, and insomnia in help-seeking adolescents with anxiety.

Keywords: adolescents, anxiety symptoms, depressive symptoms, primary health care, insomnia, sleep onset latency, sleep duration

INTRODUCTION

Sleep undergoes major changes during adolescence, and is generally characterized by short sleep duration, long sleep onset latency (SOL), and high rates of insomnia (Gradisar et al., 2011; Hysing et al., 2013). Research indicates that youth with anxiety disorders have even higher rates of insomnia (Johnson et al., 2006a; Alvaro et al., 2017), longer SOL (Forbes et al., 2008) and shorter sleep duration compared to their non-anxious peers (Roberts and Duong, 2017; Zhang et al., 2017).

Clinical research on the association between anxiety and sleep problems has primarily focused on adolescents with anxiety disorders, often in specialized treatment settings (Brown et al., 2018). We know much less about sleep in adolescents with anxiety receiving treatment within primary health care services. Such information is important because a large proportion of adolescents with symptoms of internalizing disorders (i.e., anxiety disorders and/or depression) seek help within primary health settings (Zachrisson et al., 2006). Furthermore, primary health care interventions may reach adolescents with anxiety who may not otherwise receive help (Husabo et al., 2020). By reaching adolescents early and within their everyday contexts (e.g., school), primary health services may overcome some of the barriers against seeking help for mental health problems in youth (Salloum et al., 2016; Reardon et al., 2017).

The relationship between sleep and anxiety is complex, and studies with adults, as well as with children, indicate that associations vary across sleep characteristics (Hudson et al., 2009; van Mill et al., 2014). A population-based study of adolescents reported higher prevalence of daytime sleepiness, SOL, and difficulties getting up in the morning in adolescents with anxiety and in adolescents with depression. However, short sleep duration was only reported by adolescents with depression (Orchard et al., 2020). Thus, to understand in depth the association of specific aspects of sleep with anxiety symptoms in adolescents, we need to include a broad range of sleep characteristics.

Unfortunately, the research literature on sleep and anxiety in youth is characterized by inconsistency regarding what constitutes poor sleep (Leahy and Gradisar, 2012), and the measures used to assess sleep have been questioned (Peterman et al., 2015; Brown et al., 2018). Some studies use a single item to assess insomnia, whereas others measure "sleep-related problems" applying composite scores, with items drawn from anxiety, depression, and/or general child behavioral problem checklists. Items in these composite scores are often related to bedtime behaviors, closely aligned with anxiety (e.g., resistance getting to bed, refusal to sleep alone). This represents a problem of item overlap between sleep and anxiety, that may inflate the sleep-anxiety associations (Peterman et al., 2015). The less frequent use of measures directly assessing sleep duration, SOL and/or insomnia leave us less informed about the nature of the association between sleep and anxiety in adolescents.

Associations between sleep and anxiety in adolescents may vary not only on the aspects of sleep that are measured, but also on the subtypes of anxiety. Some anxiety subtypes may be more strongly associated with sleep difficulties than others. For example, a clinical study reported more sleep-related problems in youth (6–17 years) with generalized anxiety disorder (GAD), and/or separation anxiety disorder (SAD), compared to youth with social anxiety disorder (SoAD) (Alfano et al., 2007). However, two community studies reported high rates of insomnia among adolescents regardless of anxiety subtypes, e.g., across panic disorder, SoAD, GAD, and obsessive-compulsive disorder (OCD) (Johnson et al., 2006a; Alvaro et al., 2017). The inconsistent findings and the limited number of studies suggest that further research on the association between sleep and subtypes of anxiety in adolescents is warranted. This knowledge might be used clinically to determine whether sleep difficulties need to be addressed in youth suffering all forms of anxiety, or only within specific subtypes (e.g., GAD).

Evidence for an association between depression and poor sleep in adolescents is strong (Chorney et al., 2007; Sivertsen et al., 2014; Berger et al., 2019). Higher rates of insomnia have been reported among adolescents with depression, compared to adolescents with anxiety disorders (Johnson et al., 2006a; Alvaro et al., 2017). The high comorbidity between poor sleep and depression, and the large overlap between anxiety and depression, indicate a need to examine how co-occurring depression affects the association between anxiety and sleep. To our knowledge, this has not been explicitly examined in previous studies with adolescents. The role of depression may have implications for the assessment, conceptualization, and interventions offered to adolescents with anxiety.

Adolescent girls usually report higher prevalence of anxiety and depression compared to same age boys (Carter et al., 2011; Leikanger et al., 2012). Sleep has been found to change across development, with a sex specific sleep pattern emerging after puberty, where boys report shorter sleep duration and older adolescents and girls report higher rates of insomnia (Johnson et al., 2006b; Hysing et al., 2013; Amarala et al., 2016). Thus, sex and age need to be considered when examining potential associations between anxiety, depression, and sleep characteristics.

In the present study, sleep (i.e., insomnia, SOL, and sleep duration) was examined in adolescents with anxiety who were seeking help within primary health care. We examined whether total anxiety symptoms and subtypes of anxiety (e.g., GAD and SAD) were associated with sleep duration, SOL, and insomnia. The potential confounding effect of depressive symptoms was also investigated, first by controlling for depressive symptoms in the analyses, and then by examining associations between anxiety and sleep in the subgroup of adolescents without co-occurring depressive symptoms.

MATERIALS AND METHODS

Data were drawn from baseline assessments of a randomized controlled trial (RCT) where adolescents with elevated anxiety participated in 10-week, group interventions delivered in junior high schools in Norway. The providers of the group interventions were mainly primary health care workers (i.e., school nurses, n = 21; community psychologists, n = 5; family therapist, n = 1) in addition to professionals from local Child and Adolescent Mental Health Services (n = 5, e.g., social workers). Details of the RCT as well as descriptions of interventions, implementation and outcomes have been published elsewhere (Haugland et al., 2017, 2020).

Procedure and Participants

Participants were informed about the anxiety-focused interventions through multiple sources (e.g., student and

parent routine meetings with school nurses; nomination by teachers; information through media). Both self-referral and referral from others were endorsed. Informed consent from caregivers and assent from the adolescents was obtained prior to data collection.

A total of 363 adolescents aged 12–16 years from 18 junior high schools (17 public and 1 private school) were referred for assessment. The schools represented both rural and urban areas. Adolescents were included if the total anxiety score (self-reported or parent-reported anxiety symptoms) was ≥25 on the Spence Children's Anxiety Scale (SCAS; Spence, 1998). This cut off was slightly above the mean total SCAS score (23.19, *SD* = 15.60) previously found in a community sample of adolescents who attended the same junior high schools as the present sample (Raknes et al., 2017). By applying this cut-off, we included adolescents ranging from mild to more severe levels of anxiety. In addition, a minimum level of interference from anxiety in daily life was required, defined as a score of >1 on the first question on the Child Anxiety Life Interference Scale (CALIS; Lyneham et al., 2013). Exclusion criteria were adolescents having (a) problems following group-rules, (b) disruptive behavior, and/or (c) learning problems causing difficulties following a manualized group-program. Inclusion and exclusion criteria were assessed by providers of the interventions, based on information from adolescents, parents, and teachers. Three adolescents fulfilled exclusion criteria, 34 did not meet inclusion criteria, 7 declined to participate, and six were not included, as some schools did not manage to recruit enough adolescents to form a group before the semester ended. Thus, the final sample comprised 313 adolescents (mean age 14.0 years, *SD* = 0.84, 84.0% girls).

The study was approved by the Regional Committees for Medical and Health Research Ethics (no 2013/2331).

Instruments

All measures were administered through an online platform. In the present study only self-report data from the adolescents were included. The sleep measures have previously been used in Norwegian population-based studies (Hysing et al., 2013, 2016; Sivertsen et al., 2014, 2017).

Demographic Information

All participants indicated their sex, age, and country of birth for themselves and their caregivers. Social class was determined by the highest-ranking occupation between the parents (reported by parents and adolescent), and in accordance with the Registrar General Social Class coding scheme, and categorized as high, medium, and low (Krølner and Holstein, 2006). Family structure was rated from the question "with whom do you live," with six possible response alternatives, later categorized as either a two-parent or a single parent family.

Sleep Characteristics

Insomnia was operationalized according to DSM-5 criteria (Hysing et al., 2013). Insomnia comprised a positive response to *Difficulties initiating and maintaining Sleep* (DIMS) with a frequency of at least 3 days per weeks over a period of at least 3 months and a positive response to sleepiness and/or tiredness. DIMS was rated on a three-point Likert-scale with response options "not true," "somewhat true," and "certainly true." Given a positive response ("somewhat true" or "certainly true"), the participants were asked how many days per week they experienced difficulties initiating and maintaining sleep, and how long this had been a problem. *Tiredness/sleepiness* was rated by a joint question on a three-point Likert-scale with response options "not true," "somewhat true," and "certainly true." Given a positive response ("somewhat true" or "certainly true") adolescents reported the number of days per week they experienced sleepiness and tiredness, respectively.

Youth indicated when they usually went to bed at night and usual rise time in the morning. *Time in bed* (TIB) was calculated by subtracting bedtime from rise-time.

Sleep onset latency (SOL) i.e., how long it usually took to fall asleep, was reported in hours and minutes, and further categorized in five levels from "less than 15 min" (lowest scores) to "120 min or more" (highest scores).

Sleep duration was calculated separately for weekday nights and weekend nights and defined as TIB minus SOL. Sleep duration was further categorized in ten levels from "less than 4 h" (lowest scores) to "12 h or more "(highest scores).

Sleep efficiency was calculated separately for weekday nights and weekend nights, as sleep duration divided by TIB and multiplied by 100 (reported as percentage).

Anxiety and Depressive Symptoms

Anxiety symptoms were assessed by the Spence Children's Anxiety Scale (SCAS) (Spence, 1998; Nauta et al., 2004) comprising 44 items, including six positive filler items. SCAS has sound psychometric properties (Nauta et al., 2004; Arendt et al., 2014). Good to excellent internal consistency was found in the current study (α = 0.91). In addition to a total anxiety score (i.e., a sum score of all 38 anxiety items), the SCAS comprises six subscales of anxiety along the lines of subtypes of anxiety disorders in the DSM-IV: "separation anxiety" (SAD), "social anxiety" (SoAD), "obsessive compulsive disorder" (OCD), "panic/agoraphobia," "physical injury fears/simple phobia" (SP) and "generalized anxiety" (GAD). Internal consistency of the anxiety subtypes, each comprising five to nine items, was acceptable for all subscales except for SP (<0.6) (SAD: α = 0.91; SoAD: α = 0.76; OCD: α = 0.76; panic/agoraphobia: α = 0.81; SP: α = 0.55 and GAD: α = 0.78). Due to poor alpha, the SP subtype was removed from further analysis.

Depressive symptoms were measured by the Short Mood and Feelings Questionnaire (SMFQ) (Angold et al., 1995), a 13-item scale, with good psychometric properties (Sharp et al., 2006; Lundervold et al., 2013). Good to excellent internal consistency was found in the current sample (α = 0.91). To divide the sample into depressed and non-depressed, the SMFQ scores were dichotomized to above clinical cut-off (*n* = 163) and below clinical cut-off (*n* = 150), applying a cutoff score of ≥12 for girls and ≥6 for boys, according to criteria suggested by Jarbin et al. (2020).

Data Analysis

Demographic characteristics, anxiety scores, depressive symptoms, and sleep characteristics are presented with mean, standard deviation (SD), numbers and percentages. Sex differences in anxiety and depressive symptoms and in sleep variables were analyzed by independent t-tests for continuous variables, and chi-square tests for categorical variables.

Relative risk (RR) with 95% confidence interval (CI) for *insomnia* was estimated for total anxiety symptoms, and anxiety subtypes by log-binomial regression. Three different models were provided: Model 1 unadjusted, model 2 including anxiety, age and sex, and model 3 including anxiety, age, sex, and depressive symptoms. The log-binomial regression failed to converge for the models with total anxiety symptoms and the models with anxiety subtype panic/agoraphobia. To overcome this problem Poisson regression with robust variance estimates was applied to estimated RR (Zou, 2004). In addition, equivalent model 1 and model 2 were applied to estimate the RR for insomnia in the subsample of adolescents scoring below clinical cut-off on depression. For these models there were no problems with convergence.

Linear regression analyses were used to explore associations between total anxiety symptoms, anxiety subtypes, and the sleep measures SOL and sleep duration. Corresponding approach as for the log-binomial regression was applied, with model 1 unadjusted, model 2 including anxiety, age and sex, and model 3 including anxiety, age, sex, and depressive symptoms. Equivalent analyses (model 1 and model 2) regarding SOL and sleep duration were performed within the subsample of adolescents scoring below clinical cut-off on depression. Beta values, 95% CI, standardized beta, and adjusted R^2 were calculated. Depressive symptoms correlated with the total anxiety symptom score (r = 0.67), potentially representing a risk for multicollinearity. However, as the variance inflation factor (VIF) was less than 2.1 for all independent variables in the linear regression analyses, multicollinearity was not considered a problem.

Missing data were low regarding sleep and clinical characteristics (0.6% of values missing, with highest missing for sleep duration 3.5%). Furthermore, data were determined to be missing completely at random, indicated by a non-significant Little's MCAR test (p = 0.312). Due to the low level of missing data, it was considered acceptable to handle missing values by a listwise deletion procedure.

IBM SPSS Statistics 25 (SPSS Inc., Chicago, IL, United States) was used for all analyses, besides the log-binomial regression, where STATA (15.1) (StataCorp, College Station, TX, United States) was used.

RESULTS

Demographic and Clinical Characteristics

Mean age of the adolescents was 14.0 years (SD = 0.84, 12–16). The sex distribution in the sample was uneven, with 84.0% girls and 16.0% boys (**Table 1**). Participants were predominately Norwegian (92.0%) (i.e., one or both parents born in Norway), with the majority living in two-parent families (78.8%), and the social class of most families (62.9%) categorized as medium. **Table 1** summarizes means and standard deviations for total anxiety symptoms, anxiety symptom subtypes, and depressive symptoms in the study sample.

Sex differences were found regarding internalizing symptoms, with boys reporting lower total anxiety symptoms and depressive symptoms compared to girls ($p < 0.001$).

Sleep Characteristics

Of the total sample, 119 adolescents (38.1%) met the criteria for insomnia (**Table 1**). Significantly more girls (41.2%) compared to boys (22.0%) reported insomnia (p = 0.010).

Two thirds of the sample (66.1%) reported having difficulties initiating and maintaining sleep, with significantly more girls (69.5%) than boys (50.0%) (p = 0.008). No sex differences were found for the remaining sleep variables.

A large majority of the adolescents (90.4%) reported being tired and/or sleepy during the daytime. A majority (83.1%) reported SOL of 30 min or more, whereas SOL was reported to last for 60 min or more for 64.5%. Sleep duration on weekday nights was below 7 h for 34.8% of the adolescents. Sleep efficiency on weekday nights was below 85.0% for 44.5% of the adolescents.

Anxiety, Depressive Symptoms, and Sleep

Insomnia

Total anxiety symptoms were positively associated with insomnia (RR: 1.03, [95% CI 1.02–1.03], $p < 0.001$) and remained associated with insomnia also after adjusting for age and sex (RR: 1.03, [1.02–1.03], $p < 0.001$) (**Table 2**). When including depressive symptoms in the model, both total anxiety symptoms (RR: 1.01, [1.01–1.02], p = 0.002), and depressive symptoms (RR: 1.04, [1.02–1.07], p = 0.001) were associated with insomnia.

All anxiety symptom subtypes (i.e., GAD, SoAD, SAD, panic/agoraphobia, and OCD) were associated with insomnia. This was the case also after adjusting for age and sex. When additionally including depressive symptoms in model 3, panic/agoraphobia symptoms remained significantly associated with insomnia, whereas associations between the other anxiety symptom subtypes and insomnia were no longer significant. However, for total anxiety and all anxiety subtypes, when including depressive symptoms in the model, depressive symptoms were associated with insomnia (RR ranging from 1.04 to 1.06, $p < 0.05$).

For the subsample of adolescents scoring below clinical cut-off on depression (n = 150) there was an association between anxiety and insomnia (unadjusted RR: 1.03, [1.02–1.04], $p < 0.001$). For the anxiety symptom subtypes, there were associations between insomnia and the anxiety subtypes GAD, panic/agoraphobia, and OCD (**Table 2**).

Sleep Onset Latency

Results from the linear regression analyses showed that total anxiety symptoms were positively associated with SOL (β = 0.25, $p < 0.001$), and remained associated with

TABLE 1 | Baseline demographic information, anxiety and depressive symptoms, and sleep characteristics among adolescents with anxiety (N = 313).

		n	%	*M*	*SD*
Demographic variables					
Age				13.99	0.84
Gender:	Female	263	84.0		
Nationality[a]	Norwegian	301	96.2		
Family structure	Two-parent families	246	78.8		
	Single-parent families	66	21.2		
Social class[b]	High	83	26.6		
	Middle	197	62.9		
	Low	32	10.3		
Internalizing symptoms					
Total anxiety symptoms (SCAS)				43.44	16.46
SAD				4.77	2.79
SoAD				10.09	3.76
GAD				9.22	3.49
Panic/agoraphobia				7.51	5.48
OCD				6.68	3.69
Depressive symptoms (SMFQ)				11.48	6.81
Below clinical cut-off[c]		150	47.9		
Sleep characteristics					
Insomnia (DSM-V)	Yes	119	38.1		
DIMS	Yes	207	66.3		
Tired/sleepy	Yes	283	90.4		
SOL	<30 min	53	16.9		
	30–59 min	58	18.5		
	60–119 min	93	29.7		
	120+ min	109	34.8		
Sleep duration-weekdays	<5 h	36	11.9		
	5–7 h	69	22.9		
	≥7 h	198	65.2		
Sleep efficiency-weekdays	<75	78	25.3		
	75.0–84.9	59	19.2		
	85.0–89.9	60	19.5		
	≥90	111	36.0		

[a] *Norwegian ethnicity defined as 1 or both parents born in Norway.*
[b] *Determined by occupation of the highest-ranking parent, in accordance with the Registrar General Social Class coding scheme and categorized as high, medium, and low.*
[c] *Clinical cut-off for depressive symptoms ≥6 for boys and ≥12 for girls according to Jarbin et al. (2020).*
DIMS, difficulties initiating and/or maintaining sleep; GAD, generalized anxiety disorder; OCD, obsessive compulsive disorder; SAD, separation anxiety disorder; SCAS, spence children's scale; SMFQ, short mood and feeling questionnaire; SOL, sleep onset latency; SoAD, social anxiety disorder.

SOL (β = 0.23, $p < 0.001$) after adjusting for age and sex (**Table 3**). When including depressive symptoms into the model, total anxiety was no longer associated with SOL, whereas depressive symptoms were (β = 0.28, $p < 0.001$). The full model including total anxiety symptoms, age, sex, and depressive symptoms accounted for 9% of the variance in SOL [$F(1,310) = 9.02$, $p < 0.001$]. All anxiety symptom subtypes were associated with SOL, both before and after adjusting for age and sex (**Table 3**). However, when including depressive symptoms in the model, the different anxiety subtypes were no longer associated with SOL, whereas depressive symptoms were (β ranging from 0.25 to 0.33, $p < 0.001$).

For the subsample of adolescents below clinical cut-off on depressive symptoms (n = 150), an association was found between total anxiety symptoms and SOL (β = 0.29, $p \leq 0.001$), as well as associations between symptoms of SoAD, Panic/agoraphobia, OCD and SOL (**Table 3**).

Sleep Duration

Total anxiety symptoms were negatively associated with sleep duration (β = −0.18, $p < 0.01$), and remained associated with sleep duration (β = −0.15, $p < 0.01$) after adjusting for age and sex (**Table 4**). When including depressive symptoms in the model, total anxiety was no longer associated with sleep duration, whereas depressive symptoms were (β = −0.30, $p < 0.001$). The model including total anxiety symptoms, age, sex, and depressive symptoms accounted for 8% of the variance in sleep duration [$F(1,299) = 7.60$, $p < 0.001$].

In the unadjusted models, the subtypes SoAD, Panic/agoraphobia, and OCD were associated with sleep duration, with higher levels of anxiety associated with lower sleep duration. These anxiety subtypes remained associated with sleep duration after adjusting for age and sex. However, when entering depressive symptoms to the model, none of the anxiety subtypes were associated with sleep duration, whereas associations between depressive symptoms and sleep duration emerged (β ranging from −0.25 to −0.33, $p < 0.001$).

For the subsample of adolescents below clinical cut-off on depressive symptoms (n = 150), no association was found between total anxiety symptoms and sleep duration. There were no associations between the subtypes of anxiety and sleep duration, except for the unadjusted association between symptoms of panic/agoraphobia and sleep duration (**Table 4**).

DISCUSSION

The findings indicate that sleep should be addressed among adolescents with anxiety seeking help from primary health care services. A considerable proportion of the adolescents (12–16 years) in this study reported high rates of insomnia, long sleep onset latency (SOL), and short sleep duration. Self-reported anxiety was positively associated with insomnia and SOL across all subtypes of anxiety, indicating that we need to address insomnia and SOL in adolescents regardless of anxiety subtypes. Also, some of the anxiety subtypes (i.e., SoAD, panic/agoraphobia, and OCD) were associated with sleep duration. Although co-occurring depressive symptoms accounted for most of the associations between anxiety and the sleep variables, associations between anxiety and insomnia, as well as SOL, were still found among adolescents who scored below clinical cut-off on depressive symptoms. Hence, poor sleep should be addressed among

TABLE 2 | Relative risk (RR) of insomnia in adolescents with anxiety by total anxiety symptoms (SCAS), and anxiety subtypes, adjusted for age, sex, and depressive symptoms (SMFQ), including sub-analyses on adolescents below clinical cut-off for depression, estimated from log-binomial regressions.

		Full sample (*N* = 313)		Depression below clinical cut-off[b] (*n* = 150)	
		Insomnia		Insomnia	
	Independent variables	RR	95% CI	RR	95% CI
Model 1	Total anxiety symptoms[a]	1.03***	1.02, 1.03	1.03***	1.02, 1.04
Model 2	Total anxiety symptoms[a]	1.03***	1.02, 1.03	1.03***	1.01, 1.04
Model 3	Total anxiety symptoms[a]	1.01**	1,01, 1.02		
	Depressive symptoms	1.04**	1.02, 1.07		
Model 1	GAD symptoms	1.12***	1.09, 1.14	1.22***	1.11, 1.34
Model 2	GAD symptoms	1.11***	1.07, 1.14	1.20***	1.08, 1.33
Model 3	GAD symptoms	1.04	1.00 1.09		
	Depressive symptoms	1.04*	1.01 1.07		
Model 1	SoAD symptoms	1.10***	1.06, 1.14	1.06	0.99, 1.14
Model 2	SoAD symptoms	1.08***	1.04, 1.12	1.04	0.96, 1.12
Model 3	SoAD symptoms	1.02	0.97, 1.06		
	Depressive symptoms	1.06***	1.03, 1.08		
Model 1	SAD symptoms	1.07***	1.03, 1.11	1.06	0.97, 1.16
Model 2	SAD symptoms	1.06**	1.02, 1.11	1.08	0.98, 1.18
Model 3	SAD symptoms	1.01	0.97, 1.05		
	Depressive symptoms	1.06***	1.04, 1.09		
Model 1	Panic/agoraphobia symptoms[a]	1.08***	1.06, 1.10	1.07***	1.03, 1.12
Model 2	Panic/agoraphobia symptoms[a]	1.07***	1.05, 1.09	1.06*	1.01, 1.10
Model 3	Panic/agoraphobia symptoms[a]	1.04**	1.02, 1.07		
	Depressive symptoms	1.04**	1.02, 1.07		
Model 1	OCD symptoms	1.07***	1.05, 1.10	1.09***	1.04, 1.14
Model 2	OCD symptoms	1.06***	1.04, 1.09	1.10***	1.05, 1.16
Model 3	OCD symptoms	1.01	0.98, 1.04		
	Depressive symptoms	1.06***	1.03, 1.09		

Model 1: unadjusted; Model 2: adjusted for age and sex; Model 3: including anxiety, age, sex, and depressive symptoms.
[a]For the full sample Poisson regression was used to estimate RR.
[b]Clinical cut-off for depressive symptoms ≥6 for boys and ≥12 for girls according to Jarbin et al. (2020).
GAD, generalized anxiety disorder; OCD, obsessive compulsive disorder; SAD, separation anxiety disorder; SCAS, spence children's anxiety scale; SMFQ, short mood and feelings questionnaire; SoAD, social anxiety disorder.
**p < 0.05, **p < 0.01, ***p < 0.001.*

adolescents with elevated anxiety, even in the absence of co-occurring depression.

Sleep Duration, Sleep Onset Latency, and Insomnia in Adolescents With Anxiety

The 38.1% insomnia rate in the present sample was considerably higher than a prevalence of 18.5% found in a general population-based study of Norwegian adolescents, using the same definition of insomnia (Hysing et al., 2013). Also, the percentage of adolescents reporting SOL ≥30 min, was higher in the sample of adolescents with anxiety (83.1%) compared to the adolescents in the population-based study (65%) (Hysing et al., 2013). However, as the population-based sample comprised older adolescents (16–18 years) compared to the current sample of adolescents with anxiety (12–16 years), the comparisons must be interpreted with caution. Other results from the same population-based study, however, indicate that sleep problems increase during late adolescence (Sivertsen et al., 2017). Thus, based on age alone, adolescents in the current sample should have had better, and not poorer sleep, compared to the population-based sample.

In line with previous findings of increased SOL in youth with anxiety disorders (Forbes et al., 2008; Orchard et al., 2020), most of the participants in the current study reported long SOL, with over half of the adolescents (64.5%) spending more than 1 h each night trying to fall asleep. The prevalence of insomnia in the present sample (38.1%) also appears to be higher than the 10.7% rate of insomnia found in a population-based study of American adolescents (13–16 years), using similar methodology to measure insomnia (Johnson et al., 2006a). The rate of insomnia in our sample was more in line with, and even somewhat higher than, the rate of insomnia (25.6%) reported by adolescents who fulfilled criteria for anxiety disorders in the same study (Johnson et al., 2006a).

About one third (35%) of the adolescents slept less than 7 h on weekday nights, which is considered short, according to expert-based guidelines recommending 8–10 h of sleep for

TABLE 3 | Associations between sleep onset latency (SOL), total anxiety symptoms (SCAS), and anxiety subtypes, in adolescents with anxiety, adjusting for age, sex, and depressive symptoms (SMFQ), including sub-analyses for youth below clinical cut-off for depression, estimated from linear regression.

		Full sample (*N* = 313)				Depression below clinical cut-off[a] (*n* = 150)			
		Sleep onset latency (SOL)				Sleep onset latency (SOL)			
	Independent variables	β	***B***	**95% CI**	**Adj. R^2**	β	***B***	**95% CI**	**Adj. R^2**
Model 1	Total anxiety symptoms	0.25***	0.02	0.01, 0.03	0.06	0.29***	0.03	0.01, 0.05	0.08
Model 2	Total anxiety symptoms	0.23***	0.02	0.01, 0.03	0.06	0.28**	0.03	0.10, 0.05	0.08
Model 3	Total anxiety symptoms	0.06	0.00	−0.01, 0.02	0.09				
	Depressive symptoms	0.28***	0.05	0.02, 0.08					
Model 1	GAD symptoms	0.16**	0.06	0.02, 0.09	0.02	0.12	0.06	−0.02, 0.13	0.01
Model 2	GAD symptoms	0.14*	0.05	0.01, 0.09	0.03	0.11	0.05	−0.02, 0.13	0.02
Model 3	GAD symptoms	−0.04	−0.01	−0.06, 0.03	0.09				
	Depressive symptoms	0.33***	0.06	0.03, 0.08					
Model 1	SoAD symptoms	0.20***	0.07	0.03, 0.10	0.04	0.20*	0.07	0.02, 0.13	0.04
Model 2	SoAD symptoms	0.18**	0.06	0.02, 0.10	0.04	0.18*	0.06	0.00, 0.12	0.04
Model 3	SoAD symptoms	0.01	0.00	−0.04, 0.05	0.09				
	Depressive symptoms	0.30***	0.05	0.03, 0.08					
Model 1	SAD symptoms	0.12*	0.05	0.00, 0.10	0.01	0.14	0.07	−0.01, 0.15	0.01
Model 2	SAD symptoms	0.12*	0.05	0.00, 0.10	0.02	0.15	0.08	0.00, 0.15	0.03
Model 3	SAD symptoms	0.01	0.00	−0.05, 0.05	0.09				
	Depressive symptoms	0.31***	0.06	0.03, 0.08					
Model 1	Panic/agoraphobia symptoms	0.26***	0.06	0.03, 0.08	0.06	0.25**	0.08	0.03, 0.14	0.06
Model 2	Panic/agoraphobia symptoms	0.24***	0.05	0.03, 0.08	0.06	0.23**	0.08	0.02, 0.13	0.06
Model 3	Panic/agoraphobia symptoms	0.09	0.02	−0.01, 0.05	0.10				
	Depressive symptoms	0.25**	0.04	0.02, 0.07					
Model 1	OCD symptoms	0.20***	0.07	0.03, 0.10	0.04	0.24**	0.09	0.03, 0.15	0.05
Model 2	OCD symptoms	0.19**	0.06	0.03, 0.10	0.04	0.25**	0.09	0.03, 0.15	0.07
Model 3	OCD symptoms	0.07	0.02	−0.02, 0.06	0.09				
	Depressive symptoms	0.27***	0.05	0.03, 0.07					

Model 1: unadjusted, Model 2: adjusted for age and sex, Model 3: including anxiety, age, sex, and depressive symptoms,
[a]*clinical cutoff ≥12 for girls and ≥6 for boys according to Jarbin et al. (2020).*
β, *standardized beta; GAD, generalized anxiety disorder; OCD, obsessive compulsive disorder; SAD, separation anxiety disorder; SCAS, spence children's anxiety scale; SMFQ, short mood and feelings questionnaire; SoAD, social anxiety disorder; *p < 0.05, **p < 0.01, ***p < 0.001.*

teenagers (Hirshkowitz et al., 2015). However, an even higher percentage in the Norwegian population-based sample (53.8%) reported sleep duration below 7 h on weekday nights (Hysing et al., 2016). This may be explained by a general decrease in hours of sleep occurring during the later adolescent years (Carskadon, 2011), given that the population-based sample had a somewhat higher age range than our sample. However, a previous study reported no difference between adolescents with and without anxiety disorders regarding sleep duration (Orchard et al., 2020). Thus, it is possible that sleep duration might be less affected by anxiety, and that adolescents with anxiety have no higher risk of short sleep duration than their peers. However, the limited evidence available, together with the high rates of insomnia and long SOL in the present sample, suggests that we need further studies before drawing firm conclusions regarding the association between anxiety and sleep duration.

In the present study, more girls met criteria for insomnia compared to boys. This is in accordance with sex differences found in studies of adolescents in the general population (Johnson et al., 2006b; Hysing et al., 2013). In the current sample, no difference was found between boys and girls regarding sleep duration, whereas shorter sleep duration was found among boys compared to girls in the comparison population-based study (Hysing et al., 2013). However, given the limited number of boys included in the present sample, the lack of sex differences should be interpreted with caution. In general, adjusting for sex and age did not change the associations between anxiety and sleep variables in this study. Total anxiety symptoms and most anxiety subtypes were associated with insomnia, SOL, and sleep duration even after sex and age were statistically controlled.

Anxiety Subtypes and Sleep

All anxiety subtypes were associated with insomnia and SOL, whereas sleep duration was negatively associated with symptoms of SoAD, panic/agoraphobia, and OCD. Previous research on associations between sleep and subtypes of anxiety is limited.

In this study subscales on the SCAS, and not diagnostic categories, were used to assess anxiety subtypes. However, a study comparing SCAS subscales with scores from diagnostic

TABLE 4 | Associations between sleep duration, total anxiety symptoms (SCAS), and anxiety subtypes in adolescents with anxiety, adjusting for age, sex, and depressive symptoms (SMFQ), including a subanalyses for adolescents below clinical cut-off on depression, estimated from linear regression.

		Full sample (*N* = 313)				Depression below clinical cut-off[a] (*n* = 150)			
		Sleep duration wk				Sleep duration wk			
	Independent variables	**β**	***B***	**95% CI**	**Adj. R^2**	**β**	***B***	**95% CI**	**Adj. R^2**
Model 1	Total anxiety symptoms	−0.18**	−0.02	−0.03, −0.01	0.03	−0.15	−0.02	0.04, 0.00	0.02
Model 2	Total anxiety symptoms	−0.15**	−0.02	−0.03, 0.00	0.04	−0.16	−0.02	−0.04, 0.00	0.05
Model 3	Total anxiety symptoms	0.03	0.00	−0.01, 0.02	0.08				
	Depressive symptoms	−0.30***	−0.07	−0.11, −0.04					
Model 1	GAD symptoms	−0.10	−0.05	−0.11, 0.00	0.01	−0.02	−0.01	−0.11, 0.08	−0.01
Model 2	GAD symptoms	−0.08	−0.04	−0.10, 0.02	0.02	−0.03	−0.01	−0.10, 0.08	0.03
Model 3	GAD symptoms	0.10	0.05	−0.02, 0.11	0.09				
	Depressive symptoms	−0.33***	−0.08	−0.12, −0.05					
Model 1	SoAD symptoms	−0.17**	−0.08	−0.13, −0.03	0.03	−0.07	−0.03	−0.10, 0.04	0.00
Model 2	SoAD symptoms	−0.14*	−0.06	−0.12, −0.01	0.03	−0.06	−0.03	−0.10, 0.05	0.04
Model 3	SoAD symptoms	0.02	0.01	−0.05, 0.07	0.08				
	Depressive symptoms	−0.28***	−0.07	−0.11, −0.04					
Model 1	SAD symptoms	−0.01	0.00	−0.07, 0.07	0.00	0.01	0.01	−0.09, 0.10	−0.01
Model 2	SAD symptoms	−0.01	0.00	−0.07, 0.06	0.01	−0.01	0.00	−0.10, 0.09	0.03
Model 3	SAD symptoms	0.11	0.07	−0.01, 0.14	0.09				
	Depressive symptoms	0.32***	−0.08	−0.11, −0.05					
Model 1	Panic/agoraphobia symptoms	−0.21***	−0.07	−0.01, −0.03	0.04	−0.18*	−0.07	−0.14, −0.01	0.02
Model 2	Panic/agoraphobia symptoms	−0.18**	−0.06	−0.09, −0.02	0.05	−0.16	−0.07	−0.13, 0.00	0.06
Model 3	Panic/agoraphobia symptoms	−0.04	−0.01	−0.06, 0.03	0.08				
	Depressive symptoms	−0.25**	−0.06	−0.10, −0.03					
Model 1	OCD symptoms	−0.13*	−0.06	−0.11, −0.01	0.01	−0.13	−0.06	−0.13, 0.01	0.01
Model 2	OCD symptoms	−0.12*	−0.06	−0.11, 0.00	0.03	−0.16	−0.07	−0.14, 0.00	0.06
Model 3	OCD symptoms	0.00	0.00	−0.06, 0.06	0.08				
	Depressive symptoms	−0.27***	−0.07	−0.10, −0.04					

Model 1: unadjusted, Model 2: adjusted for age and sex, Model 3: adjusted for age, sex, and depressive symptoms.

[a] *Clinical cutoff ≥12 for girls and ≥6 for boys according to Jarbin et al. (2020).*

β, *standardized beta; GAD, generalized anxiety disorder; OCD, obsessive compulsive disorder; SAD, separation anxiety disorder; SCAS, spence children's anxiety scale; SMFQ, short mood and feelings questionnaire; SoAD, social anxiety disorder.*

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

interviews, has shown the SCAS subscales to validly assess SoAD, GAD, panic/agoraphobia, OCD, and SAD in adolescents (Olofsdotter et al., 2015).

While we have not specifically addressed the factors that might drive the high prevalence of insomnia and long SOL, previous research with youth with anxiety disorders suggests that this may partly be explained by heightened physical and cognitive arousal, poorer emotion regulation, and vigilance to threat, all factors that may make sleep harder to initiate in youth with anxiety (Palmer and Alfano, 2017; Blake et al., 2018; Ricketts et al., 2018). These factors are probably common features of anxiety, explaining why sleep problems may be found across different anxiety subtypes.

The Role of Co-occurring Depressive Symptoms

With a few exceptions for insomnia, when depressive symptoms were included in the regression models, anxiety was no longer associated with the sleep variables. Strong associations between depression and sleep have been explained by excessive worrying, where worrying seems to precede and partly mediate the association between poor sleep and depressive symptoms in adolescents (Danielsson et al., 2013). Poor sleep may furthermore be related to poorer mood regulation, indicating a potential mechanism from poor sleep to mood disorders in adolescents (Short et al., 2020).

An alternative interpretation could be that the strong association found between depressive symptoms and sleep is a result of informant-bias – in other words, depressed youth may generally report more negative experiences due to their negative perceptions of the world. Support for this possibility is found in a study of youth (7–17 years) where those with anxiety disorders showed more sleep problems on objective sleep measures compared to depressed and non-clinical youth, whereas according to self-report, youth with anxiety had fewer sleep problems than those with depression (Forbes et al., 2008).

To further explore the association between anxiety, depressive symptoms, and sleep, we examined a subsample of adolescents scoring below clinical cutoff on depressive symptoms. In this subsample, anxiety symptoms remained associated with

insomnia and SOL. Thus, anxiety and sleep difficulties were associated also among adolescents with anxiety who reported low levels of depression. Common factors have been suggested to underly the associations between anxiety, depression, and sleep (Blake et al., 2018). Adolescents with sleep disturbances have been found to worry more about issues such as bullying, terrorist attacks, illness, and accidents, compared to adolescents who sleep well (Danielsson et al., 2016). These worries are also frequently found among youth with high levels of anxiety (Weems et al., 2000).

Perseverative cognition is repetitive cognitive processes constituting the common features between worrying and rumination. These cognitions have been found to prolong stress-related affective and physiological activation, in advance of and following stressors (Brosschot et al., 2006). The prolonged activation can make initiating and maintaining sleep difficult, and perseverative cognitions could therefore explain the long SOL and the high prevalence of insomnia found among adolescents with anxiety in the current study. Perseverative cognitions are commonly associated with both anxiety and depression (Brosschot et al., 2006), and might be a possible underlying mechanism in the association between depressive and anxiety symptoms, and sleep problems.

Strengths and Limitations

The current study expands on previous knowledge by examining sleep in a sample of adolescents with anxiety referred to early intervention. Examining sleep variables in this sample may increase our knowledge of problems and needs among adolescents seeking help within primary health care services.

A further strength of the study was the inclusion of measures specifically assessing insomnia, SOL, and sleep duration, rather than composite sleep measures that include overlapping items between sleep and anxiety. The focus on adolescents' self-reports rather than parent-reports is also a strength given that many sleep difficulties (e.g., long SOL) and anxiety symptoms are not always easily observable by caregivers. Finally, exploring the role of depressive symptoms in the associations between anxiety and sleep is novel, and needs to be explored further.

The study has several limitations. First, the cross-sectional design precludes any conclusions about causality or directionality between anxiety symptoms, depressive symptoms, and sleep. Second, no comparison group was included, making conclusions about level of sleep problems less definitive.

The large difference in the number of boys versus girls limits interpretations about sex differences. Whereas the exclusive use of subjective measures of sleep is a limitation, a recent study reports high correspondence between subjective and objective measures of sleep among adolescents (Lucas-Thompson et al., 2020). Furthermore, sleep duration was based on SOL subtracted from time in bed. To get a more accurate measure, wake after sleep onset should also have been subtracted from time in bed. Wake after sleep onset was not assessed but is generally quite short during adolescence. However, this could have led to an overestimation of sleep duration in the present study. For insomnia, a clinical interview is considered the gold standard, and this would have strengthened the validity of the insomnia category.

CONCLUSION

Adolescence is a period characterized by increase in sleep problems and, at the same time, anxiety and depressive symptoms commonly increase. The co-occurrence of these problems may cause considerable impairment during these critical years of a young person's development. The high rate of insomnia and the long SOL found among adolescents with different subtypes of anxiety, suggest a need to assess sleep among all adolescents who seek help for anxiety within primary health care services, regardless of subtype of anxiety they present with. The findings further point to the need to concurrently assess depressive symptoms, which may account for a considerable portion of the common variance between anxiety and the sleep variables. Nonetheless, given that anxiety is related to insomnia and SOL even among anxious adolescents who report low levels of depression, it is important to assess sleep in all adolescents presenting with anxiety.

Interventions need to address the complex symptomatology often presented by adolescents with elevated anxiety. Cognitive behavioral therapy (CBT) programs frequently used for treatment or indicated prevention for adolescents with anxiety do not focus on potential co-occurring sleep problems (e.g., Coping Cat, Kendall and Hedtke, 2006; Cool Kids, Rapee et al., 2006). This makes it highly possible that sleep problems in adolescents with anxiety are neither recognized, nor treated. Nonetheless, a few approaches targeting sleep in adolescents, either across mental health problems (e.g., Harvey, 2016), or specifically aiming to reduce co-occurring sleep problems and anxiety (Blake et al., 2016) have been developed and evaluated.

Evidence suggests that CBT for insomnia may reduce anxiety (Belleville et al., 2011), perhaps through reducing anxious worrying (Ballesio et al., 2021). Studies have also examined the integration of CBT for insomnia with techniques specifically targeting anxious worrying (Ballesio et al., 2021). As this is research including only adult samples, further studies need to examine if CBT for insomnia have effect on anxious worrying also in adolescent samples.

In general, approaches integrating interventions for anxiety and sleep problems specifically targeting adolescents need to be developed, evaluated, and disseminated in primary health care settings.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are not readily available because confidential patient data are included. All requests must be approved by the Norwegian Regional Committees for Medical and Health Research Ethics. Requests to access the datasets should be directed to BH, bente.haugland@uib.no.

ETHICS STATEMENT

The study involved human participants and was reviewed and approved by the Regional Committee for Medical and Health Research Ethics in Western Norway (no. 2013/2331). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

All authors contributed to the study conception and design. BH, MH, VB, GW, RR, AH, ÅTH, and JB performed the material preparation, data collection, and analysis. BH wrote the first draft of the manuscript. All authors commented on the different versions of the manuscript and read and approved the final manuscript.

FUNDING

This work was supported by The Research Council of Norway, through grant no. 229020. Additional financial support was received from the Oslofjord fund, grant no. 245807, Regional Research fund western Norway, grant no. 235707, and the Norwegian Directorate of Health (reference no. 11/751-38 and 14/4285-3).

ACKNOWLEDGMENTS

We wish to thank all the adolescents who took part in the study, as well as the primary health personnel who skillfully recruited participant, delivered group interventions, and administered the data collection.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychology

ORIGINAL RESEARCH
published: 20 April 2021
doi: 10.3389/fpsyg.2021.633959

Sleep and its Association With Pain and Depression in Nursing Home Patients With Advanced Dementia – a Cross-Sectional Study

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Objective: Previous research suggests a positive association between pain, depression and sleep. In this study, we investigate how sleep correlates with varying levels of pain and depression in nursing home (NH) patients with dementia.

Materials and methods: Cross-sectional study (n = 141) with sleep-related data, derived from two multicenter studies conducted in Norway. We included NH patients with dementia according to the *Mini-Mental State Examination* (MMSE $\leq$ 20) from the COSMOS trial (n = 46) and the DEP.PAIN.DEM trial (n = 95) whose sleep was objectively measured with actigraphy. In the COSMOS trial, NH patients were included if they were $\geq$65 years of age and with life expectancy >6 months. In the DEP.PAIN.DEM trial, patients were included if they were $\geq$60 years and if they had depression according to the *Cornell Scale for Depression in Dementia* (CSDD $\geq$ 8). In both studies, pain was assessed with the Mobilization-Observation-Behavior-Intensity-Dementia-2 Pain Scale (MOBID-2), and depression with CSDD. Sleep parameters were total sleep time (TST), sleep efficiency (SE), sleep onset latency (SOL), wake after sleep onset (WASO), early morning awakening (EMA), daytime total sleep time (DTS) and time in bed (TiB). We registered use of sedatives, analgesics, opioids and antidepressants from patient health records and adjusted for these medications in the analyses.

Results: Mean age was 86.2 years and 76.3% were female. Hierarchical regressions showed that pain was associated with higher TST and SE ($p < 0.05$), less WASO ($p < 0.01$) and more DTS ($p < 0.01$). More severe dementia was associated with more WASO ($p < 0.05$) and TiB ($p < 0.01$). More severe depression was associated with less TST ($p < 0.05$), less DTS ($p < 0.01$) and less TiB ($p < 0.01$). Use of sedative medications was associated with less TiB ($p < 0.05$).

Conclusion: When sleep was measured with actigraphy, NH patients with dementia and pain slept more than patients without pain, in terms of higher total sleep time. Furthermore, their sleep efficiency was higher, indicating that the patients had more

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Edited by:
Christian Franceschini, University of Parma, Italy

Reviewed by:
Luigi De Gennaro, Sapienza University of Rome, Italy
Valentina Alfonsi, Sapienza University of Rome, Italy

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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *26 November 2020*
Accepted: *26 March 2021*
Published: *20 April 2021*

Citation:
Blytt KM, Flo-Groeneboom E, Erdal A, Bjorvatn B and Husebo BS (2021) Sleep and its Association With Pain and Depression in Nursing Home Patients With Advanced Dementia – a Cross-Sectional Study. Front. Psychol. 12:633959. doi: 10.3389/fpsyg.2021.633959

sleep within the time they spent in bed. Patients with more severe dementia spent more time awake during the time spent in bed. Furthermore, people with more severe depression slept less at daytime and had less total sleep time Controlling for concomitant medication use did not affect the obtained results.

Keywords: sleep, pain, depression, nursing home patients, actigraphy, dementia

INTRODUCTION

Approximately 50 million people are living with dementia worldwide, and every year 10 million new cases are registered (World Health Organization [WHO], 2019). Sleep disturbances, like difficulties in initiating sleep, frequent awakenings, excessive daytime sleepiness and nighttime wandering are often seen in people with dementia (McCleery et al., 2016; Webster et al., 2020a). However, to estimate the prevalence of sleep disturbances in people with dementia is difficult due to differences in assessment methods and because of the patients' reduced communicative ability (Blytt et al., 2017).

A recent systematic review and meta-analysis conducted by Webster et al. (2020b) found a 20% pooled prevalence of clinically significant sleep disturbances in people with dementia and a 70% prevalence of sleep disturbances as measured with actigraphy. Furthermore, Webster et al. (2020a) found that sleep disturbances negatively affect physical and psychological well-being in people with dementia. In the NH setting, sleep disturbances also caused disruption for other patients and increased stress among staff (Webster et al., 2020a). Previously conducted studies have found that sleep disturbances in dementia are associated with reduced quality of life and impaired daytime functioning (Kyle et al., 2010), increased family burden and earlier nursing home (NH) admission, thereby increasing the social and economic costs for society (McCrae et al., 2016; Livingston et al., 2017).

Pain is a subjective experience that is difficult to assess for people with dementia, due to reduced capacity to give valid self-report (Blytt et al., 2017). When assessed by proxy-rater measurements, moderate to severe pain is found in approximately 40–60% of NH patients with dementia (Achterberg et al., 2010; Hemmingsson et al., 2018; Wagatsuma et al., 2020). Reduced quality of life, increased agitation and anxiety are all associated with pain in NH patients (Ballard et al., 2009). In addition, approximately 50% of people with dementia experience symptoms of depression – a condition that may reduce their quality of life and accelerate the decline in cognition and daily functioning (Enache et al., 2011).

Previous research has found a reciprocal relationship between pain and depression in people without dementia (Bair et al., 2003; Goldenberg, 2010; Kroenke et al., 2011). This relationship is known as the "pain-depression dyad," indicating that the conditions often coexist, respond to similar treatment and share common signal pathways (Chopra and Arora, 2014). In NH patients, Erdal et al. (2017) found that reduced pain intensity was associated with subsequent reduction of depressive symptoms, regardless of analgesic or antidepressant use. These associations were found in patients with mild, moderate and severe cognitive impairment. However, results on the primary outcome measures in an analgesic intervention trial did not support a direct causal relationship between pain and increased depression in NH patients with dementia (Erdal et al., 2018).

There is also considerable evidence for a reciprocal relationship between pain and sleep in people without dementia. Previous research suggests that poor sleep may affect the perception of pain (Sivertsen et al., 2015), but also that pain in itself can be a possible cause of poor sleep (Sivertsen et al., 2015; Flo et al., 2017). There is some evidence suggesting that depression may be a central underlying mechanism in the relationship between pain and sleep in people without cognitive impairment (Ravyts et al., 2018). Furthermore, pain may lead to depression, which in turn may affect the patient's sleep (Nicassio et al., 2012; Flo et al., 2017). By extension people with dementia and depression may be lying in bed, experiencing trouble falling asleep or maintaining sleep because they are in pain (Blytt, 2019). However, there is still a lack of evidence regarding this relationship in people with dementia (Flo et al., 2017).

To our knowledge, there are no previous studies investigating how sleep is associated with pain and depression in NH patients with dementia. Given the frequency and clinical implications of sleep disturbances for the patients, co-residents and staff, new knowledge regarding the relationship between pain, depression and sleep in this patient group is valuable. Consequently, we aimed to investigate the association between sleep, pain, depression and dementia in NH patients. We hypothesized that a) more pain was associated with poorer sleep; b) more severe dementia was associated with poorer sleep; and c) more severe depression was associated with poorer sleep. Because medical treatment for pain, depression and sleep disorders may also impact sleep parameters, analyses were adjusted for the use of analgesic, antidepressant and sedative-hypnotic drugs.

MATERIALS AND METHODS

Participants and Protocol

The study was based on sleep-related data derived from two independent multicenter studies conducted in Norway: the COSMOS trial (n = 46) and the DEP.PAIN.DEM trial (n = 95). The COSMOS (*Communication, Systematic pain assessment and treatment, Medication review, Organization of activities, and Safety*) trial is a multicenter cluster-randomized controlled trial over 4 months with follow-up at month 9. The study was conducted from January 2014 to December 2015. It aimed to improve the quality of life among NH patients through a multicomponent intervention (Husebo et al., 2015). A total of 765 patients were invited to participate in the COSMOS study, and 545 participants from 67 NH units were included (Husebø

et al., 2019). The COSMOS trial used the following inclusion and exclusion criteria: NH patients ≥65 years of age and life expectancy >6 months.

The DEP.PAIN.DEM trial is a multicenter, placebo-controlled randomized clinical trial over 13 weeks. The study was conducted in Norway from August 2014 to September 2016. The main aim of the DEP.PAIN.DEM trial was to investigate the efficacy of pain treatment on depression in people with dementia and depression. Patients were included if they were long-term NH patients ≥60 years with >4 week stay at inclusion, dementia according to the Mini-Mental State Examination (MMSE score ≤ 20) and depression according to the Cornell Scale for Depression in Dementia (CSDD score ≥ 8). The sleep subproject of DEP.PAIN.DEM included 106 patients from 47 NHs (Blytt et al., 2018a).

Patients with Parkinson disorder or any form of paralysis in the arms or upper body were excluded from actigraphy registrations. In the present study, we included patients who had valid actigraphy measurements and dementia according to MMSE (≤20) from both the DEP.PAIN.DEM and the COSMOS trials, which implies that we used data collected at baseline (week 0) before any intervention was conducted.

In total, 141 patients from the COSMOS (n = 46) and the DEP.PAIN.DEM (n = 95) trials had valid actigraphy measurements and dementia according to MMSE and were included in the present study. Some of the respondents did not have complete datasets for all variables (see **Table 1** for the number of observations for the different variables). Mean age was 86.2 years and 76.3% were female.

In the data collection process, the patient's medical decision-making capacity was discussed with the patient's primary nurse at the NH. Efforts were made to adjust the information for patients who had reduced capacity to give consent (MMSE score from 16 to 19). In addition, the researchers telephoned all the eligible patients' legal guardians. If the legal guardians gave presumed consent on behalf of the patient, they received written and oral information together with a consent form that they signed and mailed back. The DEP.PAIN.DEM study was approved by the Regional Ethics Committee (REC-West 2013/1474). The study's clinical trial number is NCT02267057. The COSMOS trial was also approved by the Regional Committee for Medical and Health Research Ethics, West Norway (REK 2013/1765) and registered at www.clinicaltrials.gov (NCT02238652).

TABLE 1 | Descriptive statistics: age, gender, CSDD, MOBID-2, and MMSE scores for the full sample.

	Descriptives	No. of observations
Age (mean, SD)	86.2 (7.5)	140
Female (%)	76.3	141
CSDD (mean, SD)	9.5 (4.7)	134
MOBID-2 (mean, SD)	2.6 (2.3)	120
MMSE (mean, SD)	8.8 (5.8)	141

Descriptive statistics for the full sample (n = 141). Number of observations refers to how many patients have valid data for the different parameters. Abbreviations: CSDD = Cornell Scale for Depression in Dementia, MOBID-2 = Mobilization-Observation-Behavior-Intensity-Dementia-2 Pain Scale, MMSE = Mini-Mental State Examination).

Measurements

In both studies, sleep was measured with *Actiwatch Spectrum (Philips Respironics)* for seven consecutive days.

NH patients may be quite inactive and in order to enhance the possibility that movement would be detected we placed the actigraphs on the patients' dominant wrist. Prior studies have found no discrepancy between data gathered from actigraphs placed on different locations (Sadeh et al., 1994; Jean-Louis et al., 1997). To enable better scoring of the actual time patients spent in bed, NH staff was instructed to register bedtimes and rise times by pushing the event button on the actigraph (light off at night and light on in the morning). Instructions were given both verbally and on a written instruction that was placed above the nightstand in the patients' rooms and in the call room.

The *Actiware 6 (Respironics)* scoring program and validated algorithm was used for sleep/wake scoring. An actigraph consists of an accelerometer and memory storage (Sivertsen et al., 2006). Based on differences in movements associated with wakefulness and sleep, an estimate of sleep-wake schedules is provided (Sivertsen et al., 2006). We used medium sensitivity since this is most commonly used., and sleep/waking status was determined for each one-minute epoch. A skilled technician scored all activity protocols. A standardized hierarchical approach was applied to set rest intervals for the actigraphy data, using a) event markers when possible; or b) light and activity data; or c) light or activity data. If there was clear differentiation between active and rest periods, alternatives b) and c) were implemented. If there was no such clear differentiation, the actigraphy protocol was excluded. In the main part of the DEP.PAIN.DEM study, 162 patients were enrolled (Erdal et al., 2018). However, 7 patients had Parkinson's disease, 11 did not consent to wear an actigraph, 8 patients removed the actigraph and 30 were excluded for other reasons (missing data, malfunctioning actigraphs, etc.) and were thus excluded in the actigraph sub-project. As a result, 106 were included in the actigraph subproject in the DEP.PAIN.DEM -study. 95 of these patients had valid MMSE measurements and were thus included in the present study. In the COSMOS study the actigraphy subproject included 107 patients, 24 of whom were excluded due to actigraph malfunction or because of missing data. Of these 46 had dementia according to the MMSE measurements and were thus included in the final sample. The following parameters were derived from actigraphy measurements: total sleep time (TST, min), time in bed (TiB, hrs:min), sleep efficiency (SE,% [TST/TiB]*100), sleep onset latency (SOL, min), wake after sleep onset (WASO, min), early morning awakening (EMA, min) and day time total sleep time (DTS, min). DTS is a measure of sleep during daytime (from light on in the morning to lights off at night) and TST is a measure of sleep during nighttime (from light off in the night to lights on in the morning).

We used the validated CSDD to measure depression (Barca et al., 2010). The CSDD consists of 19 items assessing five domains of depression (mood, behavioral disturbances, physical signs, cyclic functions and ideational disturbances). A cut-off

point of 8/9 has demonstrated the best accuracy for diagnosing depression, ≥11 corresponds with severe depression according to the ICD-10 criteria (Barca et al., 2010). We used the following cut-offs in classifying the categorical variables: no depression = CSDD ≤ 6, moderate depression = 7 ≤ CSDD ≤ 10, severe depression = CSDD ≥ 11 (Barca et al., 2010).

Cognitive function was assessed using the validated MMSE (Perneczky et al., 2006). The MMSE is a cognitive screening test with a 30-point scale consisting of 20 tasks, which was developed to differentiate potential dementia from normal functioning. In the present study, we used the following cut-offs: a score from 0 to 10 represents severe dementia, a score from 11 to 20 represents moderate dementia, a score from 21 to 25 represents mild cognitive impairment, and a score from 26 to 30 represents no dementia (Perneczky et al., 2006).

To measure pain, we used the Mobilization-Observation-Behavior-Intensity-Dementia-2 Pain Scale (MOBID-2), a validated staff-administered instrument (Husebo et al., 2010). The instrument provides a total score based on observations ranging from 0 to 10, in which 10 represents the worst possible pain. In line with previous research, a cut-off of ≥3 was used to indicate clinically relevant pain (Husebo et al., 2007, 2014).

Use of the following medications was registered based on daily prescriptions registered in the patient health records: N02A (opioids), N02B (other analgesics), N05C (hypnotics and sedatives) and N06A (antidepressants). Patients were registered categorically as users or non-users within each ATC group.

Statistical Analyses

Descriptive statistics (means, standard deviations and percentages) were calculated for the full sample (**Table 1**) and for the DEP.PAIN.DEM dataset and the COSMOS dataset separately (**Table 2**). In addition, we conducted independent samples *t*-tests to investigate if there were any statistically significant differences in relevant characteristics between the respondents in the two studies. Sleep characteristics were calculated for the full sample, for patients with and without pain as measured with MOBID-2, for patients with different degrees of depression according to the CSDD, and with different degrees of cognitive function according to the MMSE. We also conducted independent samples *t*-tests to investigate if there were any statistically differences between any of the different sleep parameters regarding these categories (pain/no pain, moderate dementia/severe dementia and no depression/moderate depression versus severe depression, **Table 3**).

Two-step hierarchical multiple regression were conducted to investigate how the different sleep parameters (total sleep time, sleep efficiency, sleep onset latency, wake after sleep onset, early morning awakening, time in bed and daytime total sleep time) correlated with varying levels of pain, depression and dementia in NH patients (see **Table 4**). Multicollinearity tests using variance inflation factor showed no severe correlation between independent variables that warrant corrective measures These variables were entered in the first step of the hierarchical regressions. In the second step, we adjusted for the use of analgesics, antidepressants, sedative-hypnotics and opioids. These variables were implemented in the regression models to investigate their potential effect on the associations between the main variables of interest. We used categorical variables with the cut-off points described above for pain, depression and dementia. In addition, we include age and gender in both steps. We regarded $p < 0.05$ as statistically significant in all analyses.

TABLE 2 | Descriptive statistics for age and CSDD, MOBID-2, and MMSE scores, comparing data from the DEP.PAIN.DEM and COSMOS studies.

	DEP.PAIN.DEM (*n* = 95)	COSMOS (*n* = 46)	*P*
Age (mean,SD)	85.6 (7.5)	87.6 (7.6)	0.13
CSDD (mean, SD)	11.1 (3.4)	5.5 (5.4)	0.00
MOBID-2 (mean, SD)	2.8 (2.2)	2.3 (2.4)	0.25
MMSE (mean, SD)	7.6 (6.0)	11.2 (4.5)	0.00

Descriptive statistics for the DEP.PAIN.DEM dataset and the COSMOS dataset. Independent samples t-test show statistically significant differences between the CSDD and MMSE scores.

RESULTS

Mean age in the total sample was 86.2 years and 76.3% were female (see **Table 1** for the number of observations for the different variables). The mean CSDD, MOBID-2, and MMSE scores were 9.5 (SD 4.7), 2.6 (SD 2.3), and 8.8 (SD 5.8), respectively. The patients from the DEP.PAIN.DEM trial had significantly higher depression and lower MMSE mean scores than the patients in the COSMOS trial (**Table 2**). In the total sample, 46.8% of the patients were prescribed non-opioid analgesics, 27.7% were prescribed sedative-hypnotics, 47.5% were prescribed antidepressants and 17.7% were prescribed opioids (see **Table 5**). **Table 4** reports sleep characteristics for the full sample (Panel A), for those with and without pain (Panel B), for different levels of depression (Panel C), and for various levels of cognitive impairment (Panel D).

We comment on significant associations between the predictors and the dependent variables for all models that are reported in **Table 4**, but note that some of the regression models are not statistically significant. The hierarchical regression predicting TST showed that being in pain was associated with more TST, while more severe depression was associated with less TST (**Table 4, Panel A**). The regression predicting SE showed that being in pain was associated with higher SE (**Table 4, Panel B**). There were no significant results in the regression predicting SOL (**Table 4, Panel C**). The linear regression predicting WASO (**Table 4, Panel D**) showed that more severe dementia and pain were both associated with more WASO. The regression predicting EMA showed no significant results (**Table 4, Panel E**). The regression predicting DTS showed that being in pain was associated with more DTS and that higher depression scores were associated with less DTS. The final regression predicting TiB showed that more severe dementia was associated with more TiB. More severe depression was associated with less TiB (**Table 4, Panel G**).

TABLE 3 | Panel A: Sleep outcomes for the full sample, *n* = 141 (mean, SD)

TST (min)	516.3 (127.8)
SE (%)	70.2 (14.9)
SOL (min)	39.4 (51.6)
WASO (min)	138.8 (71.6)
EMA (min)	39.3 (44.3)
DTS (min)	210.3 (116.3)
TiB (hrs:min)	12:14 (1:14)

The following abbreviations are used: TST = total sleep time, SE = sleep efficiency, SOL = sleep onset latency, WASO = wake after sleep onset, EMA = early morning awakening, DTS = daytime total sleep time, TiB = time in bed. The same abbreviations apply for all panels below.

TABLE 3 | Panel B: Sleep outcomes for patients with/without pain, *n* = 121 (mean, SD)

	No pain (*n* = 61)	Pain (*n* = 60)	*p*
TST (min)	489.0 (101.0)	542.9 (148.0)	**0.046**
SE (%)	67.6 (13.1)	73.2 (16.8)	**0.025**
SOL (min)	37.5 (41.6)	37.7 (61.5)	0.435
WASO (min)	156.1 (76.1)	123.3 (65.0)	**0.020**
EMA (min)	43.5 (40.2)	33.5 (42.0)	0.190
DTS (min)	181.3 (98.4)	239.8 (131.6)	**0.003**
TiB (hrs:min)	12:07 (1:16)	12:17 (1:10)	0.916

TABLE 3 | Panel C: Sleep outcomes for patients with degrees of depression, *n* = 133 (mean, SD)

	No depression (*n* = 26)	Moderate depression (*n* = 55)	Severe depression (*n* = 52)	*p*
TST (min)	548.5 (113.5)	521.9 (142.8)	497.7 (119.0)	0.985
SE (%)	72.9 (14.6)	71.5 (16.7)	67.9 (13.0)	0.830
SOL (min)	35.7 (47.5)	39.1 (62.1)	43.2 (44.2)	0.555
WASO (min)	138.3 (90.7)	127.5 (63.8)	150.1 (70.1)	0.281
EMA (min)	33.4 (32.3)	37.9 (48.2)	39.9 (42.8)	0.446
DTS (min)	265.5 (118.0)	211.0 (116.0)	193.4 (109.7)	0.343
TiB (hrs:min)	12:35 (1:05)	12:07 (1:08)	12:11 (1:25)	0.417

No depression = CSDD $<$ 6, moderate depression = 7 $<$ CSDD $<$ 10, severe depression = CSDD $\geq$ 11.

TABLE 3 | Panel D: Sleep outcomes for patients with different levels of dementia, *n* = 141 (mean, SD).

	Moderate dementia (*n* = 64)	Severe dementia (*n* = 77)	*p*
TST (min)	516.0 (113.6)	516.6 (139.2)	0.980
SE (%)	73.0 (11.9)	67.9 (16.8)	**0.039**
SOL (min)	32.0 (33.7)	45.6 (62.3)	0.101
WASO (min)	121.9 (50.3)	152.8 (83.1)	**0.007**
EMA (min)	34.5 (35.8)	43.4 (50.1)	0.224
DTS (min)	200.8 (114.5)	218.3 (117.9)	0.376
TiB (hrs:min)	11:45 (1:14)	12:38 (1:05)	**0.000**

No dementia = MMSE $\geq$ 26, Mild dementia = MMSE score from 21 $\leq$ MMSE $\leq$ 25 to $\geq$ 25, Moderate dementia = MMSE score from 11 $\leq$ MMSE $\leq$ 20, Severe dementia = MMSE score MMSE $\leq$ 10.

In the second step of the hierarchical regressions, we adjusted for the use of analgesics, antidepressants, sedative-hypnotics and opioids. In all the regressions, the results reported above held when adjusting for the use of these medications. In addition, we noted that in the regression predicting DTS, the negative association between the use of sedatives and DTS was only marginally insignificant ($p = 0.051$) (**Table 4, Panel F**). Furthermore, in the regression predicting TiB, the use of sedatives was associated with less TiB (**Table 4, Panel G**).

In order to correct for multiple comparisons, we conducted False Discovery Rate corrections. Overall, the results largely held when taking these corrections into account. The exception was that the significant association between depression and TST became insignificant ($p = 0.034$ with a corrected threshold of $p = 0.021$).

DISCUSSION

Contrary to our hypotheses, NH patients with more severe pain and dementia had longer total sleep time and slept more during daytime, which indicates that NH patients with dementia and pain sleep more. Furthermore, their sleep efficiency was higher, indicating that the patients had more sleep within the time they spent in bed. In line with our hypotheses, our results showed that more severe dementia was associated with more time spent awake at night. Furthermore, people with more severe dementia spent more time in bed and people with more severe depression slept less at daytime and had less total sleep time. In addition, when adjusting for the use of medications, we found that

TABLE 4 | hierarchical regression models for various sleep parameters, with and without adjusting for medication use.

Panel A: Hierarchical regression models predicting total sleep time (TST) with and without adjusting for medication use.

		Unstandardized coefficients		Standardized coefficients					
Step	**Predictor**	**B**	**SE**	**β**	**p**	**R^2**	**R^2 change**	**F**	**p**
1						0.095	0.095	2.24	0.056
	Pain	63.017	24.286	0.243	**0.011**				
	Depression	−36.388	16.941	−0.209	**0.034**				
	Dementia	8.307	25.043	0.032	0.741				
	Age	0.347	1.622	0.021	0.831				
	Gender	22.425	29.268	0.074	0.445				
2						0.147	0.052	1.96	0.052
	Pain	60.038	24.207	0.232	**0.015**				
	Depression	−34.612	17.183	−0.198	**0.047**				
	Dementia	3.150	25,756	0.012	0.903				
	Age	0.649	1.613	0.039	0.688				
	Gender	14.843	29.346	0.049	0.614				
	Analgesics	−0.435	24.880	−0.002	0.986				
	Sedatives	−55.265	29.105	−0.187	0.060				
	Antidepressants	22.888	24.473	0.088	0.352				
	Opioids	53.581	32.651	0.158	0.104				

The table reports hierarchical regression models. Step 1 reports the correlates pain, depression, dementia, age, and gender. Step 2 also adjusts for analgesics, sedatives, antidepressants, and opioids. For unstandardized coefficients, B and SE signifies beta values and standard errors. For standardized coefficients, β and p signifies beta values and p values, respectively. F signifies the F value from statistical tests and p value associated with the test. The same information applies to all other panels below. Bold values indicate p-values < 0.05.

TABLE 4 | Panel B: Hierarchical regression models predicting sleep efficiency (SE) with and without adjusting for medication use.

		Unstandardized coefficients		Standardized coefficients					
Step	**Predictor**	**B**	**SE**	**B**	**p**	**R^2**	**R^2 change**	**F**	**p**
1						0.098	0.098	2.296	0.050
	Pain	6.706	2.821	0.223	**0.019**				
	Depression	−2.388	1.968	−0.118	0.228				
	Dementia	−5.299	2.909	−0.174	0.071				
	Age	−0.011	0.188	−0.006	0.954				
	Gender	3.503	3.400	0.099	0.305				
2						0.117	0.020	1.507	0.155
	Pain	6.438	2.865	0.214	**0.027**				
	Depression	−2.262	2.034	−0.111	0.268				
	Dementia	−5.484	3.048	−0.181	0.075				
	Age	0.005	0.191	0.003	0.977				
	Gender	2.933	3.473	0.083	0.400				
	Analgesics	0.793	2.944	0.026	0.788				
	Sedatives	−3.150	3.444	−0.092	0.363				
	Antidepressants	1.189	2.896	0.039	0.682				
	Opioids	4.852	3.864	0.123	0.212				

Bold values indicate p-values < 0.05.

TABLE 4 | Panel C: Hierarchical regression models predicting sleep onset latency (SOL) with and without adjusting for medication use.

		Unstandardized coefficients		Standardized coefficients					
Step	**Predictor**	**B**	**SE**	**β**	**p**	**R^2**	**R^2 change**	**F**	**P**
1						0.024	0.024	0.520	0.760
	Pain	−2.236	10.225	−0.022	0.820				
	Depression	−1.881	7.132	−0.027	0.793				
	Dementia	15.290	10.543	0.145	0.150				
	Age	−0.209	0.683	−0.031	0.761				
	Gender	−6.753	12.322	−0.055	0.585				
2						0.046	0.022	0.552	0.833
	Pain	−1.950	10.375	−0.019	0.851				
	Depression	−1.369	7.365	−0.019	0.853				
	Dementia	18.519	11.039	0.175	0.096				
	Age	−0.284	0.691	−0.042	0.682				
	Gender	−4.465	12.578	−0.036	0.723				
	Analgesics	−8.861	10.664	−0.084	0.408				
	Sedatives	13.652	12.474	0.114	0.276				
	Antidepressants	−7.538	10.489	−0.072	0.474				
	Opioids	−6.741	13.994	−0.049	0.631				

TABLE 4 | Panel D: Hierarchical regression models predicting wake after sleep onset (WASO) with and without adjusting for medication use.

		Unstandardized coefficients		Standardized coefficients					
Step	**Predictor**	**B**	**SE**	**β**	**p**	**R^2**	**R^2 change**	**F**	**p**
1						0.127	0.127	3.093	0.012
	Pain	−37.192	13.432	−0.255	**0.007**				
	Depression	6.513	9.370	0.066	0.488				
	Dementia	36.154	13.851	0.246	**0.010**				
	Age	0.854	0.897	0.091	0.343				
	Gender	−8.130	16.188	−0.048	0.617				
2						0.152	0.025	2.038	0.042
	Pain	−36.010	13.590	−0.247	**0.009**				
	Depression	5.077	9.647	0.052	0.600				
	Dementia	31.717	14.459	0.216	**0.031**				
	Age	0.907	0.905	0.096	0.319				
	Gender	−7.616	16.475	−0.045	0.645				
	Analgesics	−0.880	13.968	−0.006	0.950				
	Sedatives	−6.878	16.339	−0.041	0.675				
	Antidepressants	8.648	13.739	0.059	0.530				
	Opioids	−24.746	18.330	−0.130	0.180				

Bold values indicate p-values < 0.05.

patients who were prescribed sedative-hypnotic medications spent less time in bed.

To the best of our knowledge, this study is the first to explore how different levels of pain and depression correlate with a wide set of actigraphy-measured sleep parameters in NH patients with dementia (see **Table 4**). The results are of key importance since they provide new and valuable insight on the relationship between NH patients' sleep, including sleep during daytime, and its associations with different levels of pain and depression. In light of previous research that has demonstrated that pain conditions are commonly associated with worse sleep in people without dementia (e.g., Andersen et al., 2018), the results from the present study are particularly interesting.

The results from the present study were unexpected. A potential explanation for these results could be that patients in pain receive more analgesics, antidepressants, sedative-hypnotics or opioids and thereby experience more sedation as an intended or adverse treatment effect. In turn, sedation and lack of movement could be recorded as sleep using actigraphy. However, we controlled for the use of different medications, rendering this explanation unlikely.

Another potential explanation of these somewhat surprising results may be that many older adults who experience chronic pain may develop behavior in which painful movements are avoided. This is known as the pain-avoidance effect (Vlaeyen and Linton, 2012; Achterberg et al., 2013). If this

TABLE 4 | Panel E: Hierarchical regression models predicting early morning awakening (EMA) with and without adjusting for medication use.

		Unstandardized coefficients		Standardized coefficients					
Step	**Predictor**	**B**	**SE**	**β**	**p**	**R^2**	**R^2 change**	**F**	**P**
1						0.069	0.069	1.560	0.178
	Pain	−11.767	7.387	−0.152	0.114				
	Depression	4.197	5.153	0.080	0.417				
	Dementia	8.122	7.618	0.104	0.289				
	Age	−0.189	0.493	−0.038	0.703				
	Gender	−14.590	8.903	−0.161	0.104				
2						0.075	0.007	0.923	0.508
	Pain	−11.959	7.556	−0.154	0.117				
	Depression	3.926	5.364	0.075	0.466				
	Dementia	9.337	8.040	0.119	0.248				
	Age	0.228	0.503	−0.045	0.652				
	Gender	−13.902	9.160	−0.153	0.132				
	Analgesics	0.981	7.766	0.013	0.900				
	Sedatives	6.976	9.085	0.079	0.444				
	Antidepressants	−0.1022	7.639	−0.013	0.894				
	Opioids	0.289	10.192	0.003	0.977				

TABLE 4 | Panel F: Hierarchical regression models predicting daytime total sleep time (DTS) with and without adjusting for medication use.

		Unstandardized coefficients		Standardized coefficients					
Step	**Predictor**	**B**	**SE**	**β**	**p**	**R^2**	**R^2 change**	**F**	**P**
1						0.169	0.169	4.261	0.001
	Pain	69.229	21.608	0.289	**0.002**				
	Depression	−49.988	15.272	−0.308	**0.001**				
	Dementia	31.684	22.409	0.131	0.160				
	Age	−0.311	1.455	−0.020	0.831				
	Gender	−31.897	26.025	−0.114	0.223				
2						0.205	0.036	2.891	0.004
	Pain	71.687	21.766	0.299	**0.001**				
	Depression	−44.710	15.652	−0.275	**0.005**				
	Dementia	25.192	23.223	0.105	0.281				
	Age	−0.052	1.457	−0.003	0.972				
	Gender	−39.097	26.257	−0.140	0.140				
	Analgesics	−0.492	22.312	−0.002	0.982				
	Sedatives	−51.510	26.053	−0.189	0.051				
	Antidepressants	−19.086	22.008	−0.080	0.390				
	Opioids	12.829	29.960	0.040	0.428				

Bold values indicate p-values < 0.05.

interpretation is valid, it would imply that the patients may in fact not be sleeping but are lying still in order to avoid pain, and by extension this highlight that pain assessment is fundamental. When a patient is lying still, it may be interpreted as sleep when measured with actigraphy. The fact that DTS was also higher in NH patients with pain and dementia may indicate that painful movements/activity were avoided at daytime as well. At the same time, it is noteworthy that previous research shows more agitated behavior among patients with mild to moderate pain (Husebo et al., 2014). In Blytt et al. (2018a), which is based on sleep-related data from the DEP.PAIN.DEM trial, we found that in the full sample, pain treatment improved sleep as measured with actigraphy compared to placebo after one week with pain treatment (paracetamol and buprenorphine). The results from the DEP.PAIN.DEM trial do not allow differentiation between sedation as a side-effect of the administered treatment and actual sleep. Importantly, we found no long-term effect of pain treatment on sleep (Blytt et al., 2018b). In the present study, we registered the use of different medications that can lead to sedation as a side-effect. However, this did not affect the results, and the only finding related to medication use was that the use of sedatives was associated with less time spent in bed.

Based on the present findings, we argue that there is a need for studies examining more thoroughly and systematically the association between pain, depression and sleep. It is furthermore important to acknowledge that it is very difficult to

TABLE 4 | Panel G: Hierarchical regression models with and without predicting time in bed (TiB) adjusting for medication use.

		Unstandardized coefficients		Standardized coefficients					
Step	**Predictor**	**B**	**SE**	**β**	**p**	**R^2**	**R^2 change**	**F**	**P**
1						0.228	0.228	6.261	0.00
	Pain	618.941	765.203	0.070	0.420				
	Depression	−1651.064	533.769	−0.277	**0.003**				
	Dementia	3978.952	789.043	0.447	**0.000**				
	Age	0.48.800	51.095	0.086	0.955				
	Gender	−613.861	922.179	−0.059	0.507				
2						0.313	0.085	5.169	0.00
	Pain	511.950	740.930	0.058	0.491				
	Depression	−1611.413	525.942	−0.271	**0.003**				
	Dementia	3698.456	788.338	0.415	**0.000**				
	Age	62.678	49.355	0.110	0.207				
	Gender	−869.196	898.208	−0.084	0.335				
	Analgesics	−449.644	761.529	−0.050	0.556				
	Sedatives	−2416.144	890.838	−0.240	**0.008**				
	Antidepressants	1315.321	749.052	0.149	0.082				
	Opioids	1555.759	999.381	0.135	0.123				

Bold values indicate p-values < 0.05.

ascertain pain in people with dementia. The use of observation-based pain instruments applied by a proxy-rater who is familiar with the patients is a common method to assess pain in this population. Since a patient's behavior is typically changed in reaction to experiencing pain, it is essential to examine pain expressions in relation to the person's usual behavior (Hadjistavropoulos et al., 2014). Most tools used for classifying pain in NH patients are developed against this backdrop (Corbett et al., 2012; Flo et al., 2014; Lichtner et al., 2014). The MOBID-2 instrument has good validity, interrater and test-retest reliability, and responsiveness to change has been shown (Husebo et al., 2014). Yet, pain is a complex phenomenon, and we cannot be sure that the patient is experiencing pain, and in what intensity, location and duration.

Previous research indicates that increased wakefulness and fragmented sleep at night are common sleep problems in patients with dementia (McCleery et al., 2016). Our results showed that the patients with more severe dementia spent more time awake during the night. Sleep problems in patients with dementia may be a result of neural loss in the suprachiasmatic nuclei and/or other neuropathological changes to sleep-wake circuits (Swaab et al., 1985; Van Someren, 2000). The results of the present study indicate that as dementia progresses, sleep problems may be exacerbated. While more severe dementia was also associated with spending more time in bed, we cannot tell whether this is a result of the patient's own wishes, or NH routines.

Previous studies investigating sleep and depression have found that 60 to 80% of depressed adults and older adults report having difficulty falling or staying asleep or being tired the next day (Almeida and Pfaff, 2005; Ancoli-Israel, 2009). Furthermore, depression in people with dementia is associated with lack of initiative and reduced memory, and there is thus overlap between the core symptoms of dementia and depression (Brailean et al., 2016). The present study indicates that the patients with more severe depression was somewhat more active as we found that they slept less during daytime, had lower total sleep time and spent less time in bed. A potential explanation for this could be agitation – a symptom often seen in people with dementia and depression (Husebo et al., 2014).

TABLE 5 | Descriptive statistics for the use of analgesics, sedatives, antidepressants and opioids.

Type of medication	Percent of patients with prescriptions%	Number of observations
Analgesics (without opioids)	46.8	141
Sedatives	27.7	141
Antidepressants	47.5	141
Opioids	17.8	141

As pointed out by McCleery et al. (2016), there is a lack of evidence regarding drug treatment of sleep problems in people with dementia, and this is thus highly needed. However, the present study was not designed to look at the effect of sedatives on sleep in this population. Therefore, we cannot be sure if the patients receiving sedatives (27.7% of the total sample) were systematically different in other ways that can explain these results.

Limitations

This study has several limitations. Due to the cross-sectional design of the study, we cannot draw any causal conclusions. Furthermore, the COSMOS and the DEP.PAIN.DEM trials have somewhat different inclusion and exclusion criteria. Importantly,

the DEP.PAIN.DEM study, from which most of the data is derived, had depression and dementia as inclusion criteria (CSDD $\geq$ 8, MMSE $\leq$ 20). As the results from the independent samples *t*-tests showed, the patients from the DEP.PAIN.DEM trial had significantly higher depression scores and lower MMSE scores. This implies that the patients from the two trials may not be comparable, which may affect generalizability. The results from the present study may arguably be generalized to NH patients with dementia and probable symptoms of depression.

To measure sleep in the NH setting is challenging due to patients' reduced ability to give valid self-report (Blytt et al., 2017). Therefore, objective measurement using actigraphy or use of proxy-rater assessment tools (where health personnel or relatives answer on behalf of the patient) are the current alternatives. Both have several limitations. When using actigraphy, immobility is recorded as sleep, which makes it difficult to interpret the results. Furthermore, previous research has shown that SOL has been particularly difficult to ascertain (Marino et al., 2013). When proxy-rater assessment tools are evaluated, they are often compared with actigraphy as the gold standard (Blytt et al., 2017; Hjetland et al., 2020). This indicates that actigraphy is considered a better method for measuring sleep in this population. When sleep is evaluated using proxy-rater assessment tools like the *Neuropsychiatric Inventory* and the *Cornell Scale for Depression in Dementia*, raters report significantly fewer sleep problems compared to actigraphy (Blytt et al., 2017). This highlights that measuring sleep in this population is difficult. However, individual sleep diaries – addressed by the patient's primary nurse – would have strengthened the study.

It is furthermore important to note that we have just conducted a coarse mapping of the medications; N02A (opioids), N02B (other analgesics), N05C (hypnotics and sedatives), and N06A (antidepressants). However, effects such as sedation may differ within the different drug groups and according to the prescribed dose. Additionally, we did not assess whether the daily prescriptions were in fact administered to the patient. Only daily prescribed treatments were recorded we did not control for the use of as-needed treatment.

Another limitation in the present study was that we did not have complete datasets for all the different variables (for an overview of missing data, see the number of observations in **Table 1**). We cannot be sure whether the results would be different if we had complete data for all the relevant parameters investigated.

Together, the results of the present study revealed new and interesting insights on the relationship between sleep, pain and depression in a fragile patient group. Importantly, the results indicated that being in pain was associated with more sleep as measured with actigraphy, also when controlling for use of potentially sleep-enhancing medications like sedative-hypnotics, analgesics, opioids and antidepressants. Future research should focus on further investigating the mechanisms underlying these results.

DATA AVAILABILITY STATEMENT

The datasets generated for this study will not be made publicly available in order to maintain confidentiality of the study participants. Requests to access the datasets should be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by The Regional Ethics Committee REC-West 2013/1474 and REC-West 2013/1765. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

BH is the primary investigator of the COSMOS and the DEP.PAIN.DEM trial from which the data originates. KB designed the study, analyzed the data, and wrote the manuscript. BB, AE, EF-G and BH designed the study, helped with the analysis of the data, and wrote the manuscript. All authors have read and approved the manuscript prior to publication.

ACKNOWLEDGMENTS

We thank the patients, their relatives, and the nursing home staff for their willingness and motivation, which made this work possible. BH would like to thank the GC Rieber Foundation and the Norwegian Directorate of Health for supporting our work at the Centre for Elderly and Nursing Home Medicine, University of Bergen, Norway. The funders were not involved in the study design, collection, analysis, interpretation of data, the writing of this article or the decision to submit it for publication. A special thanks to Andrea Rørvik Marti for scoring the actigraphy data. KB had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses. A conference paper based on the same data material has been previously published as a poster at the Nordic Sleep Conference in 2019, KB, EF-G, AE, BB, and BH: "Pain, depression and their association with sleep in nursing home patients with advanced dementia – a cross-sectional study."

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychology

ORIGINAL RESEARCH
published: 07 May 2021
doi: 10.3389/fpsyg.2021.668930

Good Sleep Quality Improves the Relationship Between Pain and Depression Among Individuals With Chronic Pain

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Individuals with chronic pain often experience co-existing sleep problems and depression-related states. Chronic pain, sleep problems, and depression interrelate, and have been shown to exacerbate one another, which negatively impacts quality of life. This study explored the relationships between pain severity, pain interference, sleep quality, and depression among individuals with chronic pain. Secondly, we tested whether sleep quality may moderate the relationship between pain and depression. A cross-sectional survey was completed by 1,059 adults with non-malignant chronic pain conditions (M^{age} 43 years, 88% identified as women) and collected measures related to pain severity, pain interference, sleep quality, and depression. Multiple regression analyses found that pain severity, pain interference, and sleep quality are all significantly associated with depression. Secondly, moderated regression analyses revealed that sleep quality moderates the relationship between pain interference and depression among individuals with chronic pain such that good sleep quality attenuates the effect of pain interference on depression, and poor sleep quality amplifies the effect of pain interference on depression. These findings suggest that sleep quality may be a relevant therapeutic target for individuals with chronic pain and co-existing depression.

Keywords: chronic pain, sleep quality, depression, moderation, pain interference, pain severity

OPEN ACCESS

Edited by:
Federica Scarpina, Istituto Auxologico Italiano (IRCCS), Italy

Reviewed by:
Axel Steiger, Ludwig Maximilian University of Munich, Germany
Somayyeh Mohammadi, University of British Columbia, Canada
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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *17 February 2021*
Accepted: *09 April 2021*
Published: *07 May 2021*

Citation:
Zambelli Z, Halstead EJ, Fidalgo AR and Dimitriou D (2021) Good Sleep Quality Improves the Relationship Between Pain and Depression Among Individuals With Chronic Pain. Front. Psychol. 12:668930. doi: 10.3389/fpsyg.2021.668930

INTRODUCTION

Chronic pain conditions are prevalent and burdensome across the globe. Depression is commonly reported among individuals with non-malignant chronic pain conditions which leads to impaired functioning and poor quality of life (IsHak et al., 2018). Estimates for depression among people with chronic pain have been reported between 20% and 60%, and evidence shows these individuals report a higher prevalence of depressive symptoms compared to a general population (Fishbain et al., 1997; Breivik et al., 2006; Rayner et al., 2016). Research has implicated several predictors of depression among this population including pain severity, pain interference, and illness perception (Costa et al., 2016). Furthermore, the relationship between chronic pain and depression may be bidirectional and lead to poorer health-related quality of life, and in some cases, longer duration of physical and psychological symptoms (IsHak et al., 2018). Evidence has also suggested that individuals with chronic pain and comorbid depression experience higher rates of physical, mental, and social dysfunction, and poorer response to pain treatments than chronic pain

individuals without co-existing depression (Elliott et al., 2003; Holmes et al., 2013; Rayner et al., 2016). The co-existence of depression among chronic pain individuals further impacts the economy in addition to an individual's quality of life. Previous research conducted within NHS services found that among individuals with chronic pain, those who also met criteria for depression were more likely to be unable to work due to ill health, report higher levels of absenteeism, and that average health care costs for this group were higher compared to those without depression (Rayner et al., 2016). Notably, individuals from lower income backgrounds have been found to have lower participation rates in healthcare screenings which further compounds this issue. This may be due to having more difficulty understanding and applying health information, which over time contributes to higher healthcare costs (Chan et al., 2018; Svendsen et al., 2020).

Sleep problems are a significant complaint among individuals with chronic pain, with estimates of prevalence rates as high at 88% (Smith et al., 2001). These issues have been observed across different pain groups including musculoskeletal conditions, fibromyalgia, chronic headaches, and neuropathic pain conditions (Mathias et al., 2018). The most common sleep issues are insomnia (characterized by difficulty initiating sleep, frequent night awakenings, and early morning awakening), restless leg syndrome, and sleep disordered breathing (Call-Schmidt and Richardson, 2003; Mathias et al., 2018). Furthermore, the literature examining the relationship between pain and sleep problems points to a bidirectional relationship, with evidence to suggest that pain is predictive of sleep disturbance, and equally, poor sleep quality exacerbates pain outcomes, particularly among chronic pain individuals (Smith and Haythornthwaite, 2004; Andersen et al., 2018). In addition to pain, sleep disturbance is related to mood disorders. In particular, disturbed sleep is cited as a core symptom of depression, presenting in over 90% of clinically diagnosed individuals, and is included as a diagnostic criterion for Major Depressive Episode (MDE) in the Diagnostic and Statistical Manual for Mental Disorders (DSM-5) (Murphy and Peterson, 2015; Tolentino and Schmidt, 2018). Despite this, longitudinal research has established poor sleep as an independent risk factor for depression, indicating that the relationship between sleep and depression is likely reciprocal (Buysse et al., 2008; Jaussent et al., 2011; McCrae et al., 2016). Experimental studies have suggested that sleep may impact depression-related states through various mechanisms, including increased negative reactivity to stressful stimuli, amplifying negative mood, in addition to impairing frustration tolerance and suppressing emotional intelligence (Tempesta et al., 2010; Killgore, 2013; Finan et al., 2015; Killgore et al., 2017). In all, the evidence points to complex and intertwined relationships between pain, sleep, and depression-related states, and a limited number of studies have attempted to elucidate these further through theoretical and experimental studies.

Firstly, emerging science has implicated the role of neurobiological mechanisms which may explain the co-existence of chronic pain, poor sleep, and depression-related state. Notably, the role of proinflammatory cytokines have been shown to modulate spontaneous nociceptor activity and increase stimulus sensitivity which may lead to persistent pain states. Increased cytokine levels could also promote further secretion of new cytokines which consequently influence serotonergic neurotransmission implicated in the pathophysiology of depression. Finally, there is evidence that specific proinflammatory cytokines, namely interleukin-1 (IL-1) and tumor necrosis factor (TNF-α) act as sleep regulatory substances (Boakye et al., 2016). A recent study conducted by Rosseland et al. (2018) found that inducing sleep fragmentation led to increased pain sensitivity in a cohort of healthy adults, compared to one night of undisturbed sleep. In this study, researchers also tested whether an induced mood state (akin to depression-related states) would impact pain sensitivity and whether induced sleep and mood would interact to influence pain. Results showed neither induced negative mood on its own nor the interaction between induced sleep fragmentation and induced negative mood had any significant effect on pain. Furthermore, a 2-year longitudinal study demonstrated that prior pain was predictive of subsequent sleep disturbance among individuals with rheumatoid arthritis, and that those individuals with high pain levels and high sleep disturbance were at greater risk of developing symptoms of depression over time (Nicassio and Wallston, 1992). In another example, depression-related states were shown to mediate the relationship between poor sleep and pain interference (Ravyts et al., 2019).

Studies such as these have contributed toward developing evidence-based interventions and screening measures for chronic pain populations, however, there is still a need to examine these relationships further given the high prevalence of both sleep disturbance and depression in this group. Furthermore, it is important to note the role socio-demographic factors play on accessing screening and treatments to improve physical and psychological health outcomes. Socio-economic status (SES) is a crucial determinant of health and there is a need to measure SES more frequently in health and care research, particularly where chronic pain populations are concerned as many strategies to manage pain conditions rely on self-management approaches which are often negatively impacted by low SES (Marmot, 2017; Hardman et al., 2020).

Given the extent to which pain, sleep, and depression-related states co-exist, particularly among chronic pain populations, and the detrimental impact these have on individuals and society, elucidating the relationship between these factors could contribute toward improving outcomes for chronic pain individuals. In particular, this study sought to examine whether sleep quality acts as a moderator in the relationship between pain interference and severity, and depression, among a cohort of chronic pain individuals.

Study Aims and Hypotheses

There were two aims of this cross-sectional study:

(1) To establish whether pain interference, pain severity, and sleep quality are associated with depression, replicating previous research in this area
(2) To examine whether sleep quality acts as a moderator in the relationship between pain (interference and severity) and depression, among individuals with chronic pain.

We hypothesized that pain interference, pain severity, and sleep quality would be associated with depression. Secondly, we hypothesized that sleep quality would indeed moderate the relationship between pain (inference and severity) and depression, specifically that high levels of sleep quality would attenuate the impact of high pain levels on depression.

METHODS

Design

A cross-sectional survey was conducted between February and March 2020, before a government mandated lockdown to control the coronavirus pandemic. The survey was primarily hosted on Qualtrics (www.qualtrics.com), a survey management website, and paper copies were also available upon request to any potential participants unable to complete the survey via online means. This study was granted ethical approval by University College London, Institute of Education Ethics Committee. Participants were recruited through a social media campaign, and in collaboration with UK pain charities. Participants provided informed consent prior to completing the survey and did not receive compensation for taking part. Inclusion criteria for participants were adults aged 18 years and above, with a reported diagnosis of non-malignant chronic pain, and able to consent to participation of a survey study. Exclusion criteria were diagnoses of cancer-related chronic pain, and pain duration of <3 months.

Participants

A total of 1,234 adult participants with self-reported chronic pain fully or partially completed an online or paper survey relating to their pain management, sleep, and mental health. After cleansing the data for complete responses, 1,059 fully completed surveys were included in this study. The majority of participants identified as women (88%), had a mean age of 42.88 years (SD = 13.25 years), and were of white ethnic origin (94%). In addition, nearly all (98%) reported a diagnosis of chronic pain via a healthcare professional (HCP), compared to 2% who self-diagnosed. Participants were asked to report their primary chronic pain condition, which were defined using the International Classification of Diseases (ICD) 11th edition classification. Participants reported; Chronic Widespread Pain (CWP; 33%), Musculoskeletal (MSK; 35%), Headache and Orofacial (13%), Neuropathic (16%), and Visceral pain conditions (3%). Most participants reported using pain medication to manage their pain levels (91%) and over half reported their pain duration to be more than 10 years (57%). Finally, duration of sleep problems was more than 1 year for the majority of the group (87%). Participant characteristics are reported in **Table 1**.

TABLE 1 | Participant characteristics.

Variable	*n*	%
Age**	42.88	13.25
Gender		
Men	126	12
Women	933	88
Ethnicity		
White-any background	933	94
Black/Black British	6	1
Asian/Asian British	12	1
Mixed	25	2
Other	23	2
SEP		
Very low	59	6
Low	275	26
High	323	30
Very high	402	38
Primary pain condition		
Chronic widespread pain	354	33
Musculoskeletal	373	35
Headache and orofacial	133	13
Neuropathic	164	16
Visceral	35	3
Pain duration		
<1 year	29	3
1–3 years	104	10
3–5 years	95	9
5–10 years	221	21
>10 years	602	57
Unsure	8	0
Diagnosis		
HCP diagnosed	1,037	98
Self-diagnosed	22	2
Pain medication		
Yes	959	91
No	100	9
Sleep problem duration		
<1 year	127	13
≥1 year	839	87

***Age variable displays mean and standard deviation for a continuous variable.*

Measures

Participants were required to complete background questions in addition to three validated questionnaires to measure pain interference, pain severity, sleep quality, and depression.

Demographic Information

Participants were asked to report their diagnosis (self or via HCP) of non-malignant chronic pain. Demographic and socio-economic indicators included, age, gender, ethnicity, education attainment, employment status, household income, primary chronic pain condition, and pain medication status (see section Participants).

Pain

The Brief Pain Inventory (BPI) short form is a widely used self-report measure for clinical pain (Cleeland and Ryan, 1991). The BPI includes two subscales which rate severity of pain and the

degree to which pain interferes with common dimensions of feeling and function in the past 24 h. These are referred as (1) pain severity and (2) pain interference. Both subscales range from 0 to 10 with higher scores indicating higher levels of pain severity and pain interference. These scales have good internal consistency with Cronbach's alpha of 0.85 and 0.88 for the severity and interference scales, respectively (Tan et al., 2004).

Sleep Quality

The Pittsburgh Sleep Quality Index (PSQI) is a validated measure for sleep research and consists of 24 items (Buysse, 1989). The scale comprises seven components which measure (1) subjective sleep quality, (2) sleep latency, (3) sleep duration, (4) sleep efficiency, (5) sleep disturbance, (6) daytime dysfunction, and (7) sleep medication over the past month. Each component generates a score from 0 to 3 where higher scores indicate poorer sleep outcomes. A sum of the seven component scores can be used to generate a global PSQI score ranging from 0 to 21. A global score above five indicates poor sleep quality. The PSQI has been validated among individuals with chronic pain conditions with Cronbach's alpha scores above 0.7 (Nicassio et al., 2014).

Depression

Depression was measured using the Hospital Anxiety and Depression Scale (HADS). A 14-item validated measure designed to measure anxiety and depression symptoms during the past week (Zigmond and Snaith, 1983). It comprises of two subscales assessing anxiety (HADS–A) and depression (HADS–D). Items are rated on a four-point Likert scale (e.g., 0 = not at all to 3= most of time). Five items require reverse scoring. Scores for each item are summed for each subscale, scores above eight suggest anxiety and depression with thresholds described as scores between 0 and 8 = no symptoms, 8 and 10 = mild symptoms, 11 and 14 = moderate symptoms, 15 and 21= severe symptoms (Zigmond and Snaith, 1994; Stern, 2014). The HADS-D has been validated among individuals with chronic pain conditions with Cronbach's alpha scores of 0.8 (Turk et al., 2015).

Analyses

The final sample was reduced to 1,059 participants after removing participants with missing data for the pain, sleep, depression, and demographic variables. All analyses were conducted on this sample who had a fully completed data set. A variable was created to calculate socio-economic position (SEP) using education, employment, and household income (Halstead et al., 2018). Education attainment was split into 0 = secondary school education or below and 1 = higher ed, undergraduate, and postgraduate education, employment status was split 0 = not employed and 1 = employed full or part time, finally, household income was scored 0 = low income ≤£20,000 and 1 ≥£20,000 (Cribb et al., 2018). Total SEP was calculated by summing the scores of these three indicators from the dichotomous coding, where 0 = very low and 3 = very high SEP (see **Table 1**).

Normality tests were conducted on the four main variables (pain severity, pain interference, sleep quality, depression). Descriptive analyses examined the means, standard deviations, and minimum to maximum values across the main variables (pain interference, pain severity, sleep quality, and depression), and where possible, frequencies and percentages for clinical cut-offs across the sample. A simple regression looked at the association between the components of the sleep quality measure (PSQI) and depression (HADS-D). *T*-tests were conducted to examine whether there were any differences in pain, sleep, or depression scores based on gender, diagnosis type, and pain medication type. To avoid multicollinearity between pain interference and pain severity subscales, two linear regressions (model A: pain severity and model B: pain interference) examined the relationships of all predictor variables (pain severity, pain interference, sleep quality) and demographic indicators (age, gender, SEP, pain condition group) on depression. Significant associations between demographic variables and depression were then included in the following moderated regression models as covariates.

To examine sleep quality as a potential moderator, two moderated regression analyses were conducted. The "PROCESS" macro and customs dialogue box was installed into SPSS v. 26 to conduct moderated regression analyses (Hayes, 2017). In the first analysis (model 1), pain severity, sleep quality, and demographic covariates were entered as predictors along with an interaction term between pain severity and sleep quality. In the second analysis (model 2), pain interference, sleep quality, and demographic covariates were entered as predictor variables along with an interaction term between pain interference and sleep quality. Continuous predictor variables were mean centered in both models (i.e., the variable mean is subtracted from every value of the variable). **Figure 1** illustrates the moderated regression models.

RESULTS

Descriptive Statistics and Preliminary Analyses

The mean, standard deviation, minimum, and maximum scores for each measure are displayed in **Table 2**, as well as frequencies and percentages for clinical cut-offs, where available. A full range of scores were observed across all main variables, with the exception of sleep quality, where no participants scored between 0 and 2 which would indicate very good sleep quality. Further to this, only 3% of the sample scored within range for "good sleep quality," with 97% of participants in range for "poor sleep quality" based on scores above five (Buysse, 1989). Less than half the sample scored within "normal" range for depression (indicating no symptoms), and 63% scored within range for either "mild," "moderate," or "severe" depression symptoms (Stern, 2014).

Results of a simple regression to explore the associations between the seven components of the sleep quality measure and depression are displayed in **Table 3**: $R^2 = 0.22$, $F_{(7,1,051)} = 41.24$, $p \leq 0.001$. Subjective sleep quality $\beta = 0.11$, $p = 0.01$, daytime dysfunction $\beta = 0.24$, $p \leq 0.001$, and global sleep quality $\beta = 0.26$, $p = 0.05$ were positively and significantly associated with depression.

T-tests concluded there were no significant gender differences for pain or sleep outcomes, however it was found that men had

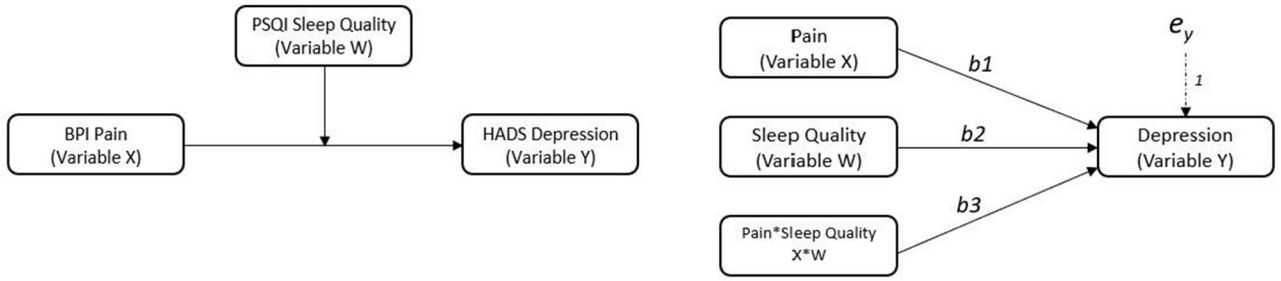

FIGURE 1 | Conceptual and statistical models showing sleep quality as a moderator on the relationship between pain and depression. Variable X is the predictor variable, variable W is the moderator, variable Y is the outcome.

TABLE 2 | Means, standard deviations, and minimum to maximum scores for all variables.

Variable	Subscale	Mean	*SD*	Min–Max
BPI pain				
	Pain interference	6.36	2.21	0–10
	Pain severity	5.46	1.86	0–10
PSQI sleep quality		13.89	3.79	2–21
HADS depression		9.19	4.44	0–21
PSQI cut-off		***N***	**%**	
	Good sleep quality	27	3	
	Poor sleep quality	1,032	97	
HADS-D cut-off				
	Normal	389	37	
	Mild	287	27	
	Moderate	246	23	
	Severe	137	13	

BPI, Brief Pain Inventory; PSQI, Pittsburgh Sleep Quality Index; HADS, Hospital Anxiety and Depression scale; Cut-offs provided for PSQI and HADS measures only.

TABLE 3 | Associations between seven PSQI components and global sleep quality score on depression.

PSQI component	Beta (β)	*p*
$R = 0.46, R^2 = 0.22, F = 41.24, p \leq 0.001$		
Subjective sleep quality	0.11	**0.01**
Sleep latency	0	0.99
Sleep duration	−0.08	0.27
Sleep disturbance	0.05	0.24
Sleep medication	−0.5	0.33
Daytime dysfunction	0.24	**<0.001**
Global sleep quality	0.26	**0.05**

Bold text displays results from the regression analysis.

slightly higher depression scores than women $t_{(1,057)} = 2.19$, $p = 0.03$, $d = 0.23$. Furthermore, there were no differences in pain severity, pain interference, or depression scores among formally diagnosed participants (via HCP) compared to self-diagnosed, and sleep quality scores were marginally higher (signifying poorer sleep quality) among those with a formal diagnosis compared to the self-diagnosed group $t_{(1,057)} = 2.00$, $p = 0.49$, $d = 0.42$. Finally, individuals taking pain medication in order to control pain symptoms, had statistically poorer sleep quality $t_{(1,057)} = -2.66$, $p = 0.008$, $d = 0.28$ and marginally higher depression $t_{(1,057)} = -1.93$, $p = 0.054$, $d = 0.20$ than individuals taking no pain medication.

When examining the linear regressions, model A revealed significant main effects of pain severity, sleep, SEP, and MSK pain on depression $R^2 = 0.20$, $F_{(8,1,050)} = 32.46$, $p = 0.001$. Model B revealed significant main effects of pain interference, sleep, gender, SEP, and chronic widespread pain on depression $R^2 = 0.29$, $F_{(8,1,050)} = 54.23$, $p = 0.001$. Non-significant variables were excluded from the subsequent moderated regression models.

TABLE 4 | Moderated multiple regression for pain severity and pain interference as predictor variables and sleep quality as moderator variable on depression.

	b	*t*	*p*
$R = 0.44, R^2 = 0.19, F = 50.75, p \leq 0.001$			
BPI pain severity	0.31	4.14	<0.001
PSQI sleep quality	0.34	9.45	<0.001
Pain severity * sleep quality	0.01	0.72	0.474
SEP	−0.74	−5.30	<0.001
MSK pain	−0.65	−2.50	0.013
$R = 0.54, R^2 = 0.29, F = 72.76, p \leq 0.001$			
BPI pain interference	0.77	12.8	<0.001
PSQI sleep quality	0.22	6.24	<0.001
Pain interference * sleep quality	0.03	2.20	0.028
Gender	−0.77	−2.14	0.033
SEP	−0.50	−3.84	<0.001
Chronic widespread pain	0.58	2.34	0.020

Bold text displays results from the moderated multiple regression analyses.

Moderation Regression Analyses

Moderated regression analyses were conducted to test whether sleep quality would moderate the relationships between pain severity and depression (model 1) and pain interference and depression (model 2), among individuals with chronic pain conditions. Results are displayed in **Table 4**.

Model 1 accounted for a significant amount of variance in depression; $R^2 = 0.19$, $F_{(6,1,052)} = 50.75$, $p \leq 0.001$. Pain severity, sleep quality, SEP, and MSK pain were all independently

significantly associated with depression. However, the interaction between pain severity and sleep quality was non-significant.

Model 2 accounted for a significant amount of variance in depression; $R^2 = 0.29$, $F_{(6,1,052)} = 72.76$, $p \leq 0.001$. Pain interference, sleep quality, gender, SEP, and chronic widespread pain were all independently significantly associated with depression. In this model, there was a significant interaction between pain interference and sleep quality; $\Delta R^2 = 0.003$, $\Delta F_{(1,1,052)} = 2.82$, $p = 0.028$. Following recommendations by Aiken et al. (1991) an interaction plot was created to aid interpretation of the interaction.

Visual inspection of **Figure 2** demonstrated there was a positive relationship between pain interference and depression (as pain interference scores increased, depression scores increased) when sleep quality scores were one standard deviation below the average; $b = 0.66$, 95%CI [0.52, 0.80], $t = 9.04$, $p \leq 0.001$, when sleep quality scores were average; $b = 0.77$, 95%CI [0.65, 0.89], $t = 12.80$, $p \leq 0.001$, and when sleep quality scores one standard deviation above the average; $b = 0.88$, 95%CI [0.72, 1.04], $t = 10.60$, $p \leq 0.001$. Taken together, it can be suggested that good sleep quality attenuated the effect of pain interference on depression scores and equally poor sleep quality amplified the effect of pain on depression scores.

DISCUSSION

The purpose of this study was to investigate variables associated with depression among a cohort of chronic pain individuals and examine whether sleep quality can moderate the effect of pain severity on depression, and pain interference on depression, among a chronic pain population. Our findings suggest that pain severity, pain interference, and sleep quality are all significantly associated with depression among this population. These results support previous research which posits pain is an antecedent to depression, and several studies which have implicated sleep quality as an initiating factor in the development of depression (Magni et al., 1994; Chang et al., 1997; Fishbain et al., 1997; Buysse et al., 2008; Jaussent et al., 2011).

Our findings also indicate that sleep quality moderates the relationship between pain interference and depression, such that better sleep quality buffers the effect of pain interference on depression, and equally poorer sleep quality exacerbates the impact of pain interference on depression in this group. This evidence supports one study conducted by Hamilton et al. (2007) in which they found sleep quality moderated the effect of pain intensity on negative affect (akin to depression) among rheumatoid arthritis and fibromyalgia patients. In addition to supporting this evidence, our study amplifies these findings among a larger sample size ($n = 1{,}059$ vs. $n = 49$) and suggests the moderating role of sleep quality may be found across several non-malignant pain groups.

Examining the relationships between pain, sleep, and depression in chronic pain populations is an important area of research, and studies have previously focused on depression-related states (e.g., negative affect, negative mood, depression) as a moderating factor between pain and sleep (Valrie et al., 2008; O'Brien et al., 2011). Subsequently, some researchers have advocated for targeting depression-related states as a therapeutic intervention among this group as a means to improve sleep quality, and in some instances, pain symptoms. Despite this, two issues arise with this approach: firstly, antidepressant medications (predominantly used in moderate to severe cases of depression) have shown to improve sleep parameters such as sleep latency and increase slow wave sleep in some instances and are recommended to be combined with a behavioral intervention (Schmid et al., 2006; Wichniak et al., 2017). However, the sleep-promoting action provided by certain antidepressants may become problematic during the maintenance phase of treatment due to over-sedation effects. Additionally, some medications used to treat depression often result in sleep disruption, whether through activating agents or through long-term increased tolerance to sedatives (Wichniak et al., 2017). Secondly, in a study which compared a behavioral intervention for sleep to a behavioral intervention for depression among individuals with both insomnia and depression, results showed that both interventions produced reductions in depression symptoms post-intervention and 3-year follow-ups, although these reductions did not differ across the two intervention groups. In addition, the group receiving the sleep treatment demonstrated significantly better improvements in sleep parameters than the depression intervention (Blom et al., 2017). The authors concluded therefore that in individuals with co-existing depression and insomnia, a behavioral sleep intervention should be included as a treatment option in addition to any pharmaco-therapy or psychological treatment for depression. Given that sleep problems are shown to be a precipitating and maintaining factor in depression, targeting depression through pharmacologic and non-pharmacologic therapies solely whilst neglecting co-existing sleep problems may only lead to short-term benefits (Tsuno et al., 2005). Several studies suggest talking therapies such as cognitive behavioral therapy for insomnia (CBT-I) are an effective intervention in reducing not only insomnia, but also improving depression outcomes significantly among clinical populations (Manber et al., 2011, 2016; Gee et al., 2019). The UK National Institute for Health and Care Excellence (National Institute for Health and Clinical Excellence, 2009) provide guidelines for treatment of depression which advocate a stepwise approach based on severity and duration of symptoms. Within these guidelines, sleep hygiene is advised for individuals with subthreshold depressive symptoms and those with recognized mild to moderate cases, and our study supports the notion that in addition to sleep hygiene, a more structured approach such as CBT-I may be considered.

Nearly all our sample met criteria for poor sleep quality (determined by the PSQI measure) and average sleep quality scores were significantly above the cut-off for "poor" sleep quality (mean PSQI scores were 13.89, nearly nine points above the cut-off of five). Our findings are similar to previous studies using this measure among chronic pain populations (Smith et al., 2000; Osorio et al., 2006; Marty et al., 2008). In addition, a significant portion of our sample also met criteria for mild, moderate, and severe depression symptoms. To contextualize, our findings suggested there is an association between sleep quality and depression and supports the notion that focusing on sleep problems could help alleviate both symptoms of insomnia and depression, as others have done previously (Asarnow and Manber, 2019). Given that depression has been shown

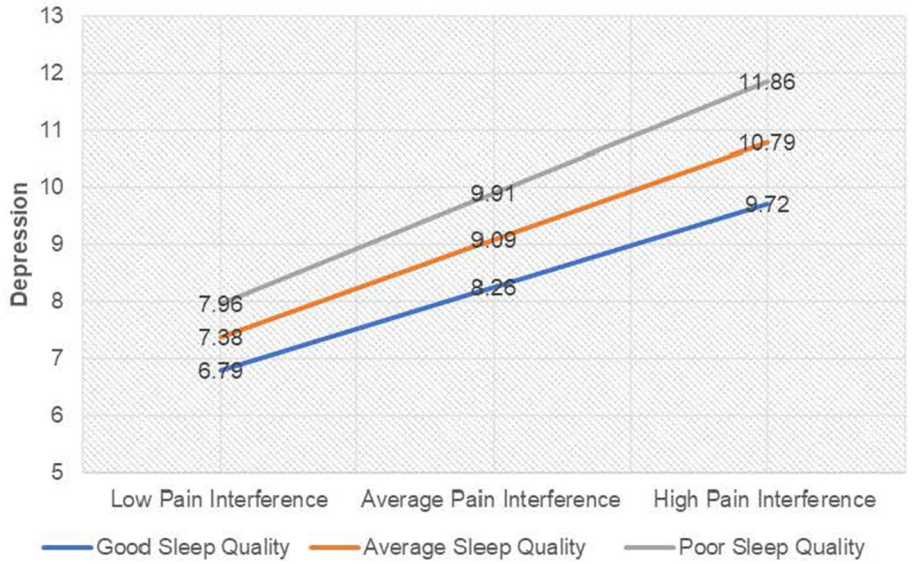

FIGURE 2 | Interaction plot for depression among individuals with chronic pain. For ease of interpretation, sleep quality labels have been raised. "Good sleep quality" as labeled on the graph denotes a score ISD below the mean on the PSQI (lower scores on the PSQI indicate better sleep quality), and "Poor sleep quality" denotes a score ISD above the mean on the PSQI (higher scores on the PSQI indicate poor sleep quality).

to impact self-management, opioid use, and health-seeking behavior among chronic pain populations, it is important to both screen for and therapeutically address sleep problems which may influence depression in this group (Jordan et al., 2006; Bair et al., 2009; Goesling et al., 2015).

Lastly, we included socio-demographic covariates in our models which were found to be significantly associated with depression among our cohort. Socio-economic position (SEP) was significant in both moderated regression models and suggests that chronic pain individuals from lower SEP backgrounds are at greater risk of experiencing comorbid depression. This supports previous findings and strengthens the basis for not only recording SEP during interactions with health and social care systems, but screening for SEP and tailoring health messaging to these groups (Freeman et al., 2016; Booher, 2019). Given the correlation between low SEP and low health-literacy rates, one strategy proposed has been to simplify text within health messaging and include illustrations where possible (Houts et al., 2006; Wilson and Wolf, 2009; Svendsen et al., 2020).

Limitations

Our study relied on self-report measures which may be less sensitive than objective measures and comprehensive clinical assessments. Despite this, self-report measures offer an effective means to data gathering across larger samples (Paulhus and Vazire, 2007). Secondly, the use of cross-sectional data limits the ability to establish temporal relationships and make causal inferences regarding pain sleep and depression. However, principal works in this field have shown that these relationships are likely reciprocal, and consequential of one another. Therefore, our results may still be meaningful in enhancing care pathways for chronic pain populations. Third, our population consisted of a community dwelling sample, which likely includes individuals with a wide range of health needs. Future research should seek to replicate this model among patients within clinical settings to assess whether the findings are replicated among those with the most complex needs. Fourth, the majority of our sample included participants who identified as women from a "White-any" ethnic background which limits generalisability of our findings to other demographic groups with chronic pain. Finally, it is possible that the association between sleep and depression may be influenced by the use of sleep-influencing medications among chronic pain populations and future research could examine this as a potential control variable.

Recommendations for Research and Practice

Given the high prevalence and impact depression has on quality of life, self-management care, and economic productivity among individuals with chronic pain, seeking strategies to reduce comorbid depression in this population is of great value. Our findings suggest sleep quality is associated with depression in this group. In light of our findings, and supported by previous research, the following recommendations are made:

1. Given that sleep quality may moderate the impact of pain interference on depression, chronic pain services should regularly include screening for sleep problems and symptoms of depression during routine assessments.
2. NICE guidelines (National Institute for Health and Clinical Excellence, 2009) for depression include sleep hygiene advice for individuals with persistent subthreshold depression, mild and moderate cases. More structured sleep interventions such as CBTI could be considered within combined treatment

approaches for individuals with co-occurring sleep problems and depression.
3. Practitioners and social care workers should be encouraged and supported to screen for SEP and address specific barriers to treatment uptake among lower SEP individuals to further improve depression outcomes in this population e.g., telehealth solutions which minimize need and expense for travel.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by UCL Institute of Education Ethics Committee. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

ZZ and EH: concept and study design and data analyses, ZZ: survey creations and data cleansing. ZZ, EH, AF, and DD: manuscript and editing. All authors contributed to the article and approved the submitted version.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychology

BRIEF RESEARCH REPORT
published: 26 May 2021
doi: 10.3389/fpsyg.2021.681569

Dream Activity in Narcoleptic Patients During the COVID-19 Lockdown in Italy

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Some studies highlighted that patients with narcolepsy type-1 (NT1) experience high lucid dream frequency, and this phenomenon has been associated with a creative personality. Starting from the well-known "pandemic effect" on sleep and dreaming, we presented a picture of dream activity in pharmacologically treated NT1 patients during the Italian lockdown. Forty-three NT1 patients completed a web-survey during Spring 2021 and were compared with 86 matched-controls. Statistical comparisons revealed that: (a) NT1 patients showed greater sleepiness than controls; (b) controls showed higher sleep disturbances than NT1 patients, and this result disappeared when the medication effect in NT1 was controlled; (c) NT1 patients reported higher lucid dream frequency than controls. Focusing on dreaming in NT1 patients, we found that (a) nightmare frequency was correlated with female gender, longer sleep duration, higher intrasleep wakefulness; (b) dream recall, nightmare and lucid dream frequency were positively correlated with sleepiness. Comparisons between low and high NT1 lucid dreamers showed that patients more frequently experiencing lucid dreams reported a greater influence of dreaming during wakefulness, especially concerning problem-solving and creativity. Overall, our results are consistent with previous studies on pandemic dreaming carried out on healthy subjects. Moreover, we confirmed a link between lucidity and creativity in NT1 patients. Considering the small sample size and the cross-sectional design, our findings cannot provide a causal relationship between lucid dreams and the COVID-19 lockdown. Nevertheless, they represent a first contribution to address future studies on this issue, suggesting that some stable characteristics could interact with changes provoked by the pandemic.

Keywords: COVID-19 pandemic, creativity, lucid dreaming, nightmares, dream recall, sleep, narcolepsy

OPEN ACCESS

Edited by:
Federica Scarpina, Istituto Auxologico Italiano (IRCCS), Italy

Reviewed by:
Armando D'Agostino, University of Milan, Italy
Franca Crippa, University of Milano-Bicocca, Italy

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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *16 March 2021*
Accepted: *29 April 2021*
Published: *26 May 2021*

Citation:
Scarpelli S, Alfonsi V, D'Anselmo A, Gorgoni M, Musetti A, Plazzi G, De Gennaro L and Franceschini C (2021) Dream Activity in Narcoleptic Patients During the COVID-19 Lockdown in Italy. Front. Psychol. 12:681569. doi: 10.3389/fpsyg.2021.681569

INTRODUCTION

Narcolepsy type 1 (NT1) is a neurological disorder characterized by excessive daytime sleepiness and sleep abnormalities, mainly dissociated manifestations of Rapid Eye Movement (REM) sleep. Indeed, rapid access into REM sleep at sleep onset, sleep paralysis, hypnagogic and/or hypnopompic hallucinations, and the pathognomonic symptom cataplexy are key features of this disorder [American Academy of Sleep Medicine (AASM), 2014].

Narcoleptic patients frequently report unusual and emotional dream experiences (Schredl, 1998; Schiappa et al., 2018). Further, the available literature underlined that NT1 patients often experience a scarce insight of what refers to dream content rather than real experience, leading to "delusional confusion" between dreaming and reality (Hays, 1992; Szucs et al., 2003; Wamsley et al., 2014).

Some studies revealed that narcoleptic patients report a more significant level of awareness during sleep mentation than healthy subjects (Lequerica, 1999; Fosse, 2000). More directly, it has been highlighted that narcolepsy is associated with experiencing lucid dreaming (i.e., the phenomenon of being aware of dreaming during dreaming) (Dodet et al., 2015; Rak et al., 2015). Specifically, Rak et al. (2015) carried out an investigation based on phone-interview and showed that 60 narcoleptic patients had higher dream recall frequency, nightmares, and lucid dreams than controls. This finding was supported by an experimental study, revealing that patients had more lucid dreams and were able to indicate their awareness while they were asleep using a defined eye movement signal (Dodet et al., 2015). Other findings underlined a link between the high metacognition during sleep and creativity personality profile (Zink and Pietrowsky, 2013). Interestingly, in narcoleptic patients lucid dreaming is associated with a higher creative profile, and hypnagogic hallucinations lead to higher creative success and potential, impacting on the creative identity of NT1 patients (Lacaux et al., 2019; D'Anselmo et al., 2020).

The latter findings open new perspectives in the investigation of the lucid dreaming process in narcolepsy (Dodet et al., 2015; Rak et al., 2015), and claim for systematic targeted studies comparing healthy and narcoleptic patients.

Further, dream activity and emotional processing are strictly related (Scarpelli et al., 2019a). In this regard, a recent review highlighted that the neurobiological basis of narcolepsy and patients' mental sleep activity appears to be closely associated (Schiappa et al., 2018). Indeed, neuroimaging studies found that narcolepsy is characterized by limbic dysfunction (Poryazova et al., 2009; Meletti et al., 2015; Vaudano et al., 2019). The amygdala and hypothalamus are also involved in processing emotional memory and fear during wakefulness (Richter-Levin, 2004), which may be responsible for disturbing dreams. In this view, dream experiences could be considered the expression of patient well-being or distress and could be clinically relevant.

We have to underline that recent studies highlighted that, during the COVID-19 pandemic, people reported sleep alterations and, in parallel, high dream recall and nightmare frequency (e.g., Iorio et al., 2020; MacKay and DeCicco, 2020; Gorgoni et al., 2021; Scarpelli et al., 2021a). During the pandemic, people's dreams showed a greater negative emotional charge (e.g., Iorio et al., 2020; Schredl and Bulkeley, 2020; Gorgoni et al., 2021; Scarpelli et al., 2021a) and pandemic-related contents (e.g., Iorio et al., 2020; Schredl and Bulkeley, 2020). Moreover, fragmented and lighter sleep has proven to be linked to dreaming during lockdown in healthy subjects (Scarpelli et al., 2021a), consistently to the "arousal-retrieval hypothesis" pointed out that dream recall may be promoted by awakenings during sleep (Koulack and Goodenough, 1976). Further, a gender difference was observed since females revealed a larger dream recall rate according to the previous literature (e.g., Barrett, 2020; Iorio et al., 2020; Scarpelli et al., 2021a). In addition, aging was associated with a drop in dream recall frequency also during lockdown (Scarpelli et al., 2021a).

Here, for the first time, we present a picture of dream activity in pharmacologically treated narcoleptic patients during the pandemic. We intend to provide a better understanding of dreaming in narcolepsy, reporting the results from a cross-sectional study in which we have compared NT1 and healthy subjects. In light of the current background, we expected that NT1 patients had a greater dream activity (dreams, nightmares and lucid dreams) than controls. We also hypothesized that (1) poor sleep quality and high arousal (i.e., frequent awakenings) are associated with dream frequency in NT1 patients; (2) gender and age are related to dream activity during the pandemic in NT1 patients; (3) lucid dream frequency and creativity are linked in NT1 patients, as highlighted by previous literature.

MATERIALS AND METHODS

Study Design, and Participants

Patients who met diagnostic criteria for narcolepsy type 1 (NT1) and followed at the Outpatients Clinical for Narcolepsy at the IRCCS—Institute of the Neurological Sciences of Bologna were requested to fill out a web-survey on the Microsoft Azure platform. Specifically, NT1 subjects had to meet the international criteria for NT1 [American Academy of Sleep Medicine (AASM), 2014].

Also, the web-survey was promoted by means of university communication systems and virtual learning environments to recruit healthy subjects. The survey lasted about 30 min and was addressed to over-18 exclusively.

All questionnaires were collected during spring 2020. Specifically, the survey was available online from March 10, 2020, to May 4, 2020.

Firstly, subjects filled out a self-administered questionnaire on socio-demographic information. In addition, psychological measures, sleep measures and dream variables were collected by specific self-reported questionnaires.

All subjects signed an electronic informed consent before accessing the questionnaires. The subjects also explicitly agreed to provide an email contact and created an identification code to anonymize it. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethic committee (Comitato Etico Indipendente di Area Vasta Emilia Centro—CE-AVEC).

Overall, 60 NT1 patients received the link to fill out the web-survey. A total of 43 NT1 patients completed the survey (response rate: 71.67%). In keeping with many studies including patients with rare conditions (e.g., Fortuyn et al., 2010) we chose to compare NT1 patients and healthy controls with a ratio case/matched controls of 1:2 to increase statistical power. Hence, 86 healthy controls were extracted from respondents to the web-survey (Franceschini et al., 2020b) and were matched for age, gender, Italian area, and days elapsed since the beginning of lockdown.

All NT1 patients were on pharmacological treatment: 28 patients on pharmacotherapy with Sodium oxybate; 15 patients on pharmacotherapy with other medications (e.g., Pitolisant; Modafinil). Data from healthy subjects reported in the current study have been presented elsewhere (Franceschini et al., 2020b; Scarpelli et al., 2021a) and were part of a wider project, "Resilience and the COVID-19: how to react to perceived stress. Effects on sleep quality and diurnal behavior/thoughts," with different objectives concerning the impact of lockdown in the Italian population.

Measures

The webform was composed of 4 sections:

Socio-Demographic and COVID-19-Related Information

This section allowed us to collect the following variables: age, gender, marital status, presence/absence of children, education level, Italian area, occupation, forced quarantine, having COVID-19-infected friends or relatives.

Psychological Measures

Psychological measures were evaluated by the Italian version of the Depression Anxiety Stress Scale (DASS-21) short form (Bottesi et al., 2015), a self-administered questionnaire in which subjects rate the frequency and severity of depression, anxiety, and stress symptoms. The 21 Items refer to the previous week and each item is scored on a 4-point scale (0 = "Did not apply to me at all," to 3 = "Applied to me very much, or most of the time"). Anxiety, depression and stress scores result from the sum of the responses to the items from each subscale multiplied by 2 to suit the original 42 items. The cut-offs for severe rating of depression, anxiety and stress are ≥21, ≥15, and ≥26, respectively (Lovibond and Lovibond, 1995).

Sleep Measures

Sleep measures were assessed by the Italian adaptation of the Medical Outcomes Study- sleep scale (MOS-SS) (Palagini and Manni, 2016), a self-reported questionnaire including 12 items to assess sleep quality and quantity within a 4-week period. Ten of the 12 MOS-SS items are scored on a 6-point categorical scale ranging from "1 = all of the time" to "6 = none of the time." The question about the time required to fall asleep uses a 5-point categorical response scale ranging from "0 to 15 min," to "more than 60 min." "Sleep duration" is reported by subjects as the average number of hours they sleep each night. All domains except sleep duration are converted from 0 to 100, and item 2 is recorded as the average number of hours slept per night (0–24 h). This instrument provides six measures for sleep quality: sleep disturbance, snoring, awakening short of breath or with headache, sleep adequacy, somnolence and sleep duration/optimal sleep. Finally, MOS-SS has a global index to assess quality of sleep defined Sleep Index II or Sleep problem index, an aggregate measure of responses to nine of the questions about the four sleep domains (sleep disturbance, awakening short of breath or with headache, sleep adequacy and sleepiness). Scores for the MOS-SS Sleep Index II range from 0 to 100, with higher scores indicating greater sleep problems (cut-off = 25.8; Hays et al., 2005). In keeping with previous work (Scarpelli et al., 2021a), we have taken into consideration also self-reported evaluation of the intrasleep wakefulness (item 8), dichotomized as follows: "high intrasleep wakefulness" (answer "3," "4," "5") and "low intrasleep wakefulness" (answer "1," "2").

Dream Variables

Dreaming was assessed by the Italian adaptation of the Mannheim Dream Questionnaire (MADRE) (Settineri et al., 2019), a self-reported questionnaire with 20 items. Dream recall frequency (item 1) was rated by a 7-point scale format (0 = never and 6 = almost every morning). Nightmare frequency (item 4) and lucid dream frequency (item 10) was rated by an 8-point scale (0 = never and 8 = several times a week). The dream and nightmare frequency were asked with reference to the last month. Also, emotional intensity, emotional tone and nightmare distress were evaluated (item 2, 3, 5). Individuals' attitudes toward dreams (i.e., the personal meaning of one's own dreams and the impression that dreams provide impulses or pointers for waking life) were assessed by item 12, consisting of eight sentences with a 5-point format (0 = Not at all/4 = Totally). The impact of dream on daily life (the frequency of dream sharing, the recording of dreams, the dreams affecting day-time mood, the creative. dreams, and the problem-solving dreams, from item 13 to 17). Dream variables eliciting utilizations of dreams (i.e., frequency of dream sharing, recording of dreams, dreams affecting day-time mood, creative dreams, problem-solving dreams) were in 8-point scale with 0 = never and 8 = several times a week.

Further, the questionnaire required information on presence/absence and percentage of recurring nightmares (item 6, 7) and on and deja-vu experiences based on dream (item 18). Additionally, the questionnaire includes specific items on age of first lucid dream (item 11); reading about dreams (item 19, rated using a 3-points scale) and helpful dream literature (item 20, rated using a 5-points scale).

Statistical Analysis

Descriptive analyses were conducted to outline the sociodemographic characteristics of the sample, considering the following features: age, gender, marital status, presence/absence of children. education level, occupation, forced quarantine, having COVID-19-infected friends or relatives.

Firstly, the Mann-Whitney U tests were used to compare differences between the NT1 and control group concerning the psychological measures extracted from DASS (anxiety, depression and stress) and sleep variables extracted from MOS-SS (sleep disturbances, snoring, awakening short of breath or with headache, sleep adequacy, sleepiness, and sleep problem index) and the oneiric measures regarding dream frequency (dreams, nightmares, lucid dreams) and qualitative emotional features (emotional intensity, emotional tone and nightmares distress).

We performed non-parametric Spearman's correlations (rank bivariate or rank biserial, depending on the variable type) to assess the relationship between NT1 dreaming (dream recall

frequency, nightmare frequency, lucid dream frequency) and (1) demographic factors (age, gender) previously associated to oneiric activity (Scarpelli et al., 2021a) and (2) sleep measures (sleep duration and intrasleep awakenings extracted from MOS-SS, sleep disturbances, snoring, sleepiness) to test the arousal-retrieval hypothesis.

In order to better understand the relationship between lucid dreaming and the waking-correlates of oneiric activity in narcolepsy, we carried out statistical comparisons between high and low lucid dreamers (Mann-Whitney U test), considering the following independent variables: attitude toward dreams (items 12—averaged score), and items regarding utilization of dreaming during wakefulness (item 13-frequency of dream sharing, item 14-recording of dreams, item 15- dreams affecting day-time mood, item 16- creative dreams, item 17- problem-solving dreams). Item 10 about lucid dreaming was dichotomized, as follows: "low lucid dreamers" (answer from 0-never to 5-about 2/3 times a month; $N = 27$) and "high lucid dreamers" (answer from 6-about once a week to 7-several times a week; $N = 16$).

The statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 25.0 and Matlab R2019a. *P*-values of <0.05 were considered statistically significant.

RESULTS

Characteristics of Samples

The characteristics of participants are shown in **Table 1**. In short, 37.2% of the samples were young subjects (age 18–25). Female gender was represented by 58.1% of the samples. Subjects were mainly single, both in NT1 (37.2%) and HC group (36%). Further, most of the participants received high school education in NT1 (55.8%) and HC group (33.7%). A high percentage of respondents were employed both in NT1 (55.8%) and HC group (58.1%). Further, 58.1% came from the North of Italy in both groups. Also, more than 70% of the individuals of each sample did not have children. The majority of the respondents from both groups did not experience a forced quarantine (97.7 %). Among healthy individuals, 14% had COVID-19-infected friends or relatives, while in the NT1 group only a subject had a significant other infected.

TABLE 1 | Socio-demographic and COVID-19-related characteristics.

	Controls ($N = 86$) N (%)	Narcoleptic patients ($N = 43$) N (%)
Age		
18–25	32 (37.2)	16 (37.2)
26–30	10 (11.6)	5 (11.6)
31–40	20 (23.3)	8 (18.6)
41–50	20 (23.3)	12 (27.9)
51–60	4 (4.7)	2 (4.7)
Gender		
Male	36 (41.9)	18 (41.9)
Female	50 (58.1)	25 (58.1)
Marital status		
Single	31 (36)	16 (37.2)
Married	22 (25.6)	7 (16.3)
Cohabitating	12 (14)	10 (23.3)
Engaged	20 (23.3)	8 (18.6)
Divorced/separated/widower	1 (1.2)	2 (4.7)
Education level		
Until middle School	1 (1.2)	4 (9.3)
High school	29 (33.7)	24 (55.8)
Bachelor's degree	25 (29.1)	8 (18.6)
Master's degree	24 (27.9)	4 (9.3)
PhD/postgraduate school	7 (8.1)	3 (7)
Occupation		
Student	29 (33.7)	14 (32.6)
Employed	50 (58.1)	24 (55.8)
Retired	1 (1.2)	0 (0)
Unemployed	6 (7)	5 (11.6)
Italian area		
North Italy	50 (58.1)	25 (58.1)
Center and South Italy	36 (41.9)	18 (41.9)
Having children		
Yes	25 (29.1)	11 (25.6)
No	61 (70.9)	32 (74.4)
Forced quarantine		
Yes	2 (2.3)	1 (2.3)
No	84 (97.7)	42 (97.7)
COVID-19-infected friends/relatives		
Yes	12 (14)	1 (2.3)
No	74 (86)	42 (97.7)

Comparisons Between Narcoleptics and Controls

Table 2 summarized the statistical comparisons between the NT1 and control group, considering psychological, sleep and dream measures. The results revealed no difference in psychological measures. Conversely, concerning sleep variables, NT1 patients reported significantly higher sleepiness than controls ($p < 0.001$). Also, healthy individuals reported higher sleep complaints than NT1 patients ($p < 0.001$). Considering that the NT1 group was on pharmacological treatment, we performed a control analysis to check whether the pharmacotherapy could impact self-reported sleep disturbances among patients (please, see the **Supplementary Material**). This supplementary analysis showed that the difference in sleep disturbances between controls and NT1 subjects is maintained only when patients were treated with Sodium oxybate, a pharmacological treatment promoting slow-wave sleep and sleep quality (Franceschini et al., 2020a). Conversely, the difference in sleep disturbances disappears comparing controls with NT1 patients treated with other types of medications.

Crucially, patients showed higher lucid dreams than controls ($p = 0.014$). No other significant difference was found regarding dream frequency and dream emotionality.

TABLE 2 | Mean rank of psychological, sleep and dream measures and results of statistical comparisons (Mann-Whitney U Test) between controls and narcoleptic patients.

		Mean rank	U-values	Z-scores	*p-values*
Anxiety	C	63.74	1740.5	−0.549	0.483
	NT1	67.52			
Depression	C	66.44	1,725	−0.633	0.225
	NT1	62.12			
Stress	C	67.81	1,607	−1.212	0.534
	NT1	59.37			
Sleep disturbances	C	73.08	1,154	−3.485	**<0.001**
	NT1	48.84			
Snoring	C	62.55	1,638	−1.222	0.222
	NT1	69.91			
Awakenings (short of breath or headache)	C	65.69	1,790	−0.371	0.710
	NT1	63.63			
Sleep adequacy	C	60.58	1,469	−1.914	0.056
	NT1	73.84			
Sleepiness	C	53.01	818	−5.200	**<0.001**
	NT1	88.98			
Sleep problem index	C	67.26	1,655	−0.971	0.332
	NT1	60.49			
Dream recall frequency	C	63.21	1,695	−0.789	0.430
	NT1	68.58			
Nightmares frequency	C	65.58	1,799	−0.253	0.800
	NT1	63.84			
Lucid dream frequency	C	59.36	13,643	−2.449	**0.014**
	NT1	76.28			
Emotional intensity	C	65.97	1,766	−0.434	0.664
	NT1	63.07			
Emotional tone	C	64.06	1,768	−0.435	0.663
	NT1	66.88			
Nightmares distress	C	62.31	1,618	−1.191	0.234
	NT1	70.37			

α = 0.05. Values in bold indicate significant difference.
C, Controls; NT1, narcoleptic patients type 1.

Demographic and Sleep Features Related to Dream Frequency

Spearman's correlation analyses (see **Table 3**) showed that (a) nightmare frequency in the NT1 group was related to female gender ($p = 0.030$), longer sleep duration ($p = 0.043$), higher intrasleep wakefulness ($p = 0.006$); (b) dream recall frequency, nightmare frequency and lucid dream frequency were positively correlated with sleepiness ($p = 0.003$).

Comparisons Between High and Low Lucid Dreamers

Table 4 summarized the statistical comparisons between low and high NT1 lucid dreamers revealing that high lucid dreamers, as compared to low lucid dreamers: (a) had higher mean score in the factor "attitude toward dream" ($p = 0.010$); (b) more frequently recorded their dreams ($p = 0.036$); (c) more frequently had dreams influencing their creativity during wakefulness ($p = 0.011$); (d) more frequently had dreams influencing their problem-solving during wakefulness ($p = 0.001$).

DISCUSSION

For the first time, the current study aimed to investigate pandemic's dream activity in NT1 patients. Overall, we revealed that NT1 patients showed greater sleepiness than healthy subjects, consistently to their diagnosis [American Academy of Sleep Medicine (AASM), 2014]. In contrast, the healthy group reported higher sleep disturbances than NT1 patients as measured by MOS-SS. This result could appear surprising, nevertheless, we showed that the difference disappeared when matched-controls were compared with NT1 patients treated with medications different from Sodium oxybate. In other words, the observed difference considering the whole NT1 group can be ascribed to effective treatment with Sodium oxybate on nocturnal sleep, which reduced disturbed sleep across the night

TABLE 3 | Features related to dream frequency in narcoleptic patients: Spearman's correlation coefficients.

	Dream recall frequency		Nightmare frequency		Lucid dream frequency	
	Correlation	***p*-values**	**Correlation**	***p-values***	**Correlation**	***p-values***
Age	−0.116	0.457	−0.067	0.667	−0.174	0.264
Gender	0.079	0.612	0.331	**0.030**	0.010	0.951
Sleep duration[a]	0.123	0.461	0.331	**0.043**	0.016	0.924
Intrasleep wakefulness	0.138	0.379	0.411	**0.006**	0.138	0.379
Sleep disturbances	0.110	0.481	0.258	0.095	0.069	0.661
Snoring	−0.11	0.942	0.024	0.877	0.016	0.918
Sleepiness	0.443	**0.003**	0.465	**0.002**	0.391	**0.009**

[a]*Correlations performed on 38 narcoleptic patients for missing data on this item.*
$\alpha = 0.05$. *Values in bold indicate significant difference.*

TABLE 4 | Mean rank of attitude toward dreams (averaged score), items regarding utilization of dream during wakefulness and results of statistical comparisons (Mann-Whitney U Test) between narcoleptic patients with low and high lucid dreamers.

		Mean rank	**U-values**	**Z-scores**	**p-values**
Attitude toward dreams	LLD	18.22	114	−2.568	**0.010**
	HLD	28.38			
Dream sharing	LLD	21.52	203	−0.330	0.741
	HLD	22.81			
Recording of dreams	LLD	20.02	162.5	−2.092	**0.036**
	HLD	25.34			
Dreams affecting day-time mood	LLD	19.61	151.5	−1.652	0.099
	HLD	26.03			
Creative dreams	LLD	18.37	118	−2.544	**0.011**
	HLD	28.13			
Problem-solving dreams	LLD	17.52	95	−3.242	**0.001**
	HLD	29.56			

$\alpha = 0.05$.
LLD, low lucid dreamers; HLD, high lucid dreamers.
Values in bold indicate significant difference.

(Franceschini et al., 2020a). In parallel, it should be noted that our data were collected during Spring 2020. In this regard, several studies demonstrated that the pandemic is provoking remarkable sleep alterations in healthy subjects (Blume et al., 2020; Casagrande et al., 2020; Cellini et al., 2020; Franceschini et al., 2020b; Wright et al., 2020), especially causing insomnia symptoms (i.e., COVID-Somnia; Gupta and Pandi-Perumal, 2020).

However, studies that investigated nocturnal sleep quality in narcoleptic patients during lockdown reported mixed results. Changes in sleep quality resulted related to changes in work habits in adult NT1 patients in the study of Postiglione et al. (2021). They found no significant alterations in patients working or studying at home and increased sleep disturbances in patients that do not change their working schedule (Postiglione et al., 2021). A study on NT1 and NT2 patients reported an increase in sleep fragmentation in 43.4% and not change in 35.5% of the sample (Rodrigues Aguilar et al., 2020). Finally, recent data on pharmacologically treated NT1 children and adolescents reported no differences in sleep quality during lockdown compared to an earlier period (Filardi et al., submitted).

Concerning the primary objective of our investigation, we revealed that only lucid dreams frequency significantly differed between groups. In line with previous literature (Dodet et al., 2015; Rak et al., 2015), patients with narcolepsy had higher lucid dreams frequency than healthy subjects. Surprisingly, no difference was found in emotional dream features.

Consistently to the findings on healthy subjects during lockdown (e.g., Scarpelli et al., 2021a), we found that nightmares in NT1 patients were more frequent in women. This result is also in line with the evidence that females reported higher rates of negative emotions in their sleep mentation during pandemic (Barrett, 2020). Barrett suggests that this gender difference may be explained in light of the "continuity-hypothesis," considering women more vulnerable to anxiety and mood alteration than men during lockdown (Barrett, 2020). The impact of gender on dream activity is well-established (Schredl and Reinhard, 2008) and may be independent by the COVID-19 health emergency.

It should be noted that the cross-sectional protocol makes it difficult to draw definitive conclusions about the link between pandemic and the differences highlighted between NT1 patients and control subjects. Moreover, the small sample size of NT1 patients and a response rate of around 70% could represent a serious weakness of our study. On the one hand, the limited number of patients involving in the study is not surprising since NT1 is a rare condition affecting 0.02–0.06% of adults, as highlighted from epidemiological studies in the United States and Europe (e.g., Mignot et al., 1997; Longstreth et al., 2007; Kornum et al., 2017). On the other hand, we have to mention that the small NT1 sample size did not allow us to study directly the impact of adverse events (forced quarantine, COVID-19-infected relatives or friends) on emotional dream features since the pandemic-related conditions were reported in ∼2% of our sample. In fact, all patients and healthy controls spent that period in conditions similar to quarantine due to the lockdown from March 10, 2020, to May 4, 2020, that forced people to stay at home in confinement. For all these reasons, our considerations should be taken with caution. Actually, we can only describe a picture of dream activity in narcolepsy during Spring 2020 without disentangling whether we observed a stable phenomenon in NT1 or a condition influenced by the COVID-19 emergency (i.e., stay-at-home in confinement).

Although we showed that sleep disturbances were attenuated by pharmacotherapy in the NT1 group, we revealed that sleepiness was correlated with dream recall, nightmare, and lucid dream frequency. In keeping with the activation-hypothesis (D'Atri et al., 2019; Scarpelli et al., 2021b) and the so-called arousal-retrieval model (Koulack and Goodenough, 1976), this result may be interpreted as an index of lighter nocturnal sleep. More directly, a greater amount of intrasleep wakefulness was positively associated with nightmare frequency, as highlighted by previous evidence (Scarpelli et al., 2021a). Awakenings during sleep would guarantee the elaboration of dream material and its transfer from short-term memory storage to long-term storage (Koulack and Goodenough, 1976; Scarpelli et al., 2021b).

Interestingly, NT1 patients, as well as control subjects (see Scarpelli et al., 2021a) reported an association between frightening dreams and higher sleep duration. This finding is only apparently in conflict with the activation/arousal-retrieval model. In fact, the phenomenon of sleep extension during lockdown has been described by Bottary et al. (2020) highlighting that even if people spontaneously prolonged their sleep duration, the rest could be featured by poor quality and fragmentation, and confirmed by recent data (Alfonsi et al., 2021).

The comparisons between high and low lucid dreamers confirmed that the increased awareness of their own mental sleep activity was linked to the perception that the oneiric dimension has a remarkable impact on daily-life. Specifically, the greater problem-solving and creative dreams in high lucid dreamers are consistent with the studies suggesting that lucid dreaming and dissociated REM sleep manifestations are associated with creativity in narcoleptic patients (Lacaux et al., 2019; D'Anselmo et al., 2020). Additionally, it is worth noting that a greater awareness of dreams may have a role in emotional regulation (Scarpelli et al., 2019a). Again, it should be mentioned that our results cannot provide a direct association between pandemic, creativity and lucid dreams in NT1 patients. However, in keeping with the available literature (Dresler et al., 2014; Rak et al., 2015; Schiappa et al., 2018), we can speculate that narcoleptic patients with more frequent experiences of lucid dreams have developed a coping strategy in their dream experience to face the negative emotional contents linked to the COVID-19 emergency. In this view, narcoleptic patients reporting high lucid dreams felt that lucidity provides relief for their nightmares (Rak et al., 2015). We have also to consider that high lucid dreamers in our sample reported a greater attitude toward oneiric experience, being more prone to record their dreams. In other words, these subjects reported high dream salience (Cohen, 1979) that may be considered an intraindividual stable and COVID-unrelated feature affecting dream recall frequency (Schredl and Göritz, 2015).

CONCLUSIONS

The main finding of the current study is the presence of higher lucid dreams frequency in NT1 patients than healthy subjects during pandemic. In line with previous studies, we highlighted that sleep measures influenced oneiric activity (Bottary et al., 2020; Gorgoni et al., 2021; Scarpelli et al., 2021a) and female gender was linked with higher nightmare frequency (Barrett, 2020; Scarpelli et al., 2021a). In addition, NT1 high lucid dreamers had more dream salience and their oneiric activity appeared to significantly affect the wakefulness (Schiappa et al., 2018). Interestingly, we confirmed a link between lucid dreaming and the creative dimension in NT1 patients.

Although we reported for the first time a picture of dreaming and sleep pattern in NT1 patients during pandemic, we have to emphasize that our findings cannot provide a causal relationship between lucid dreams and the COVID-19 lockdown. Only a longitudinal design could clarify whether the changes detected are linked to the pandemic or whether they are stable features in the investigated groups. Indeed, using retrospective questionnaires represents an important limitation of our study. In this regard, the literature points to that perspective diaries and collecting dream reports immediately after awakening are more reliable methods to obtain information on dreaming (Scarpelli et al., 2019b). Similarly, an intrinsic limitation of the study concerning the use of a self-reported questionnaire to assess sleep patterns without the support of any objective measures (e.g., actigraphy).

Finally, we believe that the present study offers a first contribution to address future research on COVID-19 outbreak and individual's well-being, suggesting that some trait-like characteristics such as individual attitude toward dreams, gender and also underlying sleep disorders could interact with changes provoked by the pandemic.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

This study was conducted in accordance with the Declaration of Helsinki and the study protocol was approved by the local ethics committee (Comitato Etico Indipendente di Area Vasta Emilia Centro—CE-AVEC). Electronic informed consent was obtained from each participant prior to starting the investigation. Participants could withdraw from the survey at any moment without providing any justification. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

SS and VA provided substantial contributions to the conception of the work, deep analysis of the literature, study design, development, and final approval of the manuscript. CF and LD contributed in the design of the study and participated in the development and revision of the work and agreement for final approval of the manuscript. AD'A and MG contributed to data analysis and agreement for final approval of the manuscript. AM and GP contributed to the revision of the work and agreement for final approval of the manuscript. GP, LD, and CF contributed to deep revision of the work, with literature analysis and agreement for final approval of the manuscript contributed to deep revision of the work, with literature analysis and agreement for final approval of the manuscript. All authors contributed to the article and approved the submitted version.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2021.681569/full#supplementary-material

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Conflict of Interest: GP is a consultant and participated in advisory board for UCB Pharma, Jazz pharmaceuticals, Bioprojet, Takeda, and Idorsia outside the submitted work.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychology

ORIGINAL RESEARCH
published: 31 May 2021
doi: 10.3389/fpsyg.2021.672238

Sleep, Well-Being and Academic Performance: A Study in a Singapore Residential College

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We examined the relationship between sleep and the affective components of subjective well-being as well as psychological well-being, and between sleep and academic performance, of full-time undergraduate students in a residential college at the National University of Singapore. The aspects of sleep considered were self-reported sleep duration, sleep efficiency, frequency of sleep disturbances, daytime dysfunction, sleep latency and overall sleep quality, as measured by the Pittsburgh Sleep Quality Index. Academic performance was measured using self-reported cumulative average point scores, typically known as grade point average in other institutions. Psychological well-being and the affective components of subjective well-being were assessed using the Flourishing Scale and the Scale of Positive and Negative Experience, respectively. With the exception of sleep latency, our univariate analysis revealed significant associations between the abovementioned facets of sleep, and the affective components of subjective well-being. The analysis also revealed significant associations between the above sleep variables and psychological well-being, except sleep latency and frequency of sleep disturbances. Only daytime dysfunction was found to be significantly correlated with academic performance in our univariate analysis. In addition, our multivariate analysis shows that psychological well-being, affect balance and academic performance each has a direct effect on overall sleep quality. The relationship between overall sleep quality and psychological well-being is U-shaped, while that between overall sleep quality and affect balance is linear and moderated by psychological well-being. The relationship between overall sleep quality and academic performance is either U-shaped or an inverted-U, depending on the level of psychological well-being, which moderates the relationship. These nonlinear relationships indicate that individuals with the highest levels of psychological well-being are not the best sleepers (in terms of overall sleep quality), neither are the highest academic achievers necessarily the best sleepers.

Keywords: psychological well-being, positive/negative affect, overall sleep quality, academic performance, university students

OPEN ACCESS

Edited by:
Christian Franceschini, University of Parma, Italy

Reviewed by:
Gianluca Ficca, University of Campania 'Luigi Vanvitelli, Italy
Sara Marelli, Scientific Institute for Research, Hospitalization and Healthcare, Italy

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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *01 March 2021*
Accepted: *27 April 2021*
Published: *31 May 2021*

Citation:
Armand MA, Biassoni F and Corrias A (2021) Sleep, Well-Being and Academic Performance: A Study in a Singapore Residential College. Front. Psychol. 12:672238. doi: 10.3389/fpsyg.2021.672238

INTRODUCTION

It is known that sleep/wake timing shifts later due to pubertal changes of the circadian timing and homeostatic sleep systems during the second decade of life. Consequently, adolescents and young adults can experience sleep loss and excessive daytime sleepiness as they attempt to synchronize their natural delayed schedule with the requirements of everyday societal schedules such as school and office hours (Crowley et al., 2007; Alfonsi et al., 2020). University students living in halls of residence face additional challenges that can further affect their quality of sleep. Problems in their sleep environment may include noise and roommates' different habits (Qin and Brown, 2017). The demands to contribute to the communal life of the hall and to integrate socially in its high-density living environment (Zhai et al., 2018), the stress from short-term academic workload and long-term anxiety related to independent adult life (Lemma et al., 2012; Laidlaw et al., 2016), and the lack of knowledge and practice of good sleep hygiene (Suen et al., 2010; Dinis and Braganca, 2018), further add to these problems. Not surprisingly, university students are viewed as being chronically sleep-deprived (Curcio et al., 2006; Fonseca and Genzel, 2020).

Sleep and Well-Being

Since the 90's, psychological research has highlighted the fundamental subjective nature of well-being. Subjective well-being is defined as "a person's cognitive and affective evaluations of his or her life" (Diener et al., 2009) and comprises three components: satisfaction with life, presence of positive emotions and moods, and absence of negative emotions and moods. An individual is said to have high subjective well-being if she experiences high satisfaction with life, frequent positive affect and infrequent negative affect. Within the conceptual framework of well-being, the idea of psychological well-being emerged as a state in which an individual realizes her own potential, relating to the social and physical environment satisfactorily and being able to cope with stressors (Ryan and Deci, 2001; Keyes et al., 2002; Hernandez-Torrano et al., 2020). Given the U-shaped relationship between sleep duration and morbidity and mortality established in epidemiological studies (Ikehara et al., 2009; Kronholm et al., 2011; Li et al., 2015), a nonlinear relationship between sleep and well-being is expected (Hamilton et al., 2007b).

Richter (2015) found sleep deprivation to be negatively correlated with psychological well-being within a university student population. Zhai et al. (2018), taking into exam the role of sleep quality in the psychological well-being of final year undergraduate students, reported that poor sleep quality is associated with high levels of negative psychological well-being. Similarly, in a study involving subjects of age 18 and above (the majority being students), Freitag et al. (2017) found that sleep disturbances were related to decreased levels of psychological well-being. In addition, from a large sample of university students from 16 countries, Allgower et al. (2001) found that excessive (>9 h) or insufficient (<7 h) sleep was linked to increased risk in social isolation, thus implying an inverted U-shaped relationship between psychological well-being and sleep duration. Several studies have found sleep quantity and/or quality to be related to the affective components of subjective well-being. For example, Pilcher et al. (1997) found that average sleep quality was better related to affect balance than average sleep quantity among college students who slept an average of 7 h a night. Lemma et al. (2012) and Lund et al. (2010) found poor sleep quality among university students to be associated with higher degrees of negative affect including anger, confusion, depression and tension. Similarly, Li et al. (2020) found that both poor sleep quality and insufficient sleep were associated with depression in university students. Fulgini and Hardway (2006) found that shorter sleep was associated with more negative and less positive moods. Interestingly, Lima et al. (2018) reported a U-shaped relationship between happiness–which constitutes positive affect–and sleep duration in adults aged 20 and older, with a prevalence of unhappy individuals among short ($\leq$6 h) and excessively long ($\geq$9 h) sleepers.

Sleep and Academic Achievement

In the last decade, a number of studies on the interaction between subjective sleep and academic achievement of university students have emerged. Ahrberg et al. (2012), Baert et al. (2015), and Toscano-Hermoso et al. (2020) reported a positive relationship between sleep quality and academic scores. Gomes et al. (2011) found poor sleep quality and insufficient sleep to be significantly associated with poorer academic performance. Zeek et al. (2015) and Raley et al. (2016) similarly found that longer sleep the night prior to an examination was associated with higher course grades. Academic performance has also been found to be negatively correlated with sleep latency (Chiang et al., 2014; Leak et al., 2020). In addition, Datta et al. (2019) reported a substantially higher proportion of students with disturbed sleep among those with average exam marks compared to students with good marks. Similarly, Maheshwari and Shaukat (2019) found a negative association between frequency of sleep disturbances and GPA scores. They also reported that most students with low GPAs had sleep efficiencies of only 75–84% and experienced daytime dysfunction almost every day. Departing from these studies, Okano et al. (2019) found that both objective sleep quantity and quality for the month and week before a test positively correlated with academic grades.

There are nevertheless studies that report contrary findings. For example, Dokuka and Smirnov (2020) found high academic performance to be associated with shorter sleep among young adults between 20 and 21 years of age including university students. Also, Hangouche et al. (2018) did not find excessive daytime sleepiness (i.e., uncontrollable dozing off and drowsiness during the daytime) to be related to academic performance. At the other end of the spectrum, a few studies have reported no association between sleep and academic achievement. For example, Sweileh et al. (2011) and Jalali et al. (2020) found no significant difference in sleep quality between students with high grades and those with low grades. In addition, Eliasson et al. (2010) found that total sleep duration (from daytime naps plus nocturnal sleep) does not correlate with academic performance. In another objective sleep study, King et al. (2018) reported no difference in project grades between students who averaged

at least 8 h of sleep for five nights leading up to the project's due date and those who did not. In short, recent findings reported in the literature on the relationship between sleep and academic performance have not fully converged to a consensus, as noted by Jalali et al. (2020).

The Present Study

The present study had two main objectives. The first was to understand how psychological well-being, the affective components of subjective well-being, and academic performance are related to self-reported sleep of full-time undergraduate students residing at the College of Alice and Peter Tan (CAPT) at the National University of Singapore. The targeted endpoint was a model for subjective sleep quality that would reveal the nature of these relationships (e.g., linear versus quadratic) and how the different dependent variables might interact. The second objective was to compare how CAPT students fair compared to university students in other countries in terms of subjective sleep quality as well as psychological and affective well-being.

MATERIALS AND METHODS

Instruments

The Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) is a self-rated questionnaire which assesses sleep quality and disturbances over a 1-month time interval. It measures seven dimensions of sleep: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, frequency of various sleep disturbances, frequency of usage of sleep medication, and frequency and severity of daytime dysfunction. Each subscale is scored on a 4-point scale ranging from 0 to 3. Summing the score of all seven subscales yields the Global PSQI score which represents overall sleep quality. The Global PSQI score therefore ranges between 0 and 21. A higher Global PSQI indicates poorer overall sleep quality. A higher score for each subscale is likewise a poorer score. An individual with a Global PSQI score greater than 5 is viewed to be a poor sleeper (Buysse et al., 1989). Conversely, an individual with a Global PSQI score not exceeding 5 is considered a good sleeper. The PSQI questionnaire consists of 10 questions of which Q.1–Q.9 are designed for self-assessment while Q.10 is to be completed by a roommate or bed partner, based on sleeping patterns over the past month. The rooms at the residential college considered in this study are all individual rooms and, as such, Q.10 was not scored, and only Q.1–Q.9 were used in our survey.

In the PSQI scoring procedure, the scores assigned to Q.5b–Q.5j are added together and the sum, which ranges between 0 and 27, is then mapped to a final score ranging between 0 and 3 to represent the frequency of sleep disturbances. Since this mapping causes us to lose the granularity of the information inherent in the original sum (e.g., distinct sums such as two and eight become indistinguishable once mapped to one), we used the sum and not the final score as the measure of this sleep dimension. Larger sums represent higher frequencies of sleep disturbances. For the same reason, we used the sum of scores assigned to Q.8 and Q.9 and not the final score derived from the sum, to represent the extent of daytime dysfunction experienced. Similarly, a larger sum represents more frequent and/or more severe daytime dysfunction.

The Scale of Positive and Negative Experience (SPANE; Diener et al., 2010) is a 12-item questionnaire designed to assess subjective feelings of well-being and ill-being, that is to measure the affective components of well-being. Six items measure the frequency of experiencing a range of positive feelings over the past four weeks, while the other six measure the frequency of experiencing a range of negative feelings over the same period. Each item is scored using a 5-point scale ranging from 1 to 5, with larger scores representing higher frequencies. Summing the scores for the six items measuring positive (respectively, negative) affect yields the overall positive (respectively, negative) affect score, denoted SPANE-P (respectively, SPANE-N), which ranges between 6 and 30. Larger SPANE-P (respectively, SPANE-N) scores represent higher frequencies of experiencing positive (respectively, negative) affect. Subtracting SPANE-N from SPANE-P yields the affect balance score, denoted SPANE-B, which ranges between -24 and +24. Increasingly positive (respectively, negative) SPANE-B scores represent increasingly higher (respectively, lower) frequencies of experiencing positive affect compared to negative affect. For both the positive and negative items, three of the items are general (e.g., positive and negative) and three per subscale are more specific (e.g., joyful and sad). Because of the general items included in the scale, it can assess not only the pleasant and unpleasant emotional feelings that are the focus of most scales, but also reflect other states such as interest, flow, positive engagement, and physical pleasure.

The Flourishing Scale (FS; Diener et al., 2010), is a brief 8-item summary measure of the respondent's self-perceived success in important areas such as relationships, self-esteem, purpose, and optimism. The scale provides a single psychological well-being score. The survey comprises several items on satisfaction with social relationships (having supportive and rewarding relationships, contributing to the happiness of others, and being respected by others), an item on having a purposeful and meaningful life, and one on being engaged and interested in one's activities, and one on feeling competent and capable in the activities that are important to the respondent. Finally two items are included tapping self-respect and optimism. Thus, FS assesses major aspects of social–psychological functioning from the respondent's own point of view. Each item is scored using a 7-point scale ranging from 1 to 7 to represent strongly disagree to strongly agree. Summing the scores yields the (overall) FS score which ranges between 8 and 56. An individual with a high FS score has many psychological resources and strengths (Diener et al., 2010).

Participants and Bad Data Points

As previously mentioned, the subjects of our study were full-time undergraduate students from the College of Alice and Peter Tan (CAPT), a residential college within the National University of Singapore. In any given semester, the college is home to approximately 500 students. The gender ratio in the population is close to 50–50 with a slight predominance of female students. The age range of female students is 18–22 while that of male students

is 18–24. The wider age range among male students is due to the national service obligations that Singaporean males have to fulfill prior to entering university. In total, 144 students participated in the survey. Demographic data, such as age and gender, was not captured in the survey.

Upon inspecting the completed questionnaires, we found meaningless responses from four participants pertaining to Q.1–Q.4 in the PSQI questionnaire, which we believe to be mainly due to the open-ended nature of these four questions. Two of these participants answered "all the time" and "Yes" in response to Q.3 instead of stating their typical waking times, thus rendering the data they provided incomplete. The other two participants provided answers to Q.1, Q.2, and Q.4 that resulted in sleep efficiencies (i.e., the percentage of hours slept of the total time in bed) that did not make sense, such as 133%. These four participants were therefore removed from our sample, reducing our sample size to 140.

Note, however, that not all the participants had a CAP at the time the survey was conducted. This is due to the fact that some respondents were freshmen in their first semester at NUS and therefore had not yet obtained any grade. Consequently, for analyses involving academic performance, the sample size had to be further reduced to 106.

Statistical Methods

In our univariate analyses, we examined the strength of association between sleep and psychological well-being, as well as between sleep and CAP scores, using the Spearman rank correlation coefficient as well as the Kendall rank correlation coefficient (As both correlation measures resulted in the same set of statistically significant associations, we report our findings in terms of the former measure for brevity). We did not use the Pearson product-moment correlation coefficient for cases where the variables were both continuous to take into account the possibility of nonlinear relationships between such variables.

For our multivariate analysis, we used moderated linear regression to model overall sleep quality. The dependent variable is Global PSQI while the linear terms among the independent variables are SPANE-B, FS, and CAP. As we believed that the relationship between overall sleep quality, and SPANE-B, FS, and CAP, could be nonlinear, we included quadratic terms SPANE-B^2, FS^2, and CAP^2. As we also believed that these 6 explanatory variables may interact, the following second and third order product terms were included: SPANE-B × FS, SPANE-B × FS^2, SPANE-B^2 × FS, CAP × SPANE-B, CAP × SPANE-B^2, CAP^2 × SPANE-B, CAP × FS, CAP × FS^2, and CAP^2 × FS. Consequently, we had a total of 15 explanatory variables to begin with. To reduce multicollinearity, we adopted the standard practice of mean-centering the linear terms (Iacobucci et al., 2016). For example, each FS score was transformed by subtracting the sample mean m_{FS} of the FS scores. Squaring the transformed linear terms then yielded the corresponding quadratic terms. From the six transformed linear and quadratic terms, the corresponding second and third-order product terms were then generated. The resulting transformed variables are distinguished from the original ones by adding the prefix "c" to each variable's label. For instance, the transformed versions of FS, FS^2, and FS^2 × CAP are denoted cFS, cFS^2, and cFS^2 × cCAP, respectively. Finally, backward elimination was applied on the transformed explanatory variables. That is, starting with all 15 of them, the least significant variable was discarded one by one until only significant variables remain–a variable is viewed to be insignificant if its p-value is 0.05 or greater.

To compare the sleep quality and well-being of CAPT students to that of other student populations, we used a two-tailed Welch's t-test to conduct two (independent) sample means tests with unequal variance. The sample means involved in these tests were the mean SPANE-P, SPANE-N, FS, and Global PSQI scores. Even though the frequency distributions of these variables are skewed, there are sound reasons to use Welch's t-test instead of a non-parametric test. Firstly, due to the Central Limit Theorem, the t-test is increasingly robust to deviations from normality as sample size increases, and is robust even to heavily skewed distributions when the sample size is 200 (Fagerland and Sandvik, 2009). In addition, Fagerland (2012) compared the rejection rates of the Wilcoxon rank sum test and Welch's t-test for samples drawn from pairs of Gamma and lognormal distributions of increasing sizes. For both distribution types, it was observed that the rejection rate of the Wilcoxon rank sum test increases rapidly with sample size whereas the rejection rate of the t-test remains stable at roughly the expected rejection rate of an unbiased test. Consequently, Fagerland (2012) asserts that non-parametric tests are most useful for small studies but for large sample sizes, t-tests should be used, even for heavily skewed data. Lumley et al. (2002) similarly showed that the t-test can perform well in moderately large sample sizes even for very non-normal distributions.

Procedure

College of Alice and Peter Tan students were invited via email to participate in an online survey comprising the above three instruments plus a question to indicate their CAP score if they had one. The online survey was accessible to students for a period of three weeks, during which they could complete the different questionnaires at their own pace. To mitigate the risk that students do not complete the survey within the 3-weeks time frame, several student leaders within CAPT were engaged to help promote the survey among their peers. Each participant was given a $5 supermarket voucher as a token of appreciation for completing the survey.

In particular, they received information that their participation in the present study was voluntary and that they could withdraw at any moment without any consequence in which case, their collected data would be discarded immediately. The study obtained the approval of the National University of Singapore's Institutional Review Board.

RESULTS

The Relationship Between Sleep and Well-Being/Academic Performance

Recall, the different aspects of sleep considered were (i) overall sleep quality, i.e., the Global PSQI score, (ii) sleep duration (in

TABLE 1 | Spearman's correlation between different sleep and well-being measures and the corresponding *p*-values.

	Global PSQI	Sleep Duration	Sleep Efficiency	Freq. of Sleep Disturbance	Daytime Dysfunction	Sleep Latency
SPANE-P	−0.441 (4.96E-8**)	0.189 (0.025*)	0.245 (3.46E-3**)	−0.211 (0.012*)	−0.354 (1.75E-5**)	−0.046 (0.587)
SPANE-N	0.348 (2.55E-5**)	−0.120 (0.157)	−0.078 (0.359)	0.190 (0.025*)	0.384 (2.85E-6**)	0.044 (0.607)
SPANE-B	−0.454 (1.71E-8**)	0.169 (0.046*)	0.176 (0.038*)	−0.232 (5.76E-3**)	−0.421 (2.25E-7**)	−0.073 (0.388)
FS	−0.374 (5.24E-6**)	0.253 (2.53E-3**)	0.177 (0.037*)	−0.074 (0.388)	−0.291 (4.91E-4**)	−0.047 (0.581)
CAP	−0.114 (0.245)	−0.019 (0.85)	−0.082 (0.402)	−0.156 (0.111)	−0.240 (0.013*)	−0.166 (0.089)

**Denotes $p < 0.05$. **Denotes $p < 0.01$.*

hours), (iii) sleep efficiency, (iv) frequency of sleep disturbances, (v) daytime dysfunction, and (vi) sleep latency (in minutes). **Table 1** summarizes the resulting correlation coefficients and corresponding *p*-values (two-tailed).

Both Global PSQI and daytime dysfunction correlate moderately with the four well-being measures (All eight correlation indices are significant at the 0.01 level). Sleep duration and sleep efficiency, on the other hand, correlate weakly with SPANE-P, SPANE-B, and FS (All eight correlation indices in this case are significant at the 0.05 level or lower). Similarly, the correlation indices of frequency of sleep disturbance and SPANE-P, SPANE-N, and SPANE-B are weak but statistically significant at the 0.05 level or lower. Sleep duration and sleep efficiency, and frequency of sleep disturbance, do not appear to be related to SPANE-N and FS, respectively.

Turning to academic performance, we see that daytime dysfunction correlates weakly with CAP scores (The correlation index is significant at the 0.05 level). There is, however, insufficient evidence of any association between CAP scores and the other sleep variables including Global PSQI.

A Model for Overall Sleep Quality

In this section, we present a model–called the *full* model–for overall sleep quality obtained through moderated linear regression. **Table 2** summarizes the results of the final iteration of the backward elimination procedure. From this table, we have the following regression equation:

$$\begin{aligned}\text{Global PSQI} \;=\; & b_0 + b_2\text{cFS}^2 + \left(b_1 + b_4\text{cFS}\right. \\ & \left. + b_5\text{cFS}^2\right)\text{cSPANE-B} + \left(b_3 + b_6\text{cFS}\right)\text{cCAP}^2.\end{aligned}$$

The left-hand side of the equation should be understood to mean the fitted value of Global PSQI for a given set of values for cFS, cSPANE-B, and cCAP. Evidently, all six explanatory variables in the equation are significant. We see that psychological well-being is quadratically related to overall sleep quality, after controlling for the other variables in the model, i.e., when the other variables–in their original form–assume their respective mean values. In addition, there is a linear relationship between overall sleep quality and affect balance, after controlling for the other variables in the model, and this relationship is moderated by psychological well-being. Further, there is a quadratic relationship between overall sleep quality and academic performance, after controlling for the other variables, and this relationship is also moderated by psychological well-being. The constant, b_0, is the expected value of Global PSQI

TABLE 2 | Effects of the Scale of Positive and Negative Experience (SPANE)-B, Flourishing Scale (FS), and Cumulative Average Point (CAP) on Global Pittsburgh Sleep Quality Index (PSQI) in the full, reduced, and reduced-plus models.

Full model

Independent variables	Slope, b_i	Std. error	*t*-statistic	*p*-value
(0) Constant	6.608			
(1) cSPANE-B	−0.148	0.032	−4.704	8.27E-6**
(2) cFS^2	−2.62E-3	1.22E-3	−2.147	0.034*
(3) $cCAP^2$	2.369	0.755	3.139	2.24E-3**
(4) cFS × cSPANE-B	5.11E-3	2.06E-3	2.484	0.015*
(5) cFS^2 × cSPANE-B	2.66E-4	1.33E-4	1.992	0.049*
(6) cFS × $cCAP^2$	−0.532	0.118	−4.490	1.93E-5**
R^2 =0.411				
Std. Error =1.787				
F-statistic =11.508				
p-value of *F* =9.80E-10**				

Reduced model

Independent variables	Slope	Std. error	*t*-statistic	*p*-value
(0) Constant	6.535			
(1) cSPANE-B	−0.122	0.024	−5.081	1.70E-6**
(2) cFS^2	3.03E-5	0.001	0.030	0.976
(3) $cCAP^2$	1.854	0.835	2.221	0.029*
R^2 =0.241				
Std. Error =1.998				
F-statistic =10.817				
p-value of *F* =3.13E-6**				

Reduced-plus model

Independent variables	Slope	Std. error	*t*-statistic	*p*-value
(0) Constant	7.021			
(1) cSPANE-B	−0.073	0.026	–2.796	6.19E-3**
(2) cFS	−0.098	0.026	–3.761	2.84E-4**
(3) cFS^2	–3.96E-3	1.42E-3	–2.788	6.34E-3**
(4) $cCAP^2$	1.708	0.787	2.172	0.032*
R^2 =0.335				
Std. Error =1.881				
F-statistic =12.693				
p-value of *F* =2.09E–8**				

**Denotes $p < 0.05$. **Denotes $p < 0.01$.*

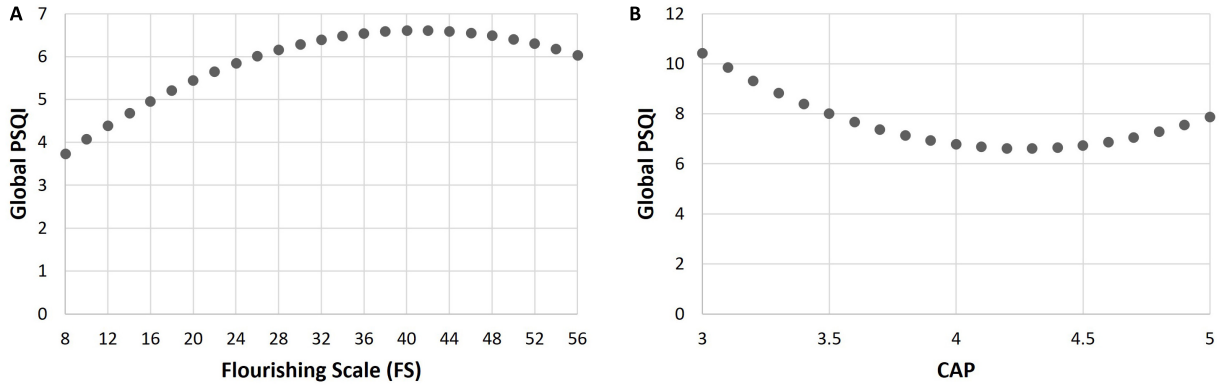

FIGURE 1 | Relationship between global Pittsburgh Sleep Quality Index (PSQI) and Flourishing Scale (FS) scores in panel **(A)**, and that between Global PSQI and Cumulative Average Point (CAP) scores in panel **(B)**, after controlling for the other variables in the full model.

when SPANE-B, FS, and CAP assume their mean values of 4.264, 41.123, and 4.269, respectively.

The abovementioned quadratic relationship between Global PSQI and FS, which is inverted U-shaped, is shown in **Figure 1A**, while that between Global PSQI and CAP is shown in **Figure 1B**. The turning points of these curves coincide with the mean FS score and mean CAP score, respectively. Although the latter relationship is depicted as being U-shaped, note that this is not always the case. One readily checks that the sign of the coefficient $\left(b_3 + b_6\text{cFS}\right)$ of cCAP^2 in the above regression equation is negative for FS scores 46 and above (i.e., $\geq m_{\text{FS}} + 0.45s_{\text{FS}}$ where s_{FS} denotes the standard deviation of the FS scores), and positive otherwise.

If we remove the interaction terms from our full model (other than the quadratic terms) to obtain a *reduced* model, the effects of the remaining independent variables on overall sleep quality are as shown in **Table 2**. The change in R^2 between the full and reduced model is 0.170, for which the associated p-value is 1.43E-5. This provides evidence that there is significant interaction between psychological well-being and affect balance, and between psychological well-being and academic performance.

The slope corresponding to cFS^2 in the reduced model is nevertheless not significant. Beginning with cSPANE-B, cFS, cCAP, cSPANE-B^2, cFS^2, and cCAP^2 and applying backward elimination, however, yields a model that also contains the three independent variables in the reduced model, plus the linear term, cFS. **Table 2** summarizes the effects of these four variables on overall sleep quality in this model, which we refer to as the *reduced-plus* model. The change in R^2 between the full model and the reduced-plus model is 0.076, for which the corresponding p-value is 2.40E-3. The full model therefore provides a significant improvement over the reduced-plus model in the quality of fit as measured by R^2.

A visualization of the contrasting effects on overall sleep quality at low and high levels of psychological well-being in our full model is provided by the interaction plots in **Figures 2A,B**. The plots in Panel A (respectively, B) correspond to SPANE-B $= m_{\text{SB}} + s_{\text{SB}} = 12.596$ (respectively, SPANE-B $= m_{\text{SB}} - s_{\text{SB}} = -4.067$) where m_{SB} and s_{SB} denote the mean and standard deviation of SPANE-B scores, respectively. Similarly, we take FS $= m_{\text{FS}} + s_{\text{FS}} = 51.967$ and FS $= m_{\text{FS}} - s_{\text{FS}} = 30.279$ to represent high and low levels of psychological well-being, and refer to these values as *high* FS and *low* FS, respectively.

The linear relationship between Global PSQI and SPANE-B is negative with a steeper (respectively, gentler) slope at low (respectively, high) levels of psychological well-being, as depicted by the interaction plot in **Figure 2C** for which CAP is held constant at the mean. At low (respectively, high) FS, the slope is $b_1 - b_4 s_{\text{FS}} + b_5 s_{\text{FS}}^2 = -0.172$ (respectively, $b_1 + b_4 s_{\text{FS}} + b_5 s_{\text{FS}}^2 = -0.062$). In other words, the expected increase in Global PSQI for a unit decrease in SPANE-B is 0.17 at low FS and 0.06 at high FS. A drop from high to low affect balance therefore translates to an expected increase in Global PSQI of 2.87 at low FS and 1.03 at high FS.

Finally, observe that for a given CAP score (other than the mean CAP), the instantaneous rate of change in overall sleep quality differs at low and high levels of psychological well-being. It is specified by the partial derivative of the regression equation with respect to cCAP, which by the chain rule, can be rewritten as

$$\frac{d\ \text{Global PSQI}}{d\ \text{CAP}} = 2\left(b_3 + b_6\text{cFS}\right)\text{cCAP}.$$

Figure 2D shows the instantaneous rate of change for low and high levels of psychological well-being.

The expected change in Global PSQI for a unit increase in CAP is then given by:

$$\frac{2\left(b_3 + b_6\text{cFS}\right)\text{cCAP} + 2\left(b_3 + b_6\text{cFS}\right)(\text{cCAP} + 1)}{2}$$
$$= \left(b_3 + b_6\text{cFS}\right)(2\text{cCAP} + 1).$$

Similarly, the expected change in Global PSQI for a unit decrease in CAP is

$$\left(b_3 + b_6\text{cFS}\right)(2\text{cCAP} - 1).$$

For example, at low FS, the expected change in Global PSQI corresponding to an increase in CAP from 3.0 to 4.0

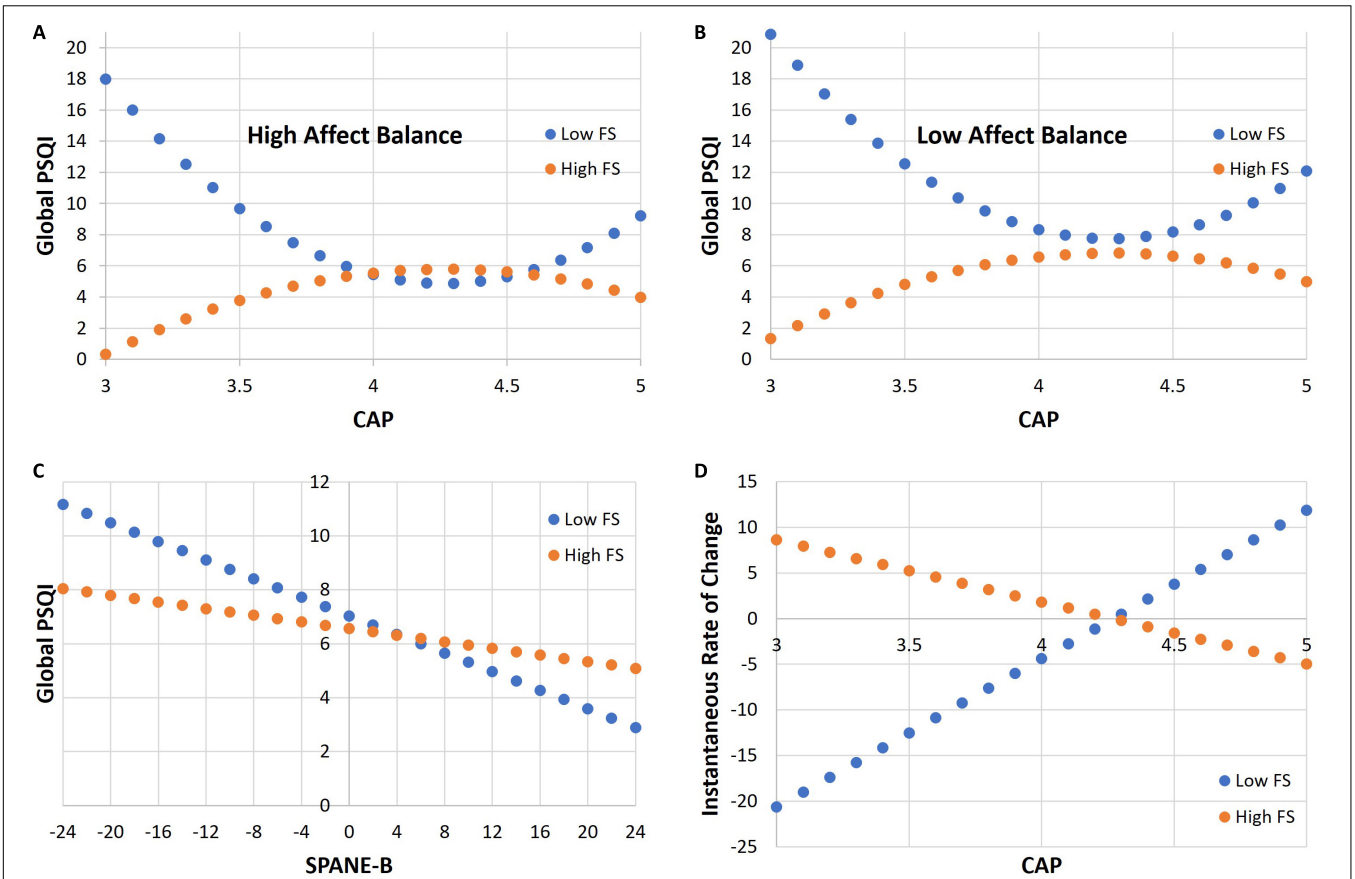

FIGURE 2 | Interaction plots of Global PSQI versus cumulative average point (CAP) scores for high affect balance in panel **(A)**; Interaction plots of Global PSQI versus CAP scores for low affect balance in panel **(B)**; Interaction plot of Global PSQI versus Scale of Positive and Negative Experience (SPANE)-B scores in panel **(C)**; Instantaneous rate of change in Global PSQI for low and high levels of psychological well-being in panel **(D)**.

is $\left(b_3 - b_6 s_{\mathrm{FS}}\right)\left(2 \times (3 - m_{\mathrm{CAP}}) + 1\right) = -12.52$ where m_{CAP} denotes the mean CAP. At high FS, however, the expected change is $\left(b_3 + b_6 s_{\mathrm{FS}}\right)\left(2 \times (3 - m_{\mathrm{CAP}}) + 1\right) = 5.23$.

Global PSQI, SPANE, and FS Scores of Other Student Populations

The overall sample mean, SD, median and interquartile range (IQR) of the Global PSQI, SPANE, and FS scores for the 140 CAPT students surveyed are presented in **Table 3**. For the purpose of comparison, we present in **Table 4** the mean and standard deviation of the SPANE-P and SPANE-N scores of n university students in seven countries: United States (Diener et al., 2010), Canada (Howell and Buro, 2015), Germany (Rahm et al., 2017), Portugal (Silva and Caetano, 2013), Japan (Sumi, 2014), Singapore (Diener et al., 2010), and South Africa (du Plessis and Guse, 2016). The students in Singapore were from the Singapore Management University (SMU). Where available, we also include in **Table 4** the mean and standard deviation of the FS scores of these student populations.

The last 3 columns of **Table 4** summarizes the p-values resulting from the application of Welch's t-test to compare the means presented in **Table 3** and their counterparts in **Table 4** (Note that infinitesimally small p-values are denoted by ε). For SPANE-P scores, the differences in the mean between CAPT students and students in United States, Canada, Germany and Portugal are significant at the 0.05 level or lower. On the other hand, the differences are not significant when comparing with students in Japan, South Africa, and not surprisingly, SMU. For SPANE-N scores, only the differences in the mean between CAPT students and students in Japan and SMU are not significant.

Finally, to determine if CAPT students also have poorer overall sleep quality compared to student populations elsewhere, we summarize in **Table 5** the mean and standard deviation of the

TABLE 3 | Descriptive statistics of Global Pittsburgh Sleep Quality Index (PSQI), Scale of Positive and Negative Experience (SPANE), and Flourishing Scale (FS) scores for College of Alice and Peter Tan (CAPT) students.

	Mean (SD)	Median (IQR)
Global PSQI	6.86 (2.25)	7 (5–8)
SPANE-P	21.17 (4.60)	22 (18–24)
SPANE-N	16.89 (4.49)	17 (14–20)
SPANE-B	4.28 (8.08)	4.5 (-1–10)
FS	41.58 (10.12)	44 (38–48)

TABLE 4 | Mean and standard deviation of Scale of Positive and Negative Experience (SPANE) and Flourishing Scale (FS) scores of other university student populations.

	n	SPANE-P Mean (SD)	SPANE-N Mean (SD)	FS Mean (SD)	SPANE-P *p*-value	SPANE-N *p*-value	FS *p*-value
United States	168	23.10 (3.20)	14.50 (3.60)	48.10 (4.90)	3.90E-5**	7.00E-7**	ε**
Canada	478	22.49 (4.08)	15.78 (4.07)	46.69 (6.73)	2.50E-3**	9.27E-3**	8.00E-8**
Germany	498	22.25 (3.88)	14.31 (4.24)		0.012*	ε**	
Portugal	194	23.51 (4.03)	13.30 (4.66)	44.51 (4.86)	2.28E-6**	ε**	1.77E-3**
Japan	520	21.01 (4.50)	16.61 (4.87)	36.63 (8.05)	0.714	0.521	2.60E-7**
Singapore	181	20.80 (3.60)	17.00 (4.00)	42.60 (6.40)	0.434	0.820	0.299
South Africa	992	21.91 (3.81)	15.96 (3.94)		0.071	0.021*	

**Denotes p < 0.05. **Denotes p < 0.01.*

TABLE 5 | Mean and standard deviation of Global Pittsburgh Sleep Quality Index (PSQI) scores of other university student populations.

	n	Global PSQI Mean (SD)	*p*-value
United States	243	5.6 (3.4)	1.73E-5**
Brazil	710	6.5 (2.6)	0.094
Belgium	621	4.802 (2.228)	ε**
Luxembourg and Germany	2831	7.22 (3.70)	0.077
Taiwan	4318	6.0 (2.5)	1.77E-5**
Indonesia	450	8.40 (3.64)	ε**
Nigeria	520	4.43 (2.67)	ε**
This study	140	6.86 (2.25)	

***Denotes p < 0.01.*

Global PSQI scores of *n* university students in eight countries: United States (Carney et al., 2006), Brazil (Mesquita and Reimao, 2010), Belgium (Baert et al., 2015), Luxembourg and Germany (Schlarb et al., 2017), Taiwan (Cheng et al., 2012), Indonesia (Herawati and Gayatri, 2019), and Nigeria (Aloba et al., 2007). For easy visual comparison, the last row of **Table 5** presents the corresponding numbers for CAPT students. The last column of the table presents the *p*-values resulting from the application of Welch's *t*-test to compare the mean Global PSQI score of CAPT students and that of these other student populations. Evidently, only the differences in the means between CAPT students and students in Brazil, and Luxembourg and Germany are not significant.

DISCUSSION

In the following discussion, it is convenient to interpret sleep duration as sleep *quantity*, and sleep efficiency, frequency of sleep disturbance, daytime dysfunction and sleep latency as individual measures of sleep *quality* (since they contribute to the overall sleep quality measure, i.e., the Global PSQI score). Also, since higher Global PSQI scores represent poorer overall sleep quality, the direction of the relationships presented in Section "A Model for Overall Sleep Quality" involving Global PSQI will have to be flipped when speaking in terms of overall sleep quality.

Reconciling Inconsistency Between the Univariate and Multivariate Analyses

It is interesting to note that despite Global PSQI and FS having a non-monotonic relationship as revealed by our multivariate analysis, we obtained a significant, negative Spearman correlation between the two variables, as reported in **Table 1**. We believe that this is due to the frequency distribution of FS scores which has a skew of -1.15 and so is highly left-skewed. In other words, the left-tail of the distribution is very long and thin, with the majority of the values falling to the right of the mean, as shown in **Figure 3A**. The relationship between Global PSQI and CAP is likewise non-monotonic. However, Spearman's correlation between Global PSQI and CAP is not significant, as highlighted in Section "The Relationship Between Sleep and Well-Being/Academic Performance". We believe that there are two main reasons. Firstly, the frequency distribution of CAP scores is apparently bimodal with one mode falling on each side of the mean, which implies that both the left and right shoulders of the distribution are pronounced, as shown in **Figure 3B**. Secondly, and as a consequence of the first reason, the distribution has a skew of -0.58 and therefore is only moderately left-skewed.

Sleep and Psychological Well-Being

Contrary to the findings of Freitag et al. (2017), our univariate analysis did not reveal any relationship between frequency of sleep disturbances and psychological well-being. Our analysis, however, revealed that sleep duration has a positive association with psychological well-being, a result that is consistent with the findings of Richter (2015). Similarly, just as Zhai et al. (2018) found a strong relationship between sleep quality and psychological well-being, our univariate analysis showed that sleep efficiency and overall sleep quality are significantly and positively correlated with the same.

Our multivariate analysis nevertheless informs that the positive association between overall sleep quality and psychological well-being is only true for above average levels of the latter. Specifically, it showed that psychological well-being has a direct, U-shaped quadratic relationship with overall sleep quality. The turning point of this quadratic relationship coincides with the mean level of psychological well-being. Thus, for above (respectively, below) average levels of psychological well-being, overall sleep quality improves with increasing

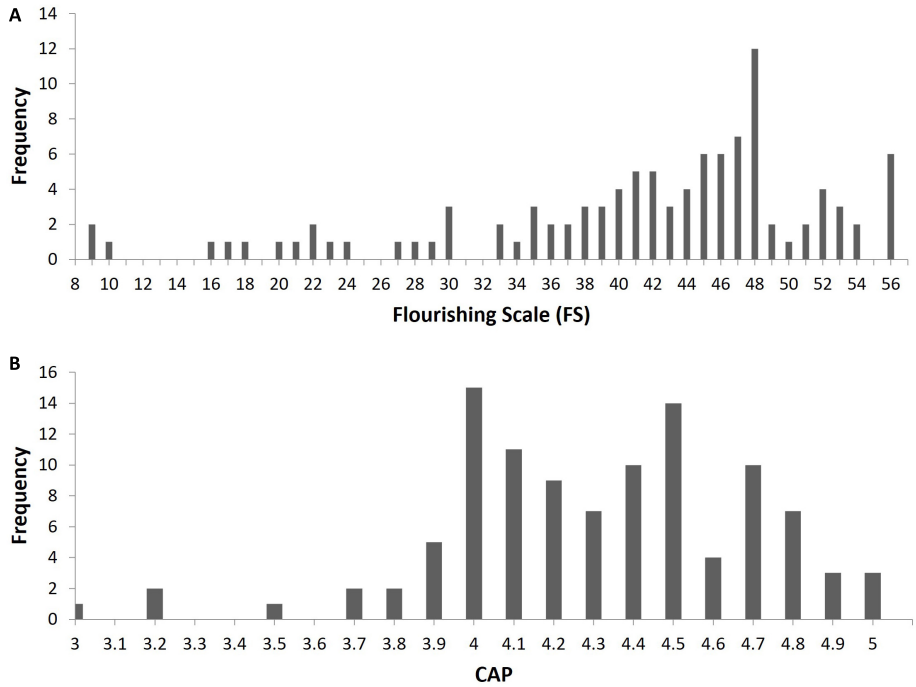

FIGURE 3 | Frequency distribution of Flourishing Scale (FS) scores in panel **(A)**; frequency distribution of Cumulative Average Point (CAP) scores in panel **(B)**.

(respectively, decreasing) levels of psychological well-being. This curvilinear relationship suggests that attaining increasingly greater psychosocial prosperity up to a certain point comes at the price of deteriorating overall sleep quality. Beyond that point, however, overall sleep quality starts to improve, meaning that above average levels of psychological well-being may be viewed as a resource for regulating overall sleep quality.

To provide a speculative explanation for this curvilinear relationship, we tap on recent findings pertaining to the relationship between perceived stress and sleep quality. Firstly, resilience has been found to be highly and positively correlated with psychological well-being among university students (Pidgeon and Keye, 2014). Secondly, it moderates (i.e., weakens) the relationship between perceived stress and sleep quality (Li et al., 2019; Du et al., 2020). We also extend the notion of sleep quality affording a protective value on subjective well-being (Weinberg et al., 2016), to psychological well-being. Finally, we make use of the fact that among the Big Five personality traits, neuroticism has been consistently found to be related to poorer psychological well-being (Brown and Ryan, 2003).

With that, we hypothesize that as an individual with poor psychological well-being starts to strengthen or expand her network of social relationships, find more purpose and meaning in her life and so on, the perceived stress engendered in the process, grows in intensity. Her level of resilience at this stage is, however, too low to negate the negative effects of the perceived stress on her overall sleep quality. On the other hand, the decrease in sleep quality is not enough to suppress the protective value it affords on her psychological well-being, thus enabling her to perceive an elevated level of the same. This trend of deteriorating overall sleep quality (but improving psychological well-being) continues until a certain level of psychological well-being unique to the individual is reached. At this point, the individual's increased level of resilience is sufficiently high to negate the effects of the perceived stress on sleep. This paves the way for the trend to reverse, with the achieved higher level of psychological well-being now serving to promote better sleep (Steptoe et al., 2008).

We expect this reversal to take place gradually, since **Figure 1A** shows an inverted "U" rather than an inverted "V". In other words, the transition from overall sleep quality protecting psychological well-being, to the latter promoting the former, is a gradual process.

Sleep and the Affective Components of Subjective Well-Being

Our univariate analysis revealed that sleep quantity and the aforementioned sleep quality measures correlated significantly with positive affect and affect balance, with the exception of sleep latency which did not appear to have any association with the affective components of subjective well-being. These results are consistent with the findings of other studies, for instance, Steptoe et al. (2008), which reported a negative association between sleep problems and positive affect, Pilcher et al. (1997), which found both sleep quantity and quality to be related to affect balance, and (Fulgini and Hardway, 2006), which found shorter sleep to be associated with less positive moods. Congruent with findings by Lund et al. (2010), Lemma et al. (2012), and Li et al. (2020), we also found that an increase in negative affect significantly correlates with increasing frequency of sleep

disturbance and daytime dysfunction. Overall, these results are consistent with the theoretical model due to Zohar et al. (2005) and Hamilton et al. (2007a) in which sleep is a resource for regulating emotional responses to goal-disruptive/-enhancing events including stressful situations.

Adding to the literature that affect balance is a resource for regulating overall sleep quality, our multivariate analysis further showed that overall sleep quality decreases linearly with affect balance, and that this relationship is moderated by psychological well-being; at lower (respectively, higher) levels of psychological well-being, the decline in overall sleep quality with affect balance is faster (respectively, slower). To provide a speculative explanation for this moderating effect, we tap on a recent finding by Ding et al. (2020) that neuroticism moderates the direct effect of trait mindfulness on sleep quality in a university student population. A higher level of trait mindfulness is associated with less sleep disturbance and hence better sleep (Garland et al., 2013). Individuals high in neuroticism, however, tend to pay more attention to negative stimuli which contributes to the maintenance of sleep disturbances (Ding et al., 2020). Thus, neuroticism serves to weaken the positive effect of trait mindfulness on sleep quality. Since neuroticism is consistently found to be associated with lower levels of psychological well-being (Brown and Ryan, 2003), we can expect that as a consequence of a negative experience (resulting in a decrease in affect balance), an individual with poor psychological well-being will have more sleep disturbance compared to one who is high in the same.

Sleep and Academic Performance

Consistent with the findings of other studies (Barahona-Corea et al., 2018; Maheshwari and Shaukat, 2019), our univariate analysis showed that daytime dysfunction was significantly correlated with CAP scores. Taking CAP to be indicative of academic performance for the semester that our survey was conducted, this result is not surprising since one would expect higher academic achievement with the absence of excessive daytime sleepiness and presence of enthusiasm to study, complete assignments and so on. Due to inconsistencies in the literature concerning the relationship between excessive daytime sleepiness and academic performance (Hangouche et al., 2018), we hypothesize that impaired sleep negatively impacts academic performance more through the consequential loss of enthusiasm to get things done–including academic motivation–than excessive daytime sleepiness. Our univariate analysis, however, did not reveal any association between sleep quantity and the other sleep quality measures with CAP. These results are consistent with the findings of Eliasson et al. (2010), Sweileh et al. (2011), Jalali et al. (2020), and King et al. (2018).

Our multivariate analysis revealed that academic performance is quadratically related to overall sleep quality, and this relationship is moderated by psychological well-being such that at low levels of psychological well-being, this relationship is an inverted-U while at high levels, it is U-shaped. Together, these U-shaped and inverted U-shaped relationships indicate that poor sleepers can have good CAPs and good sleepers can have poor CAPs. Indeed, such students were found within our sample. For example, the top student with the highest CAP among the poor sleepers typically went to bed at 3.30 a.m. and had 4.5 h of sleep out of the total time of 6 h in bed, which translates to a poor sleep efficiency of 75%. With 1.5 h of remaining awake in bed on average each night, that student clearly suffered from pronounced sleep disturbances. Not surprisingly, that student had a severe Global PSQI score of 11. Yet, he or she had a CAP of 4.92 (or 1.72 standard deviations above the mean). In contrast, the student with the lowest CAP among the good sleepers had a good Global PSQI score of 4, but a CAP of 3.63 (or 1.69 standard deviations below the mean).

The interaction plots shown in **Figures 2A,B** suggest that among CAPT students with low levels of psychological well-being, those with low affect balance will, on average, have substantially poorer overall sleep quality than those with the same CAP score but high affect balance. Among CAPT students with high levels of psychological well-being, however, those with low affect balance only have slightly poorer overall sleep quality compared to those with the same CAP but high affect balance, on average. These observations are congruent with the differing slopes shown in **Figure 2C**.

The remainder of this subsection serves to provide a speculative explanation for the trends shown in **Figures 2A,B**. For brevity, we focus on the "middle ground" of the two scenarios depicted, i.e., the case of *mean* affect balance. In this case, the two quadratic curves meet precisely at their turning points. Since the turning points coincide with the mean CAP score, we can speak of four types of students: those with *low* levels of psychological well-being and *below average* CAPs (Type 1) versus *above average* CAPs (Type 2), and those with *high* levels of psychological well-being and *below average* CAPs (Type 3) versus *above average* CAPs (Type 4).

Sutin et al. (2020) summarized that among the Big Five personality traits, lower levels of extraversion and conscientiousness and higher levels of neuroticism are associated with poorer sleep, while openness to experience and agreeableness are not associated consistently with sleep quality. Moreover, Duggan et al. (2014) found that low conscientiousness and high neuroticism are the best predictors of poor sleep. Thus, we expect Type 1 and 2, and Type 3 and 4 students to be higher in neuroticism and conscientiousness, respectively. Hakimi et al. (2011) found that all the Big Five personality traits were related to GPA scores; conscientiousness was positively correlated and was the strongest predictor, followed by neuroticism which was negatively correlated.

Next, we turn to the concept of *flow*, known colloquially as being "in the zone". Flow is a state of deep absorption in an activity wherein the individual functions at her fullest capacity and the experience itself is intrinsically rewarding such that the individual seeks to replicate it (Shernoff et al., 2003). Scholars have reported experiencing flow when engaged in their best work (Csikszentmihalyi, 1996). Hager (2015) concluded that individuals higher in extraversion, openness and conscientiousness have a greater disposition to experience flow, while high neuroticism hinders an individual from having such experiences. We therefore expect that Type 3 and 4 students have

more flow experiences than Type 1 and 2 students while engaged in learning activities.

Sumaya and Darling (2018) reported that students who experienced flow while working on a particular assignment scored significantly higher grades than students who did not. Ozhan and Kocadere (2019) concluded that flow increases academic success through increased motivation. We therefore hypothesize that for Type 3 and 4 students, conscientiousness provides the initial motivation to improve their CAPs, which is subsequently strengthened by flow experiences. We further posit that the increased motivation leads Type 3 students to engage in longer night-time study to the detriment of their sleep. Type 4 students on the other hand, are better able to replicate flow experiences and leverage these experiences to maximize their learning efficiency. As a result, these students are able to improve their CAPs without negatively impacting their sleep.

Turning to Type 1 and 2 students, Komarraju et al. (2009) suggested that anxiety provides students high in neuroticism the motivation to do better. Bratko et al. (2006) similarly suggested that anxiety and perfectionism in such students could lead to improved academic performance. On this note, we hypothesize that anxiety provides the motivation for Type 1 students to do better while both anxiety and perfectionism motivate Type 2 students. As the CAPs of Type 1 students improve, their level of anxiety falls, leading to improved sleep. For Type 2 students, however, we speculate that improved CAPs further fuel their desire for "perfect grades", leading to increased anxiety and in turn poorer sleep.

Well-Being and Academic Performance

The significant interaction between psychological well-being and CAP scores that our multivariate analysis revealed is consistent with observations made by Richter (2015) that students with higher GPAs had increased levels of certain facets of psychological well-being.

Both simple linear regression and polynomial regression (involving up to third order terms) would, however, fail to detect any association between psychological well-being and CAP scores. In fact, both the Spearman and Kendall rank correlation coefficient would also fail in this regard. This suggests that academic performance, as measured by CAP, does not have a direct effect on psychological well-being. For the same reasons, academic performance does not appear to have a direct effect on the affective components of subjective well-being as well. Therefore, contrary to what one might expect, well-being cannot mediate the relationship between academic performance and overall sleep quality. Academic performance can possibly only moderate the relationship between the affective components of subjective well-being, and psychological well-being. The present study, however, did not examine academic performance in such a role.

Comparisons With Other Student Populations

Based on the results in Section "Global PSQI, SPANE, and FS Scores of Other Student Populations", we conclude that CAPT students have lower affective well-being compared to their counterparts in America, Canada, Germany, Portugal, and South Africa, but similar affective well-being compared to students in Japan and SMU. For FS scores, only the differences in the mean between CAPT and SMU students are not significant. Thus, CAPT students apparently have lower psychological well-being compared to their overseas counterparts with the exception of students in Japan who are not doing as well in this regard. On the other hand, CAPT and SMU students have comparable psychological well-being. We also conclude that CAPT students have poorer overall sleep quality compared to their counterparts in United States, Belgium, Taiwan, and Nigeria, similar overall sleep quality compared to students in Brazil, Luxembourg, and Germany, and better overall sleep quality compared to students in Indonesia.

Limitations and Future Directions

The present study has several key limitations. First, a wider sample would have allowed for more robust results to be generated. Secondly, the availability of additional pertinent data would have enabled a better model for overall sleep quality to be obtained and more in-depth analyses to be made. This includes student demographics such as gender and year of study, and other sleep-related information such as frequency and duration of daytime naps, chronotype, consistency of sleeping patterns, as well as objective sleep measures (e.g., actigraphy-based recordings). Greater sleep consistency has been linked to better academic performance and may have a greater impact on GPA than sleep duration (Hershner, 2020). Napping has been shown to improve logical reasoning and moods, reduce subjective levels of daytime sleepiness (Milner and Cote, 2009), and improve overall sleep quality (Wang and Biro, 2021). Chronotype preference toward eveningness has been found to be associated with poorer academic performance (Gomes et al., 2011; Hershner, 2020). Thirdly, the inclusion of the Satisfaction with Life Scale by Diener et al. (1985) would have provided a more complete view of the levels of subjective well-being of our subjects. Fourthly, we believe that the inclusion of an instrument to assess the Big Five personality traits, e.g., the Big Five Inventory (John and Srivastava, 1999), would have improved the quality of fit of our model, given the growing evidence of the influence of personality traits on subjective sleep (Sutin et al., 2020). Finally, CAP is a partial measure of academic performance and achievement. Complementing it with other quantitative and qualitative measures would have provided more extensive information about the academic experience of the participants.

A future direction would be to develop separate models for objective and subjective sleep quality, taking into account the above limitations. This would allow for an in-depth investigation into the direct and indirect effects that academic achievement, well-being, personality traits and other individual differences such as chronotype preference, have on subjective and objective sleep quality. As it has been recognized that sleep and well-being affect each other (Steptoe et al., 2008; Lau et al., 2015; Zou et al., 2020), we would also include in the proposed study, an investigation into the effects of subjective and objective sleep quality on well-being. Libman et al. (2016) pointed out that sleep

quality is a construct often measured but never defined. Ness and Saksvik-Lehouillier (2018) similarly stated that sleep quality "seems to lack an established definition". Taking the cue from these authors, a key objective of the proposed study would be to determine the extent to which the proposed two models concur, in the pursuit of establishing a holistic understanding of what it means to have quality sleep, both objectively and subjectively, as well as its antecedents and consequences. Libman et al. (2016) and Harvey et al. (2008) have made a start in this direction with their findings that the daytime experience of feeling refreshed versus nonrefreshed in the morning, and the night-time experience of good versus impaired sleep continuity, characterizes perceived good versus poor sleep. Nevertheless, that still leaves much to be desired in our opinion.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Review Board, National University of Singapore. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

AC and FB conceptualized the present study. FB took charge of the well-being instruments to be used, helped to refine sections "Introduction", "Instruments" and contributed to section "Procedure," the preamble of section "Discussion," "Sleep and Psychological Well-Being," and the discussion on limitations in section "Limitations and Future Directions." MA processed the raw data, performed the statistical analyses, and wrote all sections of the manuscript including developing all the hypotheses and speculations in section "Discussion." AC wrote the background of the college at the start of section "Participants and Bad Data Points" and contributed to section "Procedure". AC suggested in part for the section "Global PSQI, SPANE, and FS Scores of Other Student Populations." All authors contributed to the article and approved the submitted version.

FUNDING

This work was funded by the College of Alice and Peter Tan at the National University Singapore under the CAPT Aspire Fund C-506-000-010-511, with additional support from the Faculty of Engineering, Faculty Board Fund C-397-000-055-001.

ACKNOWLEDGMENTS

The authors would like to thank Mr. Chan Keng Wee and Mr. Jacob Chew for their valuable help in running the survey. The authors are also grateful to Adeline Seow for insightful discussions during the initial phase of the project. Finally, the authors wish to thank the reviewers for their insightful comments and suggestions which helped improve the quality of this article.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychology

ORIGINAL RESEARCH
published: 02 July 2021
doi: 10.3389/fpsyg.2021.679804

Development and Evaluation of the CASTLE Trial Online Sleep Intervention for Parents of Children with Epilepsy

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Introduction: Many of the sleep problems experienced by children with epilepsy (CWE) have the same behavioural basis as common sleep problems seen in typically developing (TD) children. Behavioural sleep interventions (BSIs) are widely used to treat these sleep problems in TD children and are hypothesised to be effective for CWE. However, specific considerations need to be addressed and incorporated into a BSI for CWE to ensure the intervention is tailored to this population's needs. This paper details developing and tailoring an online BSI for parents of CWE, to be used in the CASTLE (Changing Agendas on Sleep, Treatment and Learning in Epilepsy) Sleep-E clinical trial.

Method: In phase one, two existing theory-driven paediatric BSIs were adapted into a novel online behavioural sleep intervention (CASTLE Online Sleep Intervention or COSI) which specifically incorporated the needs and requirements reported by nine parents of CWE. Scoping their needs included conducting interviews with three CWE so that they could contribute to the overall intervention content. In phase two, six of these parents evaluated COSI, reviewing and feeding back on COSI until parental approval for content and functionality was achieved.

Results: In phase one, a range of adaptations was made to the content and presentation of standardised intervention material to acknowledge and emphasise the key seizure-specific issues to ensure COSI best met parents of CWE's needs. Adaptations included embedding parent and child experiences in the intervention, including particular information requested by parents, such as the links between sleep and seizures and managing child and parental anxieties around sleep, as well as developing functionality to personalise the delivery of content. In phase two, parents confirmed that they found the final version of COSI to be functional and appropriate (after one round of review) for use by parents of CWE and that 100% would recommend it to other families who have CWE.

OPEN ACCESS

Edited by:
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Reviewed by:
Elizabeth Halstead, University College London, United Kingdom
Sejal V. Jain, University of Arizona, United States

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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *12 March 2021*
Accepted: *17 May 2021*
Published: *02 July 2021*

Citation:
Wiggs L, Cook G, Hiscock H, Pal DK and Gringras P (2021) Development and Evaluation of the CASTLE Trial Online Sleep Intervention for Parents of Children with Epilepsy. Front. Psychol. 12:679804. doi: 10.3389/fpsyg.2021.679804

Discussion: It is hoped that the use of evidence-based BSIs, adapted to consider salient epilepsy-specific factors, will increase parent-engagement, COSI's relevance for this particular patient group and overall efficacy in improving sleep in CWE. The effectiveness of COSI will be tested in the CASTLE Sleep-E clinical trial (https://castlestudy.org.uk/).

Keywords: intervention, epilepsy, online, sleep, e-health, telehealth, children, parents

INTRODUCTION

Epilepsy is a common neurological condition, characterised by a tendency for recurrent seizures, and is primarily a childhood-onset condition (Hauser and Hesdorffer, 1990). Epilepsy has a population prevalence of 1%, with ∼63,400 children and young people under 18 years old affected in the UK (Joint Epilepsy Council, 2011). Seizures have been found to account for 5% of the total of childhood emergency admissions (Armon et al., 2001) and epilepsy in children is commonly comorbid with cognitive, learning and behavioural difficulties which can lead to academic underachievement (Children with Epilepsy in Sussex Schools, 2014).

Sleep disturbance is a surprisingly common comorbidity for children with epilepsy (CWE) with sleep problems occurring more often than in typically developing (TD) children (Owens and Mindell, 2011). Even in the absence of nocturnal seizures, sleep problems as reported by parents are 12 times more common in 4–10 year old CWE than in children without epilepsy (Gutter et al., 2013).

There are a range of possible negative implications of the sleep problems experienced by CWE. These include daytime sleepiness, impaired cognitive functioning, behaviour, and quality of life (Stores et al., 1998; Maganti et al., 2006; Owens and Mindell, 2011). There are also a range of negative implications for the sleep of parents of CWE (Larson et al., 2012), with mothers of CWE being seven times more likely to suffer from sleep disturbance than parents of TD children (Shaki et al., 2011). Further, evidence suggests parents of CWE's sleep duration is impacted, on average obtaining only 4 h of overnight sleep with fragmented parental sleep also positively related to poorer maternal well-being and marital satisfaction (Cottrell and Khan, 2005).

Sleep and epilepsy have been described as "unfortunate bedfellows" due to their complex bi-directional relationship (Gibbon et al., 2019). This is because sleep may be disrupted due to seizures experienced during sleep, comorbid sleep disorders and/or effects of antiseizure medications. Sleep disturbance can, in turn, lower seizure threshold (da Silva Sousa et al., 2005; Gibbon et al., 2019). Many types of epilepsy have specific associations with sleep, including specific stages of sleep and circadian pattern (Loddenkemper et al., 2011; St Louis, 2011). In rolandic epilepsy (RE), the most common type of epilepsy in childhood (Cavazzuti, 1980; Sidenvall et al., 1993), seizures are most often nocturnal (Jain and Kothare, 2015), commonly occurring just after falling asleep or shortly before waking. The adverse associations with poor sleep in CWE mean that sleep issues should be an intervention target which, if successfully addressed, may have positive benefits for various child and parental outcomes, including reduced seizures.

Many of the same sleep problems experienced by CWE are commonly seen in TD children, including problems with sleep initiation (settling and falling to sleep) and/or maintenance (night or early morning waking). These disorders (as distinct from more physical sleep disorders like sleep apnoea) are commonly amenable to behavioural sleep interventions (BSIs). The aim of these interventions is to provide parents with practical strategies to modify their practises around their child's sleep so that they can support their child to "learn" appropriate sleep behaviours and, if necessary, to "unlearn" inappropriate sleep behaviours. They typically also include parental education about normal sleep and developmental aspects of sleep, as well as provide advice about good sleep hygiene, which refers to practises that promote good sleep such as regular bedtimes and limiting use of LCD screens in the bedroom (Meltzer and Mindell, 2014). BSIs have been found to be effective in randomised controlled trials for young (under 5 years) TD children, and in autism and attention-deficit hyperactivity disorder (ADHD) populations, including up to age 12 years (Mindell et al., 2006; Johnson et al., 2013; Hiscock et al., 2015). Because of this body of evidence it has been proposed that BSIs could also be modified effectively for children with epilepsy (Gibbon et al., 2019) although, to the authors' knowledge, there have been no trials which have specifically evaluated this. BSIs can be delivered in a variety of modes including face-to-face (Hiscock et al., 2015), by telephone (Stuttard et al., 2015), by written information (Gringras et al., 2012), and online/app based (Mindell et al., 2006; Espie et al., 2012).

Sleep problems in children with epilepsy are often not targeted or evaluated in clinical care or trials. For example, current NHS services for CWE are focussed on addressing seizures and are often under resourced to allow adequate time to support a BSI. The Changing Agendas on Sleep, Treatment and Learning in childhood Epilepsy (CASTLE) group consisted of lay members and professionals who contributed to the design and planning of a broad programme exploring sleep, treatment and learning in epilepsy, culminating in a national trial for an online BSI for parents of children with RE (CASTLE Sleep-E clinical trial. See: https://castlestudy.org.uk/). An online BSI was chosen for evaluation in this trial due to the RCT evidence of the efficacy of such an approach for similar childhood (Mindell et al., 2006) and adult (Espie et al., 2012) sleep problems in diverse populations. In addition, parents of CWE frequently use the internet to try to access information and support, and others have noted the need for the development of high-quality online resources for parents (Jones et al., 2019). Importantly, an online BSI (i) offers

cost effectiveness, (ii) addresses many logistical considerations of rolling out and delivering nationwide interventions, (iii) aligns with future NHS trends in telemedicine, minimising NHS staff burden and the need for staff training to deliver the intervention, and (iv) has the potential to ultimately maximise patient access to the intervention. A further advantage of the online approach is that it can also generate objective process measures of frequency and pattern of access to the materials, and, for example, scores on quizzes (as a proxy for understanding of the materials) to help inform scientific understanding about causal pathways behind a complex intervention.

Despite the good quality evidence supporting the use of BSIs, and online delivery, for children's sleep problems there are special seizure-specific considerations that could usefully be acknowledged to help ensure that the online BSI best meets the needs of this particular parent group (Cook et al., 2021). There are well-described benefits of co-creating such resources with carers and children who are "experts by experience" (D'Alessandro and Dosa, 2001; Carman et al., 2013). Our study represents an attempt at this best practise and our methods describe this process of development (phase one) and initial parent evaluation of content and functionality (phase two) of the CASTLE Online Sleep Intervention (COSI), for subsequent use in the Sleep-E clinical trial.

METHOD

Design

Phase one describes the development of COSI, an online BSI for parents of CWE, which incorporates (i) information about evidence-based BSI strategies and (ii) adaptations and additions suggested by parents of CWE. Specific requirements for this group were identified via interviews with parents of CWE (Cook et al., 2021). After an initial draft of COSI was developed by the researchers, phase two could begin. In this, parents evaluated the content and functionality of this draft during a 2-week period and then reported on the acceptability of content and functionality of the intervention website. This iterative drafting and evaluation cycle was planned to continue until parental approval (defined below under Measures) was achieved. It should be noted that in evaluating COSI parents were not asked to implement any BSI, but rather to visit the intervention website, read the text, watch the videos, see if they could easily navigate around the website etc. The effectiveness of COSI as a BSI will be assessed in the forthcoming Sleep-E clinical trial.

Participants and Recruitment

COSI Development (Phase One)

Epilepsy specific COSI adaptations were informed from interviews with nine mothers of CWE (six males, age range 5–15 years, median=10 and mean=10.3, SD=2.9), who all lived with their CWE. Further details of their children's sleep and epilepsy are available in the **Supplementary Appendix 1** but, in summary, of the children, five had Benign Rolandic Epilepsy (1 atypical), 2 had focal seizures, 1 generalised seizures and 1 unspecified. Two had been diagnosed with epilepsy < 1 year ago, 2 children between 1 and 3 years ago and 5 children >3 years ago. All the children in this sample had experienced a range of sleep problems, both currently and in the past. Participants were recruited for telephone or video interviews, between March and July 2018, via online advertisements placed on the websites of epilepsy organisations and charities and the CASTLE study and researchers' university websites.

In addition, three children with RE (2 males aged 10–14, 1 female aged 10), recruited via the CASTLE study patient and public involvement and engagement group, participated in the development of COSI in a specific way; interviews about their sleep experiences (conducted in November 2018) were used to contribute to the content of the online BSI. Anonymised quotations from the children featured in video animations created for and embedded into COSI (see Procedure, COSI Development, below).

Evaluation Study (Phase Two)

Six of the nine mothers of CWE (four males, ages ranging 5–15 years, with median=10, mean=10, SD=3.69) who had participated in the interviews also participated in the evaluation element of the study where they reviewed the developed COSI and provided their feedback about the acceptability of content and functionality (between 13th and 28th March 2019).

Measures

A COSI Evaluation Questionnaire was developed by the research team and hosted via Qualtrics (Qualtrics, Provo, UT) (see **Supplementary Appendix 2**). This allowed for parental quantitative assessments of the content and functionality of the COSI website in the evaluation study (phase two). There were four elements to this questionnaire: (i) the functionality of COSI, (ii) the acceptability of the content, (iii) the acceptability in terms of length and content of the embedded COSI parent feedback scale (which will be used to assess parents' experiences of COSI when it is used in the CASTLE Sleep-E trial) and (iv) allowing parents opportunity to make any further comments.

The Functionality of COSI

Parents were asked to rate (on a 5 point Likert scale of "Always," "Often," "Sometimes," "Rarely," and "Never") the frequency with which they could log on, access the webpages' content, see and hear the videos, access and respond to the quizzes, print off any materials they wanted and navigate easily around the intervention website. If parents responded with anything other than "Always" they were asked to explain any problems in an open text response box. Using the same 5-point scale parents were also asked if they would recommend COSI to other families of CWE.

The Acceptability of Content

For each of the possible suggested 20 behaviour change techniques (see **Supplementary Appendix 2**, section 2) which were included in COSI, parents were asked to report how acceptable they thought it was to include the technique as a suggestion (even if they personally might not use the technique). As well as explicitly listing and describing each of the techniques which the researchers considered to be included

in COSI an "Other" option was also included in case there was further content which parents perceived to be a suggested technique. Parents rated these on a 5-point Likert scale of "Very acceptable," "Acceptable," "Neither acceptable nor unacceptable," "Unacceptable," and "Very unacceptable." If they responded "Unacceptable" or "Very unacceptable" they were asked to explain their reasons in an open text response box.

The Acceptability of the COSI Parent Feedback Scale

Parents were also asked to rate the acceptability of the embedded COSI feedback scale in terms of the burden of the time taken to complete (on a 5-point Likert scale of "Far too long," "A little too long," "About right," "A little too short," and "Far too short") and the understandability of the language and phrasing used ("Very difficult," "Difficult," "About right," "Easy," and "Very easy," with open text response boxes to expand as required) as well as whether there were other questions which they felt should be included ("Yes" or "No," again with open text response boxes to expand as appropriate).

Additional Comments

Finally, there was an open text box where parents could add any additional comments about COSI.

Based on parents' responses to this questionnaire, our definition of "parent approval" was as follows:

(i) All parents reported they were able to access all elements of COSI as intended.
(ii) >65% positive rating ("Always" or "Often") on a "Friends and Family" style 5 point Likert measure answering: "How likely are you to recommend this sleep programme to other families who have children with epilepsy?"
(iii) >65% parents report acceptable burden ("About right") of embedded COSI parent feedback scale.

Procedure

Ethical approval was obtained through the Oxford Brookes University's Research Ethics Committee (UREC approval 171108).

COSI Development (Phase One)

The key content (informational and instructional content) of two existing BSIs used in randomised control trials (RCTs) of children with ADHD (Hiscock et al., 2015) and Autism (Johnson et al., 2013) was identified from the published reports and clarification with the authors as required (see **Table 1**, columns 1–3 for a summary of each BSI) and this core content was drafted into text format. The BSI content from these studies was selected for a number of reasons, including: (i) these previous studies are evidence-based level 1 studies with good effect sizes; (ii) they utilise well-defined interventions that are easy to tailor to specific family needs and goals; (iii) their relative brevity; (iv) their established effectiveness in children with neurodevelopmental disorders; and (v) their suitability to be adapted to an online intervention. Both existing BSIs comprise a number of reliable combinations of behavioural change techniques (BCT) defined as "systematic procedures included as an active component of an intervention designed to change behaviour" (Michie et al., 2011).

Based on the results of a previous interview study with parents of CWE (Cook et al., 2021) parent views about factors which should be integrated into, and issues that would need to be acknowledged as part of, any online BSI were described (see **Table 2**, column 1 for a summary). BSI content, delivery and usability were then adapted to address this parental feedback, to produce a resource which used evidence-based strategies and acknowledged the topics identified through patient and parent involvement. It was hoped this would result in a resource that parents found helpful and acceptable, and that with the contribution of CWE and their parents to its development made clear, would encourage parental trust and engagement with COSI.

To integrate the BSI content and parents' views the researchers reviewed the themes identified from the parent interviews and, for each, considered ways in which this could be included in COSI. This resulted in adapting some of the draft text content and adding new text content (see **Table 1**, column 4 for a summary of COSI content, in relation to that of the content of the existing BSIs from which it was developed), including producing video animations to embed into COSI, featuring quotes from parents. In response to parents' suggestion that children's perspectives should be included in COSI three CWE were interviewed and asked how they felt about sleep, about any problems they had with sleep (generally and related to their epilepsy) and to tell us about things they had found helpful, or not, for their sleep (see **Supplementary Appendix 3**). Quotes from the children, illustrating their opinions and experiences, were also included in the video animations.

Where appropriate, text content was reviewed for acceptability by paediatric epilepsy specialists. For example, the topic of parent concerns about Sudden Unexplained Death in Epilepsy (SUDEP) exemplified the need to combine research [i.e., evidence-based guidelines about SUDEP based on Harden et al. (2017)], clinical (comments on our draft text about SUDEP from three paediatric epilepsy specialists) and patient and parent involvement and engagement to recognise and respond to parents' concerns so that they felt willing and able to engage with any suggested strategies for sleep intervention.

Parent suggestions related to the presentation and usability of the website were addressed (see **Table 2** for details of how parents' suggestions were integrated into COSI) and the functionality and presentation of the intervention website was reviewed and tested by the researchers.

Evaluation Study (Phase Two)

Following this development, access to the COSI intervention website was provided to parents who had participated in the interview study. Participants were emailed a password protected weblink to access COSI and were asked to review and interact with the website, exploring the content and functionality. Participants were then asked to provide quantitative feedback via the COSI Evaluation Questionnaire, access to which was also sent as a weblink. Parents were offered an opportunity for further discussion with researchers to provide additional feedback however, no parents requested follow-up discussion. This process

TABLE 1 | Overlap and extension of informational and instructional content from existing BSIs and in COSI.

	Johnson et al., 2013	Hiscock et al., 2015	COSI
Normal sleep information		✓	✓
Sleep and condition-specific information			✓
Common sleep problems information		✓	✓
Explanation of basic behavioural principles	✓		✓
Prevention techniques (sleep hygiene recommendations, schedules and routines)	✓	✓	✓
Behavioural sleep management techniques for bedtime resistance, delayed sleep onset, sleep onset association, night waking and early waking (details below)	✓	✓	✓
Extinction	✓	✓	✓
Graduated extinction	✓	✓	✓
Bedtime fading	✓	✓	✓
Scheduled wakings	✓		
Stimulus control	✓	✓	✓
Reinforcement	✓	✓	✓
Behavioural techniques to address anxiety related insomnia or night fears (details below)	Optional	✓	✓
Visual imagery		✓	✓
Relaxation		✓	✓
Teaching "brave" skills	✓		✓
Systematic exposure	✓		✓
How parents can reassure	✓		✓
Additional advice for managing sleep in children with co-occurring conditions	✓		✓
Strategies for maintenance of behaviour change	✓		✓
Behaviour compliance training	Optional		
Dealing with sleep walking, sleep terrors, and nightmares		✓	✓
Troubleshooting advice	✓	✓	✓
Information to help address parental anxieties and concerns			✓
Other forms of content (details below)			
Printed handouts	✓	✓	✓
Videos modelling use of strategies	✓		
Role play	✓		
Homework activities	✓		
Videos sharing experiences of parents and children			✓
Quizzes to test knowledge			✓
Direction to additional relevant online resources			✓

of parent evaluation and re-drafting was to be continued until parent approval (as defined above) was obtained. However, parental approval was achieved after the first parent evaluation.

RESULTS

COSI Development (Phase One)

As shown in **Table 1**, core information and a range of standardised evidence-based techniques to address sleep problems in children, as used in the existing BSIs, were included in COSI. COSI was extended to include additional content highlighted as pertinent to the parents of CWE in the previous qualitative study exploring what parents of CWE wanted from an online BSI for this clinical group (Cook et al., 2021). The main content additions included (i) embedding parent and child experiences in the intervention, (ii) including information about sleep and seizures and acknowledging epilepsy-specific considerations, (iii) including information about nightmares, sleep walking and sleep terrors and (iv) including information about managing child and parental anxieties around sleep. Further, delivery and presentation of material was tailored to meet parents' identified needs, within the constraints of the online delivery platform; for example "personalising the presentation of the material" was achieved by recommending pertinent sections of COSI in response to parents' answers to a screening questionnaire where they reported on their child's sleep and offering parents a "range of management options," was supported by careful choice of words when describing the techniques to parents, so that they felt they were being offered suggestions rather than instructions. See **Table 2** for details how the key themes reported by parents were specifically acknowledged, addressed and or integrated in COSI.

Some aspects of the existing BSIs were not incorporated into COSI due to either not being possible for the current online

TABLE 2 | Illustration of how different themes reported by parents were integrated into COSI.

Theme	How integrated into COSI
Other parents' views and experiences	• Anonymised quotations from interviews with parents were used in animated videos embedded throughout COSI to weave in other parents' views and experiences (see **Figure 3** for an illustration). This represented the "personal" experiences of parents of CWE and contributed to providing support, and hopefully add credibility to, the material and ideas presented as part of COSI content • The inclusion of a frequently asked questions (FAQs) page which addresses key topics raised by parents such as what to do if child is unwell, child sleeps in multiple households, and approaches for how to manage parents' own worries (module K)
Change over time	• Parents were clearly advised that they should select options most relevant to them at the specific time of review and that this may change over time • Sleep management techniques were presented carefully to ensure factors that might impact their choice of approach were identified and acknowledged • The presentation of a range of evidence-based intervention techniques (modules G, H, I, and J) allowing parents to choose which option may be most suitable to them at different time points
Range of management options	• In any modules where behaviour-change techniques were presented (module G, H, I, and J) a variety of different evidence-based techniques were provided • In any modules where behaviour-change techniques were presented these were worded carefully to present the family with options rather than "instructions"
Personalisation of information	• Functionality embedded partly through a "sleep screener" questionnaire (module C) where recommended modules were highlighted based on parents' responses to the sleep screener questionnaire to help personalise recommended modules for parents to review • Parents completed this screener based on their child's sleep behaviour allowing them to feel their individual child's sleep was being considered • Encouraging parents to select from the range of behaviour-change approaches presented (module G, H, and I predominantly) also encouraged parents to personalise their own use of COSI • COSI provided specific evidence-based information and strategies for parents whose child may have comorbid conditions (module F)
Child anxiety around sleep	• Inclusion of a module (I) specifically aimed at supporting parents to manage sleep-related anxiety and night-time fears in their child • Also included was information (module J) designed to help parents address specific night-time behaviours (sleep walking, sleep terrors and nightmares) with their child
Practical sleep intervention suggestions	• The BSIs upon which COSI was based include a range of practical strategies that parents can select from and apply to support their child to "learn" appropriate sleep behaviours and, if necessary, to "unlearn" inappropriate sleep behaviours. • Presented in a clear step-by-step fashion making them easy to follow and implement • Inclusion of a troubleshooting section (module K) to help parents practically deal with common issues around implementing BSIs and also practical advice about how to maintain any sleep improvements
General sleep information	• The development of COSI itself was designed to address parents' desire for knowledge and information around sleep • Particular areas about which parents desired information were explicitly incorporated into COSI (i.e., general background information about sleep (module A), the relationship between sleep and seizures (module B), sleep hygiene tips (module D), understanding common sleep problems and possible approaches to managing or improving CWE's sleep (module E, G, H, I, and J)
Parental anxieties and concerns	• COSI content clearly acknowledged areas of parent anxiety (e.g., about sleep, epilepsy and intervention approaches) throughout • COSI specifically provided some information about parental worries and sleep in the FAQs page (module K) • COSI identified further useful resources of help and support for parents around possible areas of anxieties and concerns (module L)
Help, support and reassurance around sleep	• The purpose of developing COSI was to provide help, support and reassurance to parents around child sleep • Careful consideration was given to the wording throughout COSI to ensure it was written in a non-judgmental and supportive manner • Including other parents' experiences (as this was reported to be thought helpful, supportive and reassuring for them) • Acknowledging the possible challenges of intervention approaches, helping parents feel informed and supported in making the most appropriate decision for their individual child/family • Providing general sleep information to reassure parents about variability of child sleep • That there are techniques designed to improve sleep, if required, would be supportive and reassuring for some parents
Include child in intervention	• Anonymised quotations from interviews with CWE were integrated throughout COSI in animated videos, reflecting their perspectives (see **Figure 4** for an illustration)

TABLE 3 | COSI module names, descriptions and compulsory or recommended status.

Module	Module name	Outline content	Compulsory or recommended
A	What is sleep and why is it important	Education about normal sleep physiology and processes	Compulsory
B	Sleep and seizures: a vicious cycle	Information about the relationship between sleep and seizures	Compulsory
C	Personalising this advice for your child	A sleep screening questionnaire to identify key areas of concern or problems around individual child sleep	Compulsory
D	Tips on sleep hygiene for everyone	General advice about key aspects of sleep hygiene	Recommended for all
E	Advanced sleep behaviour training	Introduction to principles of behavioural sleep interventions	Recommended for all
F	Learning difficulties, ADHD and Autism spectrum disorders	Advice for parents of children with comorbid conditions	Recommended to parents who highlighted (in module C) their child may have comorbid conditions
G	Solving falling asleep problems	Sleep intervention options for typical falling asleep problems	Recommended to parents who highlighted (in module C) their child may have problems falling asleep
H	Solving difficult night wakings and early morning waking	Behavioural techniques to address typical night or early waking problems	Recommended to parents who highlight (in module C) their child may have problems with night or early morning wakings
I	Solving night time fears	Behavioural techniques to address typical night time fears	Recommended to parents who highlight (in module C) their child may have problems with night time fears
J	Sleep walking, sleep terrors, and nightmares	Information about these specific sleep disorders, what causes them and how to identify and manage different conditions	Recommended to parents who highlight (in module C) their child may have problems with sleep walking, sleep terrors, and/or nightmares
K	Troubleshooting and maintaining good sleep	How to deal with common issues, such as the child being ill or parents' disagreeing about how to manage sleep and also advice about how to maintain any benefits	Recommended to all
L	Resources	Links to additional resources of support, information and advice relating to sleep	Recommended to all
M	COSI parent feedback scale	Questionnaire in which parents are asked to report on their experiences of using COSI	Recommended to be completed by all

mode of delivery (e.g., role play, homework), not identified as a priority by the parents (e.g., videos modelling the use of strategies) or possibly unhelpful for this group (i.e., suggested use of scheduled wakings, which could increase sleep disturbance in the short term). The addition of quizzes and links to other online resources were included, not because they had been spontaneously suggested by parents but because they were obvious possible additions afforded by the online platform and, when questioned about their possible inclusion, parents reported they could be welcome additions and gave useful advice about their functionality (e.g., quizzes should be optional). COSI was a bespoke web application, purpose built for CASTLE. It was designed to allow for easy presentation of modular content, embedded animations, quizzes and data capture. As a web-based tool optimised for different devices across all platforms it was also easily accessible to all families.

COSI included 11 modules as shown in **Table 3**. The first 3 COSI modules (A, B, and C) were compulsory as they provided important information relevant to subsequent sections. Parents were required to complete each of these sequentially and were unable to access later modules until each was completed. Having completed module C (screening questionnaire) all subsequent modules were made available to parents and could be accessed at any time although, as explained, to personalise the intervention, a list of "recommended modules" specific to their child's sleep was derived based on their responses to the screening questionnaire (see **Figure 1**).

Modules D, E, K, and L were recommended to all parents alongside any of modules F, G, H, I, J, as appropriate. The COSI parent feedback scale (module M), to be completed at the end of parents' use of COSI, was embedded into the intervention website; this would allow for exploration of parents' views about the use of the COSI and the suggested intervention techniques. The structure of each information module (A, B, D-J) was the same, starting with a general introduction to the topic which was both written and also presented in an animated video (see **Figure 2** for a still of animation content).

The "scripts" for the animations included quotes from parents and CWE (spoken by actors) so that, as requested by parents, the experiences of the families, and not just clinicians' views, were embedded into COSI (see **Figures 3**, **4** for stills from animations illustrating parental and child quotes). Following the introduction for each module, a series of subheadings could be clicked to expand and reveal information and images. Common parent concerns related to the module topic were also included as subheadings. Throughout COSI hyperlinks to other relevant

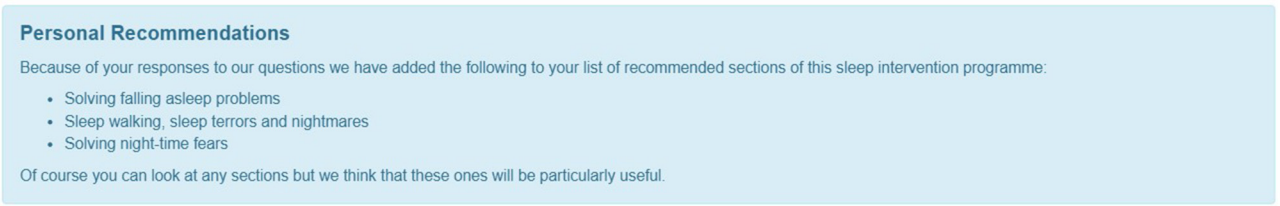

FIGURE 1 | Personalised recommendations for modules based on parental responses to screening questionnaire.

FIGURE 2 | A still of the animations used in COSI. Illustration is from the introduction to the online BSI.

FIGURE 4 | Still from COSI animation demonstrating integration of child perspective (quote).

FIGURE 3 | Still from COSI animation demonstrating integration of parental perspective (quote).

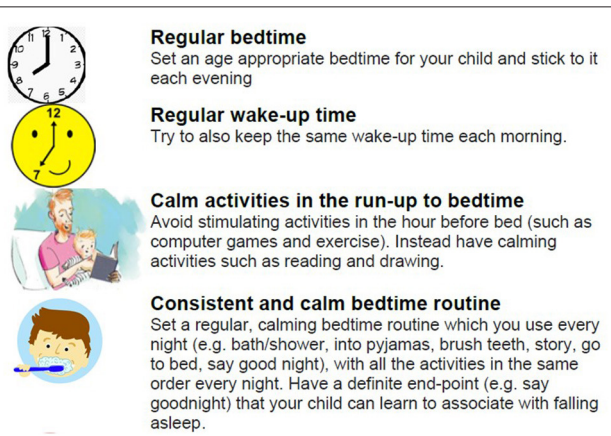

FIGURE 5 | Image of the type of advice and presentation of material for module D, sleep hygiene tips.

modules, or to other external websites, resources and videos were provided where appropriate. At the end of each module there was a quiz. If a parent did not answer correctly, the correct answer was shown.

Some modules gave general educational information, for example about normal sleep (module A) or, tailored to this particular clinical group, the links between sleep and seizures (module B). Module C included the screening questionnaire, enabling the COSI experience to be personalised by directing parents to modules which were particularly relevant for them, something which parents had reported was highly desirable. If appropriate they were guided to speak to their clinician about any sleep issues which were screened for but not addressed in COSI e.g., symptoms suggestive of a sleep related breathing disorder.

Some modules provided general advice and guidance relevant for all. For example, module D provided details about basic sleep hygiene practises and module E gave details about the underlying principles of behaviour change. See **Figure 5** for an example of the content of module D. Some modules provided targeted advice for specific scenarios. For example, module F provides advice and guidance about sleep and sleep interventions for parents whose

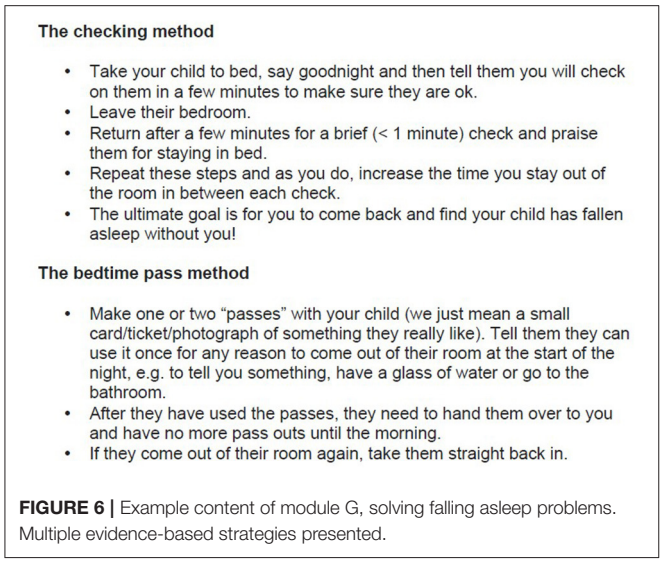

FIGURE 6 | Example content of module G, solving falling asleep problems. Multiple evidence-based strategies presented.

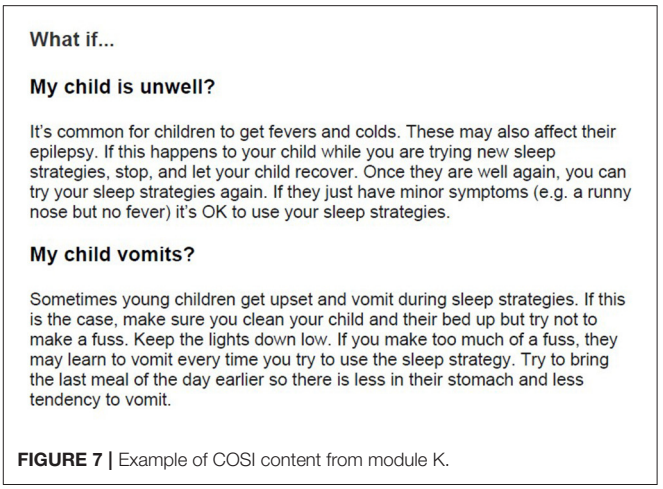

FIGURE 7 | Example of COSI content from module K.

children had other co-occurring conditions, such as ADHD and Autism spectrum disorders. The inclusion of material around co-occurring conditions was considered appropriate for this target group, to help parents feel supported and to encourage them to feel that the intervention was relevant and personal for them and their child.

For the modules giving information about behaviour change techniques (modules G, H, I, and J), all addressed a different "type" of sleep problem: falling asleep problems; difficult night or early morning waking; night-time fears; sleep walking, sleep terrors and nightmares. Each behaviour change module presented a range of possible strategies, to meet parents' desire for a variety of options from which they could choose which approach to use. As mentioned, all behavioural change methods in COSI were carefully worded as suggestions for the family to consider and were presented in a clear step-by-step fashion making them practical to follow, which was an additional key requirement reported by parents. For example, see **Figure 6** for some of the behaviour change techniques presented to parents if they have a problem with their child stalling at bedtime (also known as limit setting disorder). The explicit inclusion of material relating to addressing children's night-time fears (module I) and material relating to sleepwalking, sleep terrors and nightmares (module J) were included as parents explicitly requested help with managing or addressing their child's anxiety around sleep and requested support with these common child sleep problems. It was made clear that some of the strategies might be easy to start putting into practise at any time but for others they would need to judge when it felt right for them and their child to acknowledge the issue of changes over time, to emphasise how the material could be "personalised" and also to encourage informed parental choice.

A benefit of the online delivery was that a range of relevant links could be provided as resources for parents (module L) to help them feel further supported. These included information relevant to child sleep, epilepsy and also support for parents themselves, about coping when their own worries affected their sleep. In module K, common concerns related to implementing intervention (e.g., when the child is ill or parents disagree about management strategies) were raised alongside suggestions for how to maintain any gains over the longer-term (see **Figure 7**). It was hoped this inclusion would help to meet parents' desire for both practicality and support in dealing with any issues that arose.

Also included in this module (K) was an attempt to address one component of a theme which featured prominently in the parent interviews; that parents commonly come upon ideas for things that might help their child's sleep from anecdotal reports from other parents on social media and internet forums and that they valued this resource. Whilst we did not feel that we could endorse potential management tools and strategies for which there was no strong evidence base, we did think it was important not to ignore that parents used and valued these suggestions. In response, we decided to give parents some information to empower them about how to approach and make decisions about whether they should use unproven interventions.

The end of COSI included a parent feedback scale (module M) which will be used to evaluate COSI in the Sleep-E trial. This will ask parents to report on how easy the online intervention was to use (i.e., ease of logging on, accessing written, video and quiz content and ability to print off any required materials). Parents will also be asked to indicate which techniques they used and, if they report using specific techniques, how useful they found them to be. Alternatively, if parents report that specific techniques were not put into practise, they were asked to report the reasons for this. Finally, parents will be asked to read and rate their agreement with statements reflecting the thoughts and feelings parents may have when faced with a child that is not sleeping. These items were derived from an age-appropriate version of the Maternal Cognitions about Infant Sleep Questionnaire (Morrell, 1999), modified by excluding the three items asking about night-feeding (as used in Montgomery and Wiggs, 2015).

COSI was developed to collect quantitative, descriptive, e-learning data about parents' use of the intervention website in the Sleep-E trial. This will assess how many modules parents have looked at; how many times they have viewed a module; the duration of time on the website and individual modules, as well as parents' scores on quizzes and questionnaires. This allows for a "dose-related" exploration of the impact of parental engagement and understanding on overall efficacy.

The time required for parents to read and engage with each module will obviously vary depending on a number of factors (including whether parents chose to engage with hyperlinks to external resources and how many times they answer the quiz questions) but, as a descriptive indication of the demands COSI placed on parents, the text for each module could be read in 5–10 min at most and each animated video lasted for 1–2 min.

Evaluation Study (Phase Two)

After reviewing COSI, parent feedback assessed by the COSI Evaluation Questionnaire ($n = 6$) was unanimously positive. All parents reported they were able to access and use the online intervention as intended. One parent reported a minor error in a video animation (sub-optimal timing of text and audio presentation), which was corrected. All parents approved of COSI and reported they would recommend this sleep programme to other families who have children with epilepsy. All techniques were considered to be "acceptable" or "very acceptable" suggestions. All parents reported the embedded COSI parent feedback scale to be of acceptable burden (all "about right") and understandable (all "easy" or "about right"). Finally, whilst not a parent-approval metric, the researchers noted the "back-end" of the system successfully captured the desired e-learning analytics for all participants (e.g., time logging on, pages visited, quiz answers recorded etc.).

Following phases one and two, and with the criteria for "parent approval" exceeded, COSI was subsequently approved by the CASTLE trial programme board for use in the NIHR-funded CASTLE programme where its effectiveness will be evaluated in the Sleep-E trial (https://castlestudy.org.uk/).

DISCUSSION

We have described the co-creation of COSI, an online BSI for parents of CWE, adapted from the informational and instructional content of existing evidence-based BSIs. In doing so we took account of the special considerations, of content and delivery, for CWE and their families to help ensure COSI best met their needs. Parents' reviews of the content and functionality of COSI were universally positive and the parental "approval metric" criteria was exceeded. Of course, the clinical effectiveness of COSI cannot be determined from the current results.

Previous research has highlighted the need for high-quality online resources for parents of CWE due to the widespread reported use of the internet to access information and support (Jones et al., 2019). Whilst there are many general online sources of information about sleep available for parents, the large quantity of information can feel overwhelming for parents (Walsh et al., 2015; Cook et al., 2021) and decisions about whether or not to engage with resources can be even more difficult for families where children have particular needs or medical conditions as the advice offered may not obviously appear to be relevant or appropriate for their family circumstances (Zeng and Cheatham, 2017). COSI was designed to address this problem, in relation to the sleep of CWE, by providing salient information, evidence-based management suggestions and delivery to families in a way that accorded with parents' needs and preferences, as identified from interviews with parents of CWE.

The range of sleep-related behaviour change techniques included were not unique to COSI, but rather were specifically chosen because they had been previously demonstrated to be effective when used in various paediatric populations, including children with neurodevelopmental disorders (Mindell et al., 2006; Johnson et al., 2013; Hiscock et al., 2015) and when delivered in various ways, including online (Mindell et al., 2006; Espie et al., 2012). However, the evaluation of their use specifically in CWE is original and will be the focus of the forthcoming Sleep-E trial. What is unique to COSI is that the techniques are "packaged" as a resource which is tailored to meet this group of parents' particular needs, based on themes identified via interviews with parents of CWE (Cook et al., 2021). The main areas addressed as part of COSI's development were: (i) the inclusion of specific, desired content; (ii) presenting content in a way that was sensitive to their reported needs; and (iii) personalisation of material.

The specific additional content parents requested was a) help to manage their own and their child's anxieties and b) information about sleep and epilepsy. The latter included addressing the relationship between sleep and seizures and the consideration of SUDEP as well as wanting content to reflect the experiences and "voices" of families of CWE. In addition to the inclusion of pertinent content, conveying families' experiences was also achieved through imaginative, animated videos giving personal perspectives of parents and children, as well as by including trouble-shooting and frequently asked questions (FAQs) pages specifically covering key issues or concerns for this clinical group. As has been found in other studies (e.g., Tan-MacNeill et al., 2020), parents suggested that the inclusion of this relevant content would add credibility to the material and ideas presented as part of COSI and help parents feel that this was something that they could, and wanted to, engage with.

Also important to parents was that there was appropriate presentation of content, which was practical, non-prescriptive and flexible (over time and between families). The authors were mindful of these needs, aiming to empower parents, rather than make them feel as if they had "failed" if they were unable to put a particular strategy in place at a given moment. In adopting this approach, COSI devolves informed management decisions to parents, both about the technique to use and the timing of its use. This can be seen as a step toward increasing levels of parental self-efficacy and/or ownership of decision-making around sleep for parents of CWE, which has been identified as a beneficial approach in paediatric epilepsy care (Berg et al., 2013).

The last main area of development concerned ways to personalise COSI. Primarily this was achieved through embedding functionality to allow the recommendation of specific modules (or advice about when to seek help outside COSI, as appropriate), based on parental responses to a screening questionnaire about their child's sleep. Other more general features of "personalisation" included offering parents choices in how to approach management and specific information about use of COSI in children with co-occurring conditions of Autism, ADHD or intellectual disabilities. Their answers to any quiz questions were also responded to with personalised comments, confirming the correct answer or explaining incorrect answers. The authors were aware that there were additional ways in which COSI could have been personalised (e.g., using the child's name where appropriate) but, at review, this was not considered as necessary by parents; it appeared that "personalisation" of relevant content, rather than in more superficial ways during website/online interaction, was considered important. The importance of customisation of online intervention material has been highlighted in a large meta-analysis where tailored online health behaviour change interventions were found to result in improved health outcomes when compared to control conditions (Lustria et al., 2013). In addition, a customised approach has been shown to be beneficial when delivering sleep interventions in a sample of parents of disabled children (Beresford et al., 2010).

Overall, it is hoped that the measures undertaken in the development of COSI will provide help, information, support and reassurance around sleep to parents of CWE and, perhaps, the general approach to developing a parent resource in co-collaboration with parents, may serve as a useful model for the development of other, condition-specific online BSIs in the future.

While most of the parents' ideas for features of an online BSI were integrated into COSI there were two areas where this was challenging to achieve. For example, some parents suggested having an accompanying, parallel online sleep resource for CWE (Cook et al., 2021). This was extensively considered by the team, however, given the age range of children for which COSI was intended (5–12 years) and the amount of material covered in COSI it was felt that a single "resource for children" would not be practical as multiple, age-appropriate, child COSIs would be required. However, the development, and evaluation, of sleep-related materials designed for CWE is an interesting possibility for consideration in the future. If COSI in its current format, designed for parents of CWE, is efficacious, perhaps developing an accompanying child-specific COSI could be explored to see if this is a helpful addition to improve familial engagement with the materials and overall effectiveness of the intervention.

An additional factor suggested by a small number of parents in the study by Cook et al. (2021) was the inclusion of an interactive component such as a forum or "live" FAQs page. However, while this was considered by the team, ultimately this was avoided as it would preclude any future scaled-up, roll-out of COSI, as an ongoing website moderator would be required. Further, it was difficult to reconcile the evidence-based nature of the advice within COSI, with that which would necessarily be provided by parent anecdote. As such, a decision was taken to restrict this to a non-live FAQ and to include within that some advice for parents about how to engage with material they find on the already available parent forums. However, the inclusion and managing of a "live" or interactive component is one that could be considered in future intervention developments and may further help with parental engagement with the website, particularly as many parents reported that hearing other parents' views and experiences was highly useful and beneficial to them (Wo et al., 2018; Cook et al., 2021).

Parental reviews of the usefulness and functionality of COSI were unanimously positive. We were expectant of an extensive iterative process, involving making multiple rounds of amendments to COSI. However, the first draft version of COSI was viewed by parents as definitely beneficial in terms of its content and usability so that at first review the parental "approval metric" criteria was met. Following this creation and approval of COSI, its effectiveness will be evaluated as part of the upcoming CASTLE Sleep-E trial, where use of COSI will be compared with "standard care" in a randomised controlled-trial. Outcomes including child sleep, cost-effectiveness and a range of child and family functioning measures will be explored (see https://castlestudy.org.uk/). The clinical trial is due to begin participant recruitment of 110 participants in June 2021. It is hoped that COSI will improve the sleep of CWE with sleep problems and, as a result, also contribute to improvements in a range of broad health and well-being outcomes in CWE and their parents. We also hope that COSI will offer busy clinicians, who are aware of the importance of sleep in CWE, a specifically designed resource to which relevant families could be directed for prevention and intervention advice. An online format is scalable, translatable, has potential accessibility benefits for most families, reduces the cost and time of clinical staff's involvement and thus may offer clinical services extra time to focus on the most severe cases or those families who require more clinical input. The recent COVID pandemic emerged just after the CASTLE pilot study had opened and the ability to remotely assign an online sleep intervention was advantageous in these circumstances and will also be used in the upcoming randomised controlled-trial.

A major strength of this study is that the end users of COSI (parents of CWE), and CWE themselves, contributed to the development of COSI and helped to ensure that this online BSI, based on use of evidence-based sleep-behaviour change techniques, included adaptations and additions to meet their needs. A potential limitation of the current study is the small sample size and also that not all parents from phase one ($n = 9$) participated in the evaluation aspect of the trial ($n = 6$). Whilst broad and varied recruitment strategies were employed, recruitment remained a challenge throughout and the final sample was smaller than hoped for. In the current study we intended to use the same participants in phases one and two so that we could be confident that we had interpreted their described needs correctly and that our adaptations to COSI met with their requirements. However, a large sample of different parents will provide feedback on their experiences with using COSI as an intervention in the Sleep-E trial and this will be valuable

additional information which could inform future development of COSI more broadly.

Despite the current sample being small it is noteworthy that the parent participants in both phases of the study were mothers of CWE aged 5–15 years and this allowed us to explore their perspectives based on their experiences across childhood. These parents had dealt with a broad range of longstanding sleep-related difficulties and were well-placed to comment about general topics which were relevant for families with CWE. The method of thematic analysis yielded considerable information even from a small sample (Cook et al., 2021). A challenge and further possible limitation of the current study was the need to balance the requirement for evidence-based content with all the suggestions made by parents.

In conclusion, we have outlined the co-creation of COSI, a unique, tailored, online, BSI for use with CWE. We hope that consideration of factors, identified through patient and public involvement, as being salient for parents of CWE will help parent-engagement and optimise COSI's relevance for this patient group. If the results of the clinical trial suggest that COSI is successful in supporting parents to establish healthy sleep in CWE, then the intervention may help to address an unmet need, by offering a low-cost resource to support the many children with epilepsy and their carers who experience poor sleep.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because data are to be made available at the end of the research programme. Requests for access to be made to the Programme Manager: amber.collingwood@kcl.ac.uk.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Oxford Brookes University Research Ethics Committee (UREC approval 171108). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

All authors contributed to conception and design, acquisition of data, analysis and interpretation of data, drafted the article, and revising it critically for important intellectual content.

FUNDING

This paper presents independent research funded by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research Programme (RP-PG-0615-20007). HH was supported by a National Health and Medical Research Council (NHMRC) Practitioner Fellowship (1136222). The MCRI was supported by the Victorian Government's Operational Infrastructure Support Program.

ACKNOWLEDGMENTS

The authors would like to thank the parents and children who shared their time and views to help with the development of COSI and the charities and organisations who kindly advertised the research. The authors would also like to thank the funders.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2021.679804/full#supplementary-material

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Disclaimer: The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychology

ORIGINAL RESEARCH
published: 29 July 2021
doi: 10.3389/fpsyg.2021.628605

A Qualitative Investigation Into What Parents Want From an Online Behavioural Sleep Intervention for Children With Epilepsy

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Many of the same sleep problems seen in typically developing (TD) children are frequently experienced by children with epilepsy (CWE). Behavioural sleep interventions (BSIs) are commonly and successfully used to treat these sleep problems in TD children and in some neurodevelopmental disorder populations. Therefore, BSIs should be effective in CWE, however, there are special seizure-related considerations for CWE and their parents which may be salient to consider in any future BSI development for this group. The current study sought to identify, from parents, if there were special considerations for the content and delivery of an online BSI for parents of CWE. Semi-structured interviews were conducted with nine mothers of CWE and thematic analysis was conducted on the interview data. Ten themes were apparent which represented what parents wanted from any online BSI for CWE. Parents wanted (i) other parents' views and real-life experiences to be included, (ii) recognition of how changes over time may influence the appropriateness of using various sleep-management options, (iii) to be presented with a range of sleep management options from which they could select, (iv) personalised information and suggestions for behaviour-change options, (v) help to address child anxiety around sleep, (vi) for the advice and behaviour-change options to be practical, (vii) general educational information about sleep and the relationship between sleep and epilepsy, (viii) for parental worries and concerns to be acknowledged, (ix) to receive help, support, and reassurance around children's sleep; and (x) to include the child in the intervention. It was clear that any online BSI would require specific adaptations and additions (to content and delivery format) to best meet the needs of parents of CWE. It is hoped that having identified what parents want from on online BSI for CWE will allow these factors to be acknowledged in future intervention development, with the intention to optimise parental engagement and intervention effectiveness. Practical suggestions for how these aspects could be integrated into any online BSI are suggested.

Keywords: qualitative, epilepsy, sleep, sleep intervention, parental needs, children

OPEN ACCESS

Edited by:
Christian Franceschini, University of Parma, Italy

Reviewed by:
Chiara Fante, Istituto per le Tecnologie Didattiche (ITD), Italy
Oliviero Bruni, Sapienza University of Rome, Italy
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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *12 November 2020*
Accepted: *15 February 2021*
Published: *29 July 2021*

Citation:
Cook G, Gringras P, Hiscock H, Pal DK and Wiggs L (2021) A Qualitative Investigation Into What Parents Want From an Online Behavioural Sleep Intervention for Children With Epilepsy. Front. Psychol. 12:628605. doi: 10.3389/fpsyg.2021.628605

INTRODUCTION

Epilepsy, characterised by recurrent seizures, is a common neurological condition which affects 1% of the population, with nearly 65,000 children and young people affected in the United Kingdom (Joint Epilepsy Council, 2011). Comorbidity is common in children with epilepsy (CWE) in domains such as cognitive functioning, memory, processing speed, and learning as well as behavioural problems (Children with Epilepsy in Sussex Schools (CHESS) study, 2014).

In various populations, a factor which has been linked with functioning in all these areas throughout the lifespan is sleep; poor-quality sleep in childhood predicts future cognitive, attentional, and psychosocial problems (Gregory et al., 2005; Hill et al., 2007; Simola et al., 2014). The relationship between sleep and seizure disorders is a particularly vicious cycle and readers are referred to the paper by Gibbon et al. (2019) for a consideration of the associations between sleep and epilepsy. Nocturnal seizures can fragment sleep, while a number of factors, including sleep disorders and anti-seizure medications, cause sleep fragmentation and can worsen seizures. Establishing and obtaining healthy sleep is particularly crucial in CWE as sleep disturbance (i.e., impaired quality or quantity of sleep) can also trigger seizures (Gibbon et al., 2019). Yet CWE experience sleep problems (i.e., symptoms suggestive of a possible sleep disorder) more frequently than typically developing (TD) children (Owens and Mindell, 2011), and this is true for children with epilepsy both with and without nocturnal seizures (Cottrell and Khan, 2005). For example, in a sample of 4–10 year old children with focal epilepsy, parental reported sleep problems were 12 times more common than in children without epilepsy, even without the presence of nocturnal seizures (Gutter et al., 2013).

The sleep problems experienced by CWE can lead to daytime sleepiness and worse cognitive functioning, behaviour, and quality of life (Stores et al., 1998; Maganti et al., 2006; Owens and Mindell, 2011). The impact extends to the whole family and parents of CWE often report having disturbed sleep (Larson et al., 2012). This may include disturbance due to waking up frequently to check on their child, or in some cases choosing to bed or room share with their child in case s/he has a seizure. Parents of CWE have been found to be at seven-times higher risk of sleep disturbance in comparison to parents of children without epilepsy (Shaki et al., 2011) and spend an average of only 4 h asleep, with further associated adverse outcomes on maternal health and marital satisfaction (Cottrell and Khan, 2005). Reducing sleep disturbance in CWE is therefore a pivotal target of intervention that could potentially improve not only child sleep, but also learning, mood, behaviour, seizures, and parental quality-of-life.

The type of sleep problems experienced by CWE are varied (see Gibbon et al., 2019 and Kothare and Kaleyias, 2010 for a detailed discussion of sleep issues in children with epilepsy) but can present as similar to the sleep problems experienced by TD children and commonly take the form of issues with sleep initiation (settling and going off to sleep) and/or maintenance (night or early morning waking) (Stores et al., 1998; Owens and Mindell, 2011; Gutter et al., 2013). These symptoms could arise as a result of various sleep disorders (or other factors related to the child's epilepsy or other clinical conditions). Diagnosis and management decisions, of course, need to be based on careful individual assessment of each child and family. However, attention to behavioural factors (alone or as a component of intervention) is likely to form a part of management of many sleeplessness problems in both TD children and those with neurodevelopmental disorders (Wiggs and France, 2000; Mindell et al., 2006; Mindell and Meltzer, 2008; Bruni et al., 2018). Behavioural sleep interventions (BSIs), seek to provide parents with strategies they can implement to encourage desired sleep behaviours by manipulating their child's learned associations with sleep. BSIs can be delivered in a variety of modes including face-to-face (Hiscock et al., 2015), telephone (Stuttard et al., 2015), paper-based (Gringras et al., 2012), and online/app based (Mindell et al., 2006; Espie et al., 2012), making for the possibility of flexible and cost-effective interventions with wide-reach. BSIs have well demonstrated efficacy in randomised controlled trials for younger TD children, and older (up to 12 years of age) autism and attention-deficit hyperactivity disorder (ADHD) populations (Mindell et al., 2006; Johnson et al., 2013; Hiscock et al., 2015). Therefore, it has been proposed that BSIs could be modified effectively for CWE (Gibbon et al., 2019).

However, a "one size fits all" approach to the behavioural management of sleep in CWE fails to acknowledge potential specific seizure-related considerations for CWE (e.g., nocturnal seizures or anxiety about seizures) and their parents (e.g., concerns about the appropriateness of using some behavioural techniques with a child who might have seizures). Qualitative approaches have increasingly been used to extend our understanding of key issues and experiences of parents and their CWE (Harden et al., 2016; Wo et al., 2018; Jones et al., 2019). Others have noted the extensive potential benefits of partnering with end users in the development of healthcare systems and interventions, including those to be administered online. This approach not only benefits the end product but can also engage and empower parents and families in their own healthcare and interventions (D'Alessandro and Dosa, 2001; Carman et al., 2013). While addressing sleep problems in CWE is a possible intervention target to improve a range of outcomes for children and their parents, there is a lack of exploration around what seizure-specific considerations or adaptations may be required for any BSIs for parents of CWE to best meet their needs. The current study was conducted as part of a larger program Changing Agendas on Sleep, Treatment and Learning in Epilepsy (CASTLE) exploring the health and quality of life of CWE and their parents, and whether these can be improved by better sleep. Epilepsy is a diverse group of electroclinical syndromes and how its various manifestations are linked with sleep and sleep difficulties at different ages could not, and was not intended to, be documented by the results of the current study. Rather, the current paper reports qualitative findings from interviews with parents of CWE that sought to identify broad factors related to sleep-management which were important to parents to inform the development and delivery of an online BSI

designed for parents of CWE to be used in the CASTLE Sleep-E clinical trial[1].

MATERIALS AND METHODS

Participants and Recruitment

Nine mothers of children (six males, ages ranging 5–15 years, with median = 10 and mean = 10.3, SD = 2.9) participated in the initial interviews. The sample was generally well-educated. Descriptive information about parent-reported child sleep problems and seizure timing is shown in **Table 1**. Of the children, five had Benign Rolandic Epilepsy (one atypical), two had focal seizures, one generalised seizures, and one unspecified. Two had been diagnosed with epilepsy <1 year ago, two children between 1 and 3 years ago, and five children >3 years ago. As can be seen in **Table 1**, the children in this sample had experienced a range of sleep problems, either currently or in the past, with all children having difficulties with sleep currently and in the past. This allowed parents to provide their thoughts and experiences of dealing with longstanding sleep problems in their child with epilepsy.

Participants were recruited (between March and July 2018) via online advertisements placed on the websites of epilepsy organisations and charities (e.g., Epilepsy Action) and the CASTLE study and researchers' university websites. Online recruitment was considered appropriate given that taking part in the study required parents to have access to the internet.

Other inclusion criteria were that participants were the parent of a child with epilepsy (of any type), based in the United Kingdom and had sufficient English language skills so that they could read and interact with a draft version of the online BSI and respond to written and oral questions about it, reported in a separate paper (see Wiggs et al., 2021). There were no specific exclusion criteria and all parents who met the inclusion criteria were eligible.

Interested participants were invited to contact the researchers and once contact had been made, parents were emailed a participant information sheet explaining the study and a consent form. Potential participants were then contacted by the researchers to (i) ensure materials were received, (ii) discuss the specifics of the study and answer any parental questions, and (iii) complete an eligibility and contact details form if participants agreed to participate. Once signed consent forms were received (by post or scanned and sent via email), a convenient time was arranged to conduct the interview.

Measures and Data Analysis

The initial intention had been to run focus groups with parents to elicit their thoughts and opinions about factors related to sleep-management which were important to them with the intention of using this information to inform the development of an online BSI for parents of CWE. However, logistical issues in bringing participants together at convenient times resulted in an amendment to the data collection method and individual semi-structured interviews were conducted with parent participants instead.

Interviews

Researchers developed a semi-structured interview schedule that asked about key topics relevant to the development of an online sleep intervention (see **Supplementary Material 1**). In addition to asking about demographic factors and the child's health and epilepsy for descriptive purposes, this included questions about (i) child and parental sleep (including asking about particular difficulties with sleep faced by the family and/or child because of the child's epilepsy and the areas related to the child's sleep that parents want help with), (ii) the nature and success of sleep-related treatments or management approaches that had been attempted (including their views about why some approaches they had tried were not successful, (iii) their views and experiences of the acceptability of behavioural interventions specifically, if not already discussed, (iv) epilepsy-specific issues that would need to be considered or addressed as part of any developed intervention, and (v) parental perceptions of what would make a good or bad online intervention experience (e.g., relating to website content and usability).

Whilst parents were asked about their own and their child's particular experiences (sections i and ii), this was in the context of hoping to elicit broad issues related to sleep and sleep-management, rather than documenting their individual circumstances. Parents were fully informed at the outset about the intention of the interview and when answering encouraged, especially in sections (iii)–(v), to reflect on their own past and current experiences and the wider context of the parents of CWE community.

Interview transcripts were analysed by the researchers using thematic analysis following the standardised guidelines developed by Braun and Clarke (2006). The researchers further sought to ensure credibility, dependability and confirmability and applied a number of the "means for establishing trustworthiness" proposed by Nowell et al. (2017). An inductive data-driven thematic analysis approach was employed, whereby themes were derived from the data in a "bottom-up" approach, with participants' words being the starting point from which themes were developed.

During data familiarisation, interviews were transcribed and then repeatedly reviewed, before being systematically coded by a researcher not involved in the interview process (GC). Coding was discussed amongst the research team to address any discrepancies and reach agreement in the coding. Because of these discussions, some codes were combined and other codes that did not relate to what parents of CWE wanted from any online BSI were omitted. One of the researchers (GC) then grouped the codes into potential themes. These themes were iteratively reviewed and discussed amongst the research team to reach agreement. Next, coded extracts of raw data were re-visited and the themes were reviewed across the whole data set to ensure that themes accurately reflected interview content. Subsequently, the research team agreed names and descriptions for each theme. This involved ongoing discussion until agreement was reached. Prior to the write-up, the research team agreed that the final

[1]https://castlestudy.org.uk/

TABLE 1 | Descriptive information about children of the participants.

	Age	Gender	Seizure timing	Parent reported sleep problems*
P1	10	M	Transitioning between sleep and wake	Current: settling, night waking, sleep-related anxiety, unsettled sleep, co-sleeping
				Past: sleep terrors, sleep walking
P2	15	M	Daytime and during sleep	Current: settling, sleep-related anxiety, night and early morning waking, sleepwalking, sleep terrors, daytime sleepiness
				Past: room sharing
P3	10	F	Transitioning between sleep and wake	Current: night waking, sleep terrors, sleep-related anxiety, co-sleeping
				Past: morning waking difficulty
P4	11	M	Transitioning between sleep and wake	Current: settling, sleep-related anxiety, night waking
				Past: room sharing
P5	5	F	Daytime. 1 year without seizures (due to medication)	Current: settling, night waking, sleep terrors, sleep-related anxiety, room sharing, co-sleeping, daytime sleepiness
P6	9	M	During sleep	Current: settling, night and early morning waking
				Past: daytime sleepiness and co-sleeping
P7	13	F	During sleep and transitioning between sleep and wake	Current: settling, morning waking difficulty
P8	7	M	Transitioning between sleep and wake	Current: night and early morning waking, co-sleeping
P9	13	M	Daytime and transitioning between sleep and wake	Current: settling, night waking, poor sleep quality, daytime sleepiness, possible restless legs syndrome

**Current sleep problems refers to problems which are currently present but it should be noted that the duration of these problems is generally longstanding (since infancy or beyond), with most problems also being also present in the past. Past sleep problems refers to problems which have now resolved but which were significant problems at some point.*

themes reliably and accurately embodied the detail present in the participants' original data. The final analysis was reviewed and discussed between the team until all were confident that the findings accurately represented the raw data and presented a coherent overview of the data relevant to the topic in question.

The presence of each theme across individual participants' data was identified so that a frequency count for each theme could be generated to provide an indication of the strength of each theme across the sample. Results from the interviews allowed us to identify epilepsy-specific considerations for an online BSI for parents of CWE.

Procedure

This was a qualitative study with parents of CWE. Ethical approval was obtained through the Oxford Brookes University's Research Ethics Committee (UREC approval 171108). Following informed consent (as described in section "Participants and Recruitment") interviews were scheduled and conducted (by LW and PG) at a time and in a manner convenient to participants (two face-to-face, six telephone, and one video call). They were audio recorded, transcribed and thematically analysed to identify the key themes reported by parents relevant to the development of the online intervention.

RESULTS

Parent Interviews

Parent interviews had an average duration of 61 min. Several themes were apparent, as explained below along with supportive quotes, which highlighted key aspects parents felt should be acknowledged or addressed in any online BSI for parents of CWE. See **Table 2** for an overview of final themes and which participants made comments relating to which theme. Details of the themes are presented in **Table 3**, including the theme description, frequency count and illustrative quotes.

Other Parents' Views and Experiences

A firm preference was reported for hearing about other parents' experiences, *"for me, when I've looked at websites and researched things, the thing that I look out for most is other parents' stories"* (P1). Parents valued other parents' experiences for a number of reasons; for some parents it was useful to hear what had worked successfully for other families, *"it is good to have other parents' experiences as a backup, so if it doesn't work maybe try this"* (P5). While for others, the value was in the sharing of experiences of parents dealing with sleep in CWE, *"as far as the sleep, not the medical side of sleep but the experience side, I think I would prefer to hear from other parents"* (P2).

For many parents, hearing from other parents was crucial and was perceived as more beneficial than simply being presented with information derived from clinical experience or research data:

> *"So for me it's definitely someone going through the same thing and reading their words is something that I would find maybe more powerful than just a paragraph saying, 'well this normally happens or this can happen or that can happen'"* (P1).

Some parents specifically highlighted that an interactive component to any online resource would be useful in allowing them to obtain information and advice from other parents:

TABLE 2 | Summary of themes identified and by which participants they were reported.

	P1	P2	P3	P4	P5	P6	P7	P8	P9
Other parents' views and experiences	x	x	x	x	x	x	x	x	
Change over time	x	x	x	x	x	x	x	x	
Range of management options	x	x	x	x	x		x	x	
Personalisation of information	x		x	x	x		x	x	
Child anxiety around sleep	x	x	x	x	x		x		
Practical sleep intervention suggestions		x	x			x	x	x	x
General sleep information		x	x	x		x	x	x	
Parental anxieties and concerns	x	x	X	x	x				x
Help, support and reassurance around sleep	x	x	x	x					
Include child in intervention		x				x	x		x

"It's a shame. . .you don't have like a forum on it. . .so that parents can ask each other questions, that would be useful. . .because if there's some random question that's not answered on there. . .someone could go that's happened to us this is what we did" (P6).

Parents obviously valued hearing other parents' views and experiences for a variety of different reasons and it was clear that this aspect would need to be a key component for any BSI designed for this group.

Change Over Time

Parents reported a variety of possible ways in which they, their child and their broader family may change and develop over time, which were significant to managing their child's sleep, and which needed to be acknowledged. These included changes in the child, the child's epilepsy, age and family anxieties. Parents acknowledged that these factors may impact the relevance and/or use of different techniques at different times. For example, one parent emphasised individual child factors, and specifically age, as impacting the appropriateness of different behavioural interventions, *"I suppose it depends on. . . every child's different aren't they and I think it probably just depends on your child and the age of your child"* (P1). In addition, another acknowledged how the effectiveness of different sleep management techniques can shift and change over time, *"It helped for a while as things perhaps do"* (P7).

Parents stressed that variation could exist within a family across time. For example, one parent highlighted the difference age makes in parental monitoring and awareness of their child's sleep and sleep problems, *"there's a big difference between a 7 year old coming through going 'mummy I can't sleep' then a 15-year old saying 'oh I'll sit on my iPad at 3 in the morning for 10 min until I fall back asleep again'"* (P2). Another was already anticipating possible future change, prompted by both her child's wishes and her child's seizure state:

"But what I would like to change, what I would maybe think about if, and I'm thinking about it now because maybe the time will come and she will want to sleep alone, but maybe sleeping on her own would be something I would like to, yeah, try but not now with her epilepsy, no I wouldn't give it a shot now" (P5).

Parents clearly felt that any suggestions for managing children's sleep needed to acknowledge the variety of possible changes which might occur over time and which may influence their desired sleeping arrangements, their approach to sleep as well as the applicability and/or use of different techniques at different time points.

Range of Management Options

Parents felt strongly that they didn't want sleep management options to be prescriptive, *"I don't like anything. . .that sounds like this is the only way to go. . .it's never black and white"* (P5). Instead, what parents desired and felt would have been useful to them when dealing with their CWE's sleep was "*suggestions of things, 'you could try this', yeah and I think that would have been really helpful"* (P2).

Parents desired the ability to be informed about the range of different options, *"if there was a website there to help you, to say 'try this or try this or, you know, different things'"* (P4). Parents felt that such information would allow them to decide which approach was most appropriate for them. For example, one parent said what they desired was to *"pick some that I felt could help and try those rather than try everything. You know try some that would fit in for us"* (P3).

Parents clearly valued the opportunity to review the range of possible sleep management options and to have the ability to choose techniques that they felt were most suited to them, their individual child and/or their individualised circumstances.

Personalisation of Information

A key feature of any online BSI that parents felt was highly desirable was the personalisation of any material, where possible. For example, one parent identified the benefit of being signposted to key relevant information, *"you can be directed more specifically for your needs then that would be really good"* (P1). This desire for personalisation was emphasised, primarily for practical reasons so that parents could quickly identify information which was of relevance for them without having to spend time extracting this themselves. For example, one parent reported that:

"I literally spent hours reading about different things, so if you could just do that then leave the bits that were relevant for you, definitely useful, yeah" (P4).

TABLE 3 | Themes, description, frequency count and supportive quotes of what parents wanted to be included in an online BSI for parents of CWE (based on *n* = 9 parents).

Theme name	Theme description	Number of parents reported by	Example quotes
Other parents' views and experiences	Access to other parents' views or experiences (about parenting, sleep, interventions) were valued highly because other parents had first-hand experience and was seen as an essential aspect to include in the intervention	8	"I find it really helpful when you get stories from other parents who've tried things and if they've worked" (P4) "The real experiences from other parents" (P5) "I would more listen to other parents who would who have tried something, whether they had scientific research to back it up, if they said, 'this has worked for my son' and he's got the same thing as (child) has, I think well it's worth a go, I'll give it a go" (P4) "It's really nice to see or hear. . .or even read an excerpt from a parent" (P3)
Change over time	The need for any suggestions for behaviour change techniques to acknowledge that there are changes over time (in terms of the child's epilepsy, age, the family's anxieties) and that these affect the applicability of use of different techniques at different times	8	"Yeah, because it does massively change because I feel totally different to when he was first diagnosed. It was just none of us were getting any sleep at all. It was just really stressful" (P4) (in response to issues with putting things into practice) "I suppose it depends on. . .every child's different aren't they, and I think it probably just depends on your child and the age of your child" (P1) "That was the real crux of (child's) changing and his sleep patterns was and that's the year he really, really struggled was the change from primary school to secondary school, which apparently is meant to be one of the biggest things in a kid's life anyway" (P2) "But what I would like to change, what I would maybe think about if and I'm thinking about it now because maybe the time will come and she will want to sleep alone, but maybe sleeping on her own would be something I would like to yeah try but not now with her epilepsy, no I wouldn't give it a shot now" (P5)
Range of management options	That any suggestions for behavioural change techniques should be non-prescriptive but rather should give parents the ability to choose from a range of techniques, depending on what suited their individual child and/or circumstances	7	"if there was a website there to help you, to say 'try this or try this or, you know, different things'. . . Because obviously different things work for different people. But you know if there was one kind of point you could go to get all of that advice that would have helped" (P4) "Here's some things and see what fits in, what can you fit into your family, your circumstances, because the children will be at such a variety of ages" (P3) "If it's an option then I would try to read through it" (P5) "So yes I think maybe almost like a spiders web isn't it, so you have one and then it goes off and off and off. But you can still sort of come back in. . .:" (P2)
Personalisation of information	Parents had a desire to be directed to content which was personalised to the individual child and/or family needs as far as possible	6	"I think personalising it would make it more, have more of an impact. I mean at the end of the day the chances are if you're reading about the intervention or being involved in the intervention then something going to resonate with you in that" (P1) "It would actually get me hooked up. . . to answer the data about my child and so that it pops up what kind of situation do we have so that it narrows down the data or narrows down the sort of text that I have to read. . .it would work for me" (P5) "Signposted to the most relevant part for yourself but then so if you [want], you know, this is available" (P3) "You also hope that by entering your problems. . .it's the most interactive way to talk to the internet. . .you get some kind of answer" (P5)
Child anxiety around sleep	Many parents reported that their child struggled with anxieties around sleep. Either in relation to fear of sleep due to their epilepsy or as sleep being a time when anxieties or concerns were expressed. Some parents specifically desired information to help them support their child(ren) with any anxiety or fears around sleep	6	"He was having a lot of difficulty sleeping because he was worried that if he went to sleep, because we had quite a few instances where he went to bed as normal and when he woke up he was in hospital. . .he had a massive fear that he was going to die in his. . .sleep, so I think that's, it's not just the seizures, it's the emotional side of it as well" (P2) "She does worry about things and it all seems to come out, you know, as it does I suppose you get into bed and you think about everything" (P7) "Maybe some sort of tool to talk to him about it" (P1) "It's very hard and we've really tried but I know my husband has accidentally said it before. It's very hard so if she's resistant to want to go to bed he says 'well (child) now look you know you need to go to bed early because you know because of your seizures you know' and then you don't want to bring it into that just before you go to bed" (P3)
Practical sleep intervention suggestions	Desire for practical suggestions for ways in which they could make changes to their child's sleep	6	"I just want the end result of what to do. . .Get to the point, what do I need to do" (P7) "I think the main thing is, I think, to consider is it's got to be something you can work around other family members" (P3) "So I think practical things as well help for reassurance for him and for us as well, yeah" (P2) "I think just practical stuff might be useful" (P6)

(Continued)

TABLE 3 | Continued

Theme name	Theme description	Number of parents reported by	Example quotes
General sleep information	General sleep information (i.e., about normal sleep and the link between sleep and seizures) as well as specific "intervention" advice. Some parents had not been advised about the possible link between sleep and seizures while others were told by clinicians that good sleep was important for CWE but were not advised of ways to address child sleep	6	"Not anything that had ever been brought up or even asked. . .So no no one's ever said anything about sleep" (P2) "I just Googled and Googled...for all different like helps and things like that to kind of help them" (P4) "I've done so much research online it's ridiculous but it's just like I've just sort of found out myself really that I try" (P7) "Sleep is the one thing that we can do, help. But then not really much assistance comes along with that at that point of diagnosis so it's kind of, you know, you've got to be having 10 h, you've got to be getting them to sleep early and especially for children that are my daughters age, so 10/11, you're talking quite a bit of a lifestyle change really for them" (P3)
Parental anxieties and concerns	For parents' worries and concerns (about sleep, epilepsy and intervention approaches) to be acknowledged, even if these concerns could not all be resolved	6	"The problem for us is...that it's us that are scared of leaving him in case he has a seizure so in regards to monitoring sleep I don't really, you know, we've thought about putting a camera in his room and things but that would, we'd just be sat watching the camera" (P1) "....because you're aware of these issues and, I think, as a parent to know that it's been flagged up, that I'm not just being overreacting or being paranoid about letting my child go to a sleepover... Yeah, I think that would be nice, just to acknowledge it and say actually 'no, there are other parents out there that either don't let their child go to a sleepover"' (P2) "I got so used to waking up and having to go into him, if he has a good night I become anxious and have to go through and check he is OK and still breathing" (P9) "I do sleep like a rabbit and I hear her every move and in her every move and every episode that she has during the night I am looking for signs that it might be a seizure" (P5)
Help, support and reassurance around sleep	That information about child sleep (typical and atypical), how to manage it and how this relates to others' experiences would be reassuring and help parents feel supported. For some parents this was particularly needed at the time of diagnosis	4	"Having, yeah, reassurance I think, or even, yeah, just guidelines or something kind of like, this is what you can try for your child. . ." (P2) "It's just so nice to know that there's sort of someone out there who's trying to do some research and trying to put things out there to help" (P1) "Because at the point of diagnosis they said this is, you know, the one thing you can do (sleep). It feels more pressured. . . more challenging, because you feel that it is the only thing you can do" (P3) "It was just really, really stressful [when first diagnosed] so any kind of assistance then would have been massive because I spent hours and hours on the internet like researching different things" (P4)
Include the child in intervention	Some parents felt that the child's perspective, voice and/or feelings should be acknowledged in the intervention. It was seen as important that children's perspectives about sleep had been considered and were included as they, and their needs, are central	4	"I think from a child's point of view it's very important too and maybe it would be even worth you interviewing some children about this because I don't think they get their say about how they feel or how they would want to cope with it as well." (P2) "I've noticed a lot of information that you get given is only aimed at the parents, if you get given anything, any kind of. . .leaflet or whatever this is for a parent of the child who has epilepsy and (child) is like, well, I've got it why am I not getting any information, why have they not given me anything to read. . ." (P6) "She is at an age now where yeah. But she, yeah, I think there should be information for both of us" (P7) "For the older children you should have some advice for them, the children as well so they can be part" (P9)

Parents also felt personalisation would help material have the greatest benefit on parental engagement and how parents viewed the information, *"I think personalising it would make it more, have more of an impact"* (P1). It was clear that developing a means by which salient material could be identified and presented to parents in a personalised manner would be an important consideration for an online BSI for this group.

Child Anxiety Around Sleep

It was common for parents of CWE to report that their children experienced anxiety around sleep as a result of their epilepsy, *"I've spoken to him about it and he said he used to be a bit nervous in case he did have one (seizure)"* (P4). For other parents sleep or bedtime was a time when child anxieties or concerns were explicitly expressed, "*bedtime is usually the time in which things come out if she is worrying*" (P3).

Some parents specifically reported that they were interested in finding out about ways to help them support their child(ren) with any anxiety or fears around sleep. For example, one parent reported what would be useful was *"how to explain and how to make an entry of this new subject would be helpful"* (P5). Others acknowledged that managing a CWE was not just about seizure management but also the anxieties and fears that are bound up in the condition for some children, *"it's not just the seizures, it's the emotional side of it as well"* (P2).

It was clear that CWE's anxiety around sleep and bedtime was problematic and challenging for parents. Many parents also felt they required help and support to approach managing these issues suggesting this is an important component which should be included in any BSI for parents of CWE.

Practical Sleep Intervention Suggestions

Parents reported a desire for approaches to and management options for their child's sleep to be practical in nature. For example, when asked what would be useful one parent reported, "*I think just practical stuff might be useful*" (P6) and another "*just give people the practical stuff"* (P9).

Parents reported different motivations for desiring practical intervention suggestions including so that parents could easily identify the aspects of the intervention that they needed to implement, such as "*I just want the end result of what to do. . .Get to the point, what do I need to do" (P7).* While others wanted interventions that were practical for them and their individual circumstances:

> *"I think the main thing is, I think to consider is it's got to be something you can work around other family members*'" (P3).

Given parents' desire for practical sleep management options, it appears important that any suggested management strategies are ones that can easily be integrated into family life and also that instructions for their use are conveyed to parents in a clear and easy to understand manner.

General Sleep Information

It was evident that many parents did not feel that there was currently sufficient help and information for parents of CWE around sleep, *"we've not had any advice beyond that. Apart from get good sleep, that's the one thing you can do"* (P3). Parents reported a desire for general information about sleep (including in relation to epilepsy):

> *". . .include the quality of the sleep so that if that is such a big factor in having seizures, I'd actually like to know more about sleep and how it can affect that*" (P3).

Some other parents also reported lacking awareness or knowledge of methods that they could use to manage any difficulties with sleep "*it's a bit like I don't really know what else there is really to do"* (P6). It was clear that many parents desired knowledge and information around sleep (i.e., normal sleep, relationships with epilepsy, sleep problems, and their management) and their need to feel informed should be addressed prominently in any BSI for parents of CWE.

Parental Anxieties and Concerns

Parental anxiety was a topic which parents raised as salient and requiring acknowledgement. These anxieties were broad in nature and dealt with concerns about sleep, epilepsy and intervention approaches. For example:

> *"We're just scared, just the fear of it (seizure) happening and us not hearing him or us not being there is just, it's just unbearable to think about"* (P1).

> *"I got so used to waking up and having to go into him, if he has a good night I become anxious and have to go through and check he is OK and still breathing"* (P9).

Some parents acknowledged that the issues pertinent to them may not be able to be resolved by any intervention but it was nevertheless important that they were recognised:

> "*...because you're aware of these issues and I think as a parent to know that it's been flagged up, that I'm not just being overreacting or being paranoid about letting my child go to a sleepover, yeah I think that would be nice just to acknowledge it"* (P2).

It is clear that parents' wide-ranging worries and concerns about relevant topics need to be understood and acknowledged in a BSI for parents of CWE. In doing so, this will help provide parents with confidence that the intervention is sensitive to their needs and the challenges that they face.

Help, Support and Reassurance Around Sleep

Many parents reported not feeling adequately supported in managing and, if necessary, improving CWE's sleep. For example, "*I think any kind of help, kind of assistance with getting to sleep....because a lot of them, I think, do struggle to sleep"* (P4). Many parents felt that it would be reassuring and help parents feel supported if they had more access to information about child sleep (both typical and atypical), how to manage it and also how this information and their own experiences relate to others' experiences:

> *"Having, yeah, reassurance I think, or even, yeah, just guidelines or something kind of like, this is what you can try for your child. . ."* (P2).

For some parents it was clear that this type of help, support and reassurance was particularly pertinent at the time of diagnosis:

> *"Because at the point of diagnosis they said this is, you know, the one thing you can do (sleep). It feels more pressured. . . more challenging, because you feel that it is the only thing you can do"* (P3).

It was evident that support and reassurance for parents around managing and, if necessary, treating their child's sleep was lacking. For some parents, this was a fundamental and essential element that should feature in any BSI developed for this group.

Include Child in Intervention

Some parents felt that CWE's perspective, voice and/or feelings should be clearly acknowledged in the intervention:

"I've noticed a lot of information that you get given is only aimed at the parents, if you get given anything, any kind of leaflet or whatever this is for a parent of the child who has epilepsy and (child) is like, well, I've got it why am I not getting any information, why have they not given me anything to read. . ." (P6).

Specifically, it was felt by some that children's perspectives about sleep should be considered and included as they, and their needs, are central and this is not an aspect which is usually addressed:

"*I know with (child) nobody's ever asked him how he feels and that's one thing he keeps on about quite a lot. That nobody understands how he feels, which we don't"* (P2).

Some parents highlighted specific means by which children's perspectives could be integrated and how children could be involved in different ways in the intervention:

"I think from a child's point of view it's very important to and maybe it would be even worth you interviewing some children about this because I don't think they get their say about how they feel or how they would want to cope with it as well" (P2).

It appears important and relevant that an online BSI designed for parents also acknowledges or includes the voice of CWE themselves.

DISCUSSION

Ten themes were identified which represented the requirements of parents of CWE for any online BSI. Parents wanted (i) other parents' views and real-life experiences to be included; (ii) recognition of how changes over time may influence the appropriateness of using various sleep-management options; (iii) to be presented with a range of sleep management options from which they could select; (iv) personalised information and suggestions for behaviour-change options; (v) help to address child anxiety around sleep; (vi) for the advice and behaviour change options to be practical; (vii) general educational information about sleep and the relationship between sleep and epilepsy; (viii) for parental worries and concerns to be acknowledged; (ix) to receive help, support, and reassurance around children's sleep; and (x) to include the child in the intervention.

Sleep issues (including broader sleep-related factors which might not indicate any sleep disturbance, a sleep problem or a sleep disorder, for example to do with the sleep environment or parent anxiety) are common in CWE and parents in the current study were very clear about the need for a sleep resource. This desire for information and support is in keeping with the findings of another qualitative study with parents of CWE, which also emphasised parents' desire for both information *and* support, which extends beyond the point of diagnosis (Jones et al., 2019). Many parents felt that receiving information and support around child sleep would help them to feel reassured about their ability to manage and, if necessary, improve their child's sleep. The current study has described the key aspects that parents of CWE would want to be included in any online BSI for this group and it is hoped developing an online BSI with these considerations in mind would help to meet this need.

One of the most prominent topics reported by parents was the importance of hearing from other parents who have shared experiences. This desire has also been highlighted as an important factor for parents of CWE in a Malaysian sample (Wo et al., 2018). Based on the frequency and strength with which this theme was reported by parents in the current study it was concluded this was an essential addition to any online BSI for parents of CWE. A possible practical approach, which is increasingly recognised for its range of benefits in health research, is to involve parents in the co-production of the intervention (Hickey et al., 2018). In addition, explicitly representing the views and experiences of actual parents of CWE as part of the intervention content, perhaps in the form of videos or quotations, could also be beneficial and achievable as a way to clearly present other parents' experiences and help foster engagement (D'Alessandro and Dosa, 2001; Carman et al., 2013). Some parents in the current study expressed that they valued the use of interactive sites such as parent forums for this reason, so that they could exchange information, techniques or to obtain answers to relevant questions that they had. Peer support has been identified as a key factor in contributing to self-management in a young adult with narcolepsy (Franceschini et al., 2020), increasing feelings of social support and fostering information sharing. These benefits of peer support are similar to those outlined by the mothers in the current study, when describing the advantages associated with the peer support they received via online parenting forums. However, there may be tensions between combining anecdotal information from forums with evidence-based information included in any online BSI.

Another theme highlighted by parents was the possibility of including or representing CWE themselves in any online BSI. The nature of any sleep issues and the age range of the children targeted by the intervention would likely influence whether this was possible and the best approach for achieving this. This could perhaps, as suggested by some parents in the current study, take the format of having age-appropriate accompanying materials/online resources designed for the child which may further contribute to a feeling of partnership in managing children's sleep. A qualitative study of a young adult with narcolepsy has highlighted how peer support can improve an individuals' self-management of their condition (Franceschini et al., 2020). Perhaps an intervention approach that fostered peer support between CWE would be beneficial in the management of the child's condition and/or sleep, offering them an additional opportunity for support. Some parents in the current study also suggested having children's input into the intervention content, however, the appropriateness of this may be limited, particularly as some BSI strategies are specifically designed to eliminate parent behaviours which the child themselves may find rewarding and have little motivation to have eliminated. Involving CWE in the form of interviews and reflecting their voice and key concerns and experiences throughout the intervention would be another, perhaps more achievable, way in which children could be "included". Identifying how best to offer peer support to CWE and their parents is an important area for future investigation.

Parents were supportive of a diverse range of different behavioural techniques being provided (including those which they may not choose to use themselves) to address many types of sleep problems. The possibility for personalisation and freedom in the choice of which techniques to use was also important as it allowed parents to select strategies which were relevant, practical, and acceptable for them and their family at any given time. Including parents of CWE in decision-making has been highlighted as a key aspect of paediatric epilepsy care (Berg et al., 2013). Offering a range of possible intervention choices for dealing with each sleep problem and ensuring that these are presented as options rather than "instructions," via sensitive phrasing, could be a helpful way to best meet parents' needs.

Parents valued personalisation because it acknowledged the uniqueness of their child and family and also for practical reasons, as it limited the amount of information they would have to attend to (if they wanted to be more selective in their reading). The value of adopting a customised approach when delivering sleep interventions has also been raised by a sample of parents of disabled children (Beresford et al., 2010). The feeling of being overwhelmed by the excess of, often irrelevant, information generated from an internet search was prominently expressed by parents in the current study and in previous studies which have explored internet use in parental information seeking about child health care more broadly (Walsh et al., 2015). Ensuring any online BSI for parents of CWE was personalised may therefore help to encourage parental engagement with the material for multiple reasons.

Parents made it clear that any sleep management options should be practical. The current study explored what parents wanted from an online BSI and so, by definition, the strategies that would be presented would be behavioural in nature. These types of techniques are underpinned by the idea that parents follow clearly described strategies which are designed to be practical for parents to implement. However, additional attention to how these strategies are presented (e.g., noting possible variations which could be used, advice for coping with common situations which could arise during intervention) may help to ensure they are explicitly perceived by parents as "practical" strategies.

It was clear that parents of CWE held broad concerns and anxieties relating to their child's sleep, epilepsy and use of intervention approaches. Many parents felt that the pervasive and ongoing nature of these anxieties needed to be acknowledged in any credible BSI. Therefore, it is essential that any BSI comprehensively considers and seeks to allay, if possible, common parental anxieties. In some cases, it may be sufficient to reassure parents by providing them with evidence-based information. In others, the sensitivity with which matters are presented and discussed may be relevant. However, even where no obvious resolution to their anxieties is possible, parents believed it was important for the possible presence of such concerns to be aired and recognised, to increase the credibility of the BSI.

Parents also felt that content of any online BSI needed to acknowledge specific changes that may occur over time in the lives of parents and CWE. In the current study, these changes most notably included the status of the child's epilepsy, the child's age and the family's anxieties. Parents explicitly stated that changes in these areas could affect how they felt about any online BSI and also their views about the applicability of using different behavioural techniques at different times. Offering parents a range of optional techniques from which they can select goes some way to addressing this. In addition, material could explicitly make reference to the importance of these child and family factors, for example by ensuring that there is coverage of any sleep-related developmental changes and discussion of pertinent child and family factors which might influence parental choices about use of specific intervention strategies.

Many parents desired knowledge and information around sleep. This is in line with previous studies which found mothers of CWE in a Taiwanese cohort had relatively poor knowledge of child sleep (Tsai et al., 2018). Therefore, a key component of a BSI developed for this group should be the provision of general information regarding sleep. In the current study parents reported specifically wanting general sleep information about normal sleep processes, the links between sleep and seizures and details of specific methods that they could use to manage any difficulties with sleep in CWE. While limited, there is evidence to suggest that reduced levels of maternal knowledge about child sleep is linked to poorer and more variable maternally reported sleep in CWE (Tsai et al., 2018). Although there may be cultural influences on this reported link between maternal knowledge and reporting about sleep and these findings need further exploration, such results suggest that ensuring adequate levels of parental knowledge about sleep may be an important intervention target, helping parents to understand their child's sleep processes or to feel more confident and informed about how to manage their child's sleep.

Previous research has highlighted that CWE experience higher levels of anxiety around sleep in comparison to controls (Stores et al., 1998). It was apparent from the current study that a specific aspect of CWEs' sleep for which parents desired further support was managing sleep-related anxiety and night-time fears, which could play a role in many sleeplessness problems of CWE. Therefore, any future BSI for this group should ensure this topic is explicitly addressed so that the content reflects the type of sleep difficulties which are prominent for CWE.

A potential limitation of the current study is the small sample size, particularly as "CWE" are heterogeneous. Whilst broad and varied recruitment strategies were employed, initially for focus groups and later for interviews, recruitment remained a challenge throughout. The final sample consisted of only nine parents, all of which were mothers who were generally well-educated. However, these were mothers of CWE aged 5–15 years and this allowed us to obtain perspectives based on their experiences across childhood as these parents had dealt with a broad range of longstanding sleep-related difficulties. There generally seemed to be considerable similarity across parents in terms of their views about the priorities for factors which should be included in any online BSI for CWE with most of the themes, endorsed by the majority of parents. Greater understanding of demographic factors related to parents' views (and eventual use) of online interventions would be helpful.

Further, the current study did not attempt to relate parents' views to the particular problems with sleep or sleep-management identified by the families as these could never be representative of "CWE." Instead the intention was to highlight participants' opinions about general topics which are relevant for families, so that standardised BSIs could be developed and presented with these considerations in mind. Whilst some elements of the findings are clearly specific to parents of CWE (e.g., wanting information about the links between sleep and seizures), we don't know if other themes related to the delivery of an online sleep intervention (e.g., a desire for other parents' views and real-life experiences to be included and recognition of how changes over time may influence the appropriateness of using various sleep-management options) are specific to parents of CWE or are also important to other groups of parents or clinical groups. Future studies exploring the needs of parents in relation to child sleep interventions for discrete clinical (and other) groups are needed and could helpfully expand the number of parents involved and include fathers and children to maximise the chances of capturing diverse perspectives.

Being provided with information about management of behavioural sleep disorders will not be appropriate or the entire sleep-solution required for all parents of CWE. However, attention to behavioural factors (alone or as a component of intervention) is likely to form a part of the management of many sleeplessness problems, including in CWE. The availability of a general, online BSI resource for all parents of CWE would therefore seem useful. Whilst behavioural interventions for child sleep problems have a strong evidence base, parental insights from the current study suggest that the way management advice is delivered to parents could affect their engagement and, in addition, for parents of CWE, there are areas of additional content which should also be addressed to best meet their particular needs. The development of an online BSI (Castle Online Sleep Intervention, COSI) for parents of CWE which attempts to address the points raised by parents in the current study, is reported elsewhere (Wiggs et al., 2021) and its efficacy will be evaluated in the forthcoming CASTLE Sleep-E clinical trial (see text footnote 1). It is hoped that taking account of the special considerations of BSIs for parents of CWE will maximise the chances that the intervention is perceived as being relevant for them and their family.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because the data are qualitative interviews and cannot be shared. Requests to access the datasets should be directed to Amber Collingwood, amber.collingwood@kcl.ac.uk.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Oxford Brookes University Research Ethics Committee (UREC approval 171108). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

All authors contributed to conception and design, acquisition of data, analysis and interpretation of data, and drafting the article or revising it critically for important intellectual content.

FUNDING

This manuscript presents independent research funded by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research Programme (RP-PG-0615-20007). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care. HH was also supported by a National Health and Medical Research Council (NHMRC) Practitioner Fellowship (1136222). The MCRI was supported by the Victorian Government's Operational Infrastructure Support Program.

ACKNOWLEDGMENTS

The authors would like to thank the parents and children who shared their time and views to take part in the study. The authors also would like to thank the charities and organisations who kindly advertised the study.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2021.628605/full#supplementary-material

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychology

ORIGINAL RESEARCH
published: 05 August 2021
doi: 10.3389/fpsyg.2021.705212

Physical Activity Is Associated With Sleep Quality: Results of the ESSE-RF Epidemiological Study

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Edited by:
Christian Franceschini, University of Parma, Italy

Reviewed by:
Anita D'Anselmo, University of Bologna, Italy
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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *04 May 2021*
Accepted: *09 July 2021*
Published: *05 August 2021*

Citation:
Dubinina E, Korostovtseva LS, Rotar O, Amelina V, Boyarinova M, Bochkarev M, Shashkova T, Baranova E, Libis R, Duplyakov D, Sviryaev Y, Konradi A and Shlyakhto E (2021) Physical Activity Is Associated With Sleep Quality: Results of the ESSE-RF Epidemiological Study. Front. Psychol. 12:705212. doi: 10.3389/fpsyg.2021.705212

Background and hypothesis: Physical activity (PA) is an important behavioral factor associated with the quality of life and healthy longevity. We hypothesize that extremely low and extremely high levels of daily PA (including occupational PA) may have a negative impact on sleep quality and psychological well-being.

Objective: The aim of the study is to investigate the association between the level and type of PA and sleep problems in adult population.

Materials and methods: The sample of the study consisted of the participants from the population-based cohort of The Epidemiology of Cardiovascular Risk Factors and Diseases in Regions of the Russian Federation Study (ESSE-RF). The data of three regions (Saint Petersburg, Samara, Orenburg), varying in geographic, climatic, socioeconomic characteristics, was included into analysis. The total sample consisted of 4,800 participants (1,600 from each region; 1,926 males, 2,874 females), aged 25–64. The level of PA was evaluated using three parameters: the type of PA at work, the frequency of an intensive/high PA including sport (times a week), the mean duration of leisure-time walking (minutes a day). The measures of sleep quality were sleep duration and the frequency of difficulty falling asleep, difficulty maintaining sleep, daytime sleepiness, and sleep medication use. PA and sleep characteristics were assessed by interview carried by the trained medical staff.

Results: When controlling for gender, age and socioeconomic status (SES) extremely high occupational PA was a significant risk factor for difficulty falling asleep three or more times a week [OR(CI95%) = 1.9(1.2–3.0), $p = 0.003$] while working in a sitting position or having moderate physical load at work were not associated with sleep characteristics. Having a high physical load six or more times a week was a risk factor for difficulty falling asleep controlling for gender, age and SES [OR(CI95%) = 1.9(1.4–3.4), $p = 0.001$]. The

association between leisure-time walking and sleep characteristics was insignificant. Walking less than an hour a day was associated with increased depression scores (46.5 vs. 41.9%, $p = 0.006$).

Conclusion: High physical load at work and excessively frequent intensive PA are associated with difficulties initiating sleep and may represent a risk factor for insomnia.

Keywords: sleep quality, physical activity, anxiety, depression, socioeconomic factor, sleep duration, insomnia, sleep disorders

INTRODUCTION

Physical activity (PA), sleep, dietary pattern, and psychological well-being are known to be important factors contributing to the quality of life and healthy longevity. Interrelations between these components and other factors potentially influencing quality of life are being extensively studied.

According to a recent systematic review (Cunningham et al., 2020), PA in older adults (≥60 years) reduces risk of all-cause mortality, cognitive decline, and depression. Participants with sleep disorders improved sleep quality as a result of increased weekly activity up to 100 (Reid et al., 2010)—210 min (King et al., 2008) on a regular basis—from 16 (King et al., 1997) to 54 weeks (King et al., 2008).

In a systematic review by Yang et al. (2012) middle-aged and older adults with sleep problems who practiced physical exercise program (10–16 weeks) which consisted of either moderate intensity aerobic exercise or high intensity resistance exercise showed significantly reduced sleep latency (assessed by Pittsburgh Sleep Quality Index score) and medication use compared to the control group. In a more recent systematic review covering 14 studies all but one study found at least one significant improvement on sleep outcomes in generally healthy older adults engaged in PA programs, and no significantly detrimental effects were reported (Vanderlinden et al., 2020). The authors conclude that physical exercise may be regarded an alternative or complementary approach to existing interventions for sleep disorders.

The agreement on the optimal level of physical load beneficial for sleep quality and general physical functioning is being established. WHO recommends 150 min moderate-intensity exercise weekly World Health Organisation (WHO) (2010). According to Hartescu et al. (2015), this level of exercise is associated with better sleep and mood. Authors emphasize that these results were independent of participants' social status, health and daily light exposure. Vancampfort et al. (2018) examined the relationship between compliance with the PA recommendations of the World Health Organization (150 min of moderate to vigorous PA per week for prevention or reducing sleep problems) in 38 low- and middle-income countries (n = 204,315). After adjusting for socio-demographic characteristics, obesity, chronic physical diseases, depression, and anxiety, not complying with WHO recommendations was associated with 1.23 higher risk for sleep problems.

It is supposed that relationship between PA and sleep is bidirectional and poor sleep may also contribute to reduced PA (Kline, 2014; Dolezal et al., 2017), making a vicious circle that maintains reduced quality of life.

Studies revealed possible pathways for PA effects on sleep involving endocrine, autonomic nervous system, metabolism, circadian rhythm, and somatic functions (Uchida et al., 2012).

On the whole studies confirm beneficial effects of PA on sleep quality but, as recent studies demonstrated, this relationship is more complex than a linear association. Thus there are some controversies concerning the role of type of PA, its regimen, and intensity.

There is evidence that vigorous PA (compared to moderate PA) does not have any positive impact on sleep quality (Myllymäki et al., 2011; Pengpid and Peltzer, 2018).

According to a cross-national study, including 9,238 adults from five countries, both very low (<10 continuous min per week) and very high (>300 min per week) levels of regular physical activity are associated with the risk of insomnia (Hartescu and Morgan, 2019).

Additionally when the type of PA is considered, high occupational PA (compared to leisure-time PA) may have detrimental effects on physical and mental health, including sleep (Soltani et al., 2012; Wennman et al., 2014; Skarpsno et al., 2018a; Cillekens et al., 2020). Skarpsno et al. (2018b) studied the association of heavy physical work resulting in fatigue with risk of sleep disorders and chronic pain as a potential mediator of this association. Authors conclude that there is a link between work-related physical fatigue and musculoskeletal pain that should be considered as a target for prevention of insomnia in working populations. It can also be assumed that exposure to stress is another factor involved in an interplay between heavy physical work and sleep disturbances. Thus, the contribution of different levels and types PA to sleep quality still needs to be elucidated. It is exceptionally relevant due to high comorbidity between sleep disturbances and mental disorders. Results of epidemiological study indicate that 40% of patients with insomnia have comorbid psychiatric disorder. Major depressive disorder or dysthymia is detected in 23%, anxiety disorders in 24% (Ford and Kamerow, 1989). In a meta-analysis, covering 21 longitudinal epidemiological studies, non-depressed persons with insomnia had a twofold risk of developing depression, compared to persons who had no sleep problems (Baglioni et al., 2011). It is shown that treatment of a psychiatric disorder can lead to improvement in sleep quality, and treatment of sleep disorders can have a beneficial effect on the course of psychiatric disorder (Krystal, 2012).

Thus, it is essential for the assessment of groups at high risk of developing sleep and mental disorders and in order to plan preventive activities to understand the nature of interaction between such factors involved in quality of life as sleep, PA, and psychological well-being.

Objective of the present study is to investigate the association between the level and type of physical activity (PA) and sleep problems in adult population taking into account psychological well-being as possible mediating factor.

We hypothesize that extremely low and extremely high levels of daily PA (including occupational PA) may have a negative impact on sleep quality and psychological well-being.

The results of the study may contribute to developing recommendations for optimal level of leisure and occupational PA to prevent sleep disorders, anxiety and depression.

MATERIALS AND METHODS

Sample

The sample of the study consisted of the participants from the population-based cohort of The Epidemiology of Cardiovascular Risk Factors and Diseases in Regions of the Russian Federation Study (ESSE-RF) that was conducted in 2012–2013 and covered 13 regions of Russian Federation (Boitsov et al., 2013). The protocol was approved by the Local Ethical Committee (Almazov National Medical Research Centre), approval #193 dated by 8 October 2012. All patients/participants provided written informed consent prior participation in the study.

The data of three regions (Saint-Petersburg, Samara, Orenburg), varying in geographic, climatic, socioeconomic characteristics, was included into analysis in our study.

The total sample consisted of 4,800 participants (1,600 from each region), aged 25–64 years.

Data on socio-demographic characteristics (age, gender, education, marital status, employment status, income level), PA and sleep quality were obtained in a structured interview that was carried out by trained medical staff in presence.

Weight and height were measured during the interview by medical staff, and the body mass index (BMI) was calculated using the Quetelet equation [weight (kg)/height^2 (m^2)]. Height was assessed with the accuracy up to 0.5 cm, in the standing position, by stadiometer (Medical RP, TVES, Russia), weight was measured with the accuracy up to 100 g by medical scales (HEM-150 MASSA-K, Russia).

The sample was divided in two age groups: young (25–44 years old) and middle-aged (45–64 years old). The threshold of 45 years was chosen based on WHO classification of age groups.

The main sample characteristics are represented in the **Table 1**.

Measures

The level of PA was evaluated during interview by asking several questions from commonly used validated questionnaires (**Supplementary Table 1**). The following parameters were assessed:

1. The type of PA at work (for working participants): (a) mainly sitting, (b) mainly walking, (c) lifting and carrying small loads, and (d) heavy physical work.
2. The frequency of an intensive/high PA including sport (times a week). In the case of self-reported disease as a barrier to PA the data were excluded from the analysis.
3. The mean duration of leisure-time walking (minutes a day).

Valid data on the level of PA at work were available for 4,696 participants, valid data on the frequency of high physical load per week were available for 2,796 participants, on leisure-time walking—for 4,084 participants. The data of 49 respondents (16 males, 33 females), who indicated that their physical disease was a barrier to a high PA, were excluded from analysis in relation to a high PA.

Sleep quality was assessed based on five questions regarding sleep duration and sleep problems (described in Korostovtseva et al., 2020) (**Supplementary Table 1**).

The measures of sleep quality were the following:

1. Sleep duration.
2. Difficulty falling asleep.
3. Difficulty maintaining sleep.
4. Daytime sleepiness.
5. Sleep medication use.

In accordance with the European guideline for the diagnosis and treatment of insomnia (Riemann et al., 2017) difficulty falling

TABLE 1 | Sample characteristics.

Sample characteristics		*n*	%
Gender	Male	1,926	40.1
	Female	2,874	59.9
Age	young (25–44 years)	2,091	43.6
	middle-aged (45–64 years)	2,709	56.4
Education	Higher	2,354	49.0
Employment status	Working	4,009	83.5
	Unemployed	312	6.5
	Retired	479	10.0
Marital status	Married	3,081	64.2
	Single	822	17.1
	Divorced	602	12.5
	Widowed	295	6.1
Self-reported financial status	Wealthy	13	0.3
	Relatively wealthy	487	10.1
	Average	3,817	79.5
	Relatively poor	447	9.3
	Poor	36	0.8
Socioeconomic status (SES)[1]	Higher	2,177	45.4
	Lower	2,623	54.6
BMI	<18.5 kg/m^2	92	1.9
	≥18.5, <25 kg/m^2	1,630	34.0
	≥25, <30 kg/m^2	1,812	37.8
	≥30 kg/m^2	1,266	26.4

[1]Higher SES is defined as a combination of higher education and middle and higher financial status.

asleep, maintaining sleep, uncontrolled daytime falling asleep three and more times a week were considered as sleep problems.

The other signs of disturbed sleep and unhealthy sleep behavior were sleep duration less than 6 h and using sleep medication at least once (Sivertsen et al., 2015; Watson et al., 2015).

Anxiety and depression were assessed using a Russian validated version of the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983; Smulevich, 2007). Cut-offs for increased level of anxiety and depression were eight points and higher.

Statistical Analysis

Statistical analysis was made with IBM SPSS 21.0 software.

Assessment of differences between subgroups by quantitative variables (mean leisure-time walking, BMI) was carried out with Student's *t*-test.

Chi-square test was applied to examine the association of qualitative and rank variables such as type of PA at work, frequency of high physical load (times per week), frequency of sleep problems (more or less than three times a week), increased or normal level of anxiety and depression.

The association of PA with sleep problems was examined by logistic regression analysis with forward (likelihood ratio) method of variable selection. Simple and multiple binary logistic models were used with the following dependent variables: sleep duration less than 6 h, experience of sleep medication use, difficulties falling asleep, staying asleep and episodes of daytime sleepiness three or more times a week. When an association of PA with sociodemographic characteristics was found these variables were included into the model as covariates. Results are presented as odds ratios (OR) with 95% confidence intervals (CIs). Nagelkerke R^2 was calculated to assess the contribution of independent variables to the variation of dependent variables.

RESULTS

The Level of PA

Among working participants 2,212 (55.2%) are mainly sitting at work, 1,304 (32.5%) are predominantly walking, 353 (8.8%) are lifting and carrying small loads, 140 (3.5%) perform heavy physical work.

Females [1,359 (59.5%) compared to 853 (49.4%) males $p < 0.0001$] and participants of the higher-SES group [1,326 (68.9%) compared to 886 (42.5%) in the lower-SES group, $p < 0.0001$] more frequently reported working primarily in a sitting position.

Among those, who did not indicate some disease as a barrier to a high PA, 735 (26.8%) participants have a high physical load (including sport and intensive physical exercise) less than one time a week, 1,050 (38.2%)—one or two times a week, 732 (26.6%) participants—from 3 to 5 times a week, 230 (8.4%)—six times a week or every day.

In the whole group 391 (9.6%) participants have leisure-time walking less than 30 min a day, 1,378 (33.7%) participants are walking from 30 min to an hour a day, 1,257 (30.8%)—from one to 2 h, 1,058 (25.9%)—more than 2 h a day.

Participants of the older (45–64) age group [76.3 ± 1.1 compared to 68.4 ± 1.1 min in the younger age group (25–44), $t = -5.07$, $p < 0.0001$], females (74.4 ± 1.0 compared to 70.6 ± 1.2 min in males, $t = -2.38$, $p < 0.05$) and individuals with lower SES (78.4 ± 1.1 compared to 66.6 ± 1.1 min in the higher-SES group, $t = 7.64$, $p < 0.0001$) spend more leisure-time walking.

The data on PA in the sample are similar to the Russian national averages estimated in ESSE-RF epidemiological study for 13 regions (Balanova et al., 2014).

The characteristics of PA were not associated with BMI, but middle-aged persons (compared to younger subgroup) (28.78 ± 0.10 vs. 25.28 ± 0.10, $t = -24.38$, $p < 0.0001$) and persons with lower SES (compared to higher SES) (27.94 ± 0.10 vs. 26.41 ± 0.11, $t = 10.21$, $p < 0.0001$) had higher BMI.

PA and Sleep Characteristics

The frequency of sleep complaints was assessed in individuals with different level of PA (**Table 2**). Differences between subgroups were calculated using Chi-square and Student's *t* tests. Most salient differences concern difficulty falling asleep. This sleep problem is significantly more frequent in participants who regularly or constantly have a very high physical load. Also persons with difficulties initiating sleep as well as staying asleep spend more time walking, probably as a way to cope insomnia. In addition, more frequent sleep medication intake was found in individuals with more frequent high physical load.

Logistic regression was applied to assess the contribution of PA characteristics to the risk of sleep disturbances.

Performing heavy physical work was found to be a risk factor for difficulty falling asleep three or more times a week [OR(CI95%) = 1.9(1.2–3.0), $p = 0.003$, $B = 0.65$, and $R^2 = 0.004$], although its contribution is relatively small. When adjusted for gender, age and SES (**Table 3**) performing heavy physical work remained a statistically significant risk factor ($R^2 = 0.06$) while working in a sitting position or having moderate physical load at work were not associated with sleep characteristics.

Having a high physical load six or more times a week was a risk factor for difficulty falling asleep [OR(CI95%) = 1.9(1.3–3.0), $p = 0.003$, $B = 0.65$, and $R^2 = 0.004$). The contribution is small but statistically significant. And it remained statistically significant [OR(CI95%) = 1.9(1.4–3.4), $p = 0.001$, and $B = 0.77$] after controlling for gender [OR(CI95%) = 1.9(1.8–2.8), $p < 0.0001$, and $B = 0.55$], age [OR(CI95%) = 2.2(1.8–2.8), $p < 0.0001$, and $B = 0.80$] and SES [OR(CI95%) = 1.4(1.2–1.8), $p < 0.0001$, and $B = 0.36$]; $R^2 = 0.06$.

No association was found between leisure-time walking and sleep characteristics.

Physical Activity, Anxiety, and Depression

Characteristics of PA in the sample were also analyzed in relation to the level of anxiety and depression (HADS scores) (**Table 4**). Higher anxiety scores were found in participants with the most

TABLE 2 | Physical activity (PA) and sleep characteristics.

Characteristics of PA		Mean sleep duration		Difficulty falling asleep		Difficulty staying asleep		Sleepiness: episodes of daytime falling asleep		Sleep medication use	
		<6 h	≥6 h	≥3 times a week	no or <3 times a week	≥3 times a week	no or <3 times a week	≥3 times a week	no or<3 times a week	At least once	Never
Type of PA at work, *n* (%)	sitting	96 (4.3)	2,116 (95.7)	231 (10.4)	1,981 (89.6)	170 (7.7)	2,042 (92.3)	94 (4.2)	2,118 (95.8)	306 (13.8)	1,906 (86.2)
	walking	48 (3.7)	1,256 (96.3)	140 (10.7)	1,164 (89.3)	110 (8.4)	1,194 (91.6)	54 (4.1)	1,250 (95.9)	182 (14.0)	1,122 (86.0)
	carrying loads	23 (6.5)	330 (93.5)	57 (16.1)	296 (83.9)	39 (11.0)	314 (89.0)	24 (6.8)	329 (93.2)	66 (18.7)	287 (81.3)
	heavy physical work	8 (5.7)	132 (94.3)	27 (19.3)	113 (80.7)	14 (10.0)	126 (90.0)	5 (3.6)	135 (96.4)	23 (16.4)	117 (83.6)
Chi-square/p-level		5.99/0.112		19.13/ < 0.0001		5.16/0.16		5.36/0.15		6.54/0.09	
Frequency of high physical load, *n* (%)	<1 time a week	43 (5.9)	692 (94.1)	125 (17.0)	610 (83.0)	74 (10.1)	661 (89.9)	35 (4.8)	700 (95.2)	117 (15.9)	618 (84.1)
	1–2 times a week	38 (3.6)	1,012 (96.4)	143 (13.6)	907 (86.4)	110 (10.5)	940 (89.5)	47 (4.5)	1,003 (95.5)	154 (14.7)	896 (85.3)
	3–5 times a week	37 (5.1)	695 (94.9)	100 (13.7)	632 (86.3)	75 (10.2)	657 (89.8)	42 (5.7)	690 (94.3)	146 (19.9)	586 (80.1)
	>5 times a week	8 (3.5)	222 (96.5)	52 (22.6)	178 (77.4)	33 (14.3)	197 (85.7)	18 (7.8)	212 (92.2)	43 (18.7)	187 (81.3)
Chi-square/p-level		5.94/0.12		14.95/0.002		3.73/0.29		5.07/0.17		9.62/0.02	
Mean leisure-time walking, min., M ± m		78.9 ± 4.072.6 ± 0.8		80.4 ± 2.371.7 ± 0.8		78.8 ± 2.572.2 ± 0.8		78.3 ± 4.172.6 ± 0.8		74.5 ± 2.072.6 ± 0.8	
t/p-level		1.7/0.09		3.75/ < 0.001		2.59/0.01		1.52/0.13		0.89/0.37	

TABLE 3 | Logistic regression model for prediction of difficulty falling asleep.

Variable	B	OR	p-level	CI95%
Heavy physical work	0.77	2.2	0.001	1.4–3.4
Female	0.55	1.7	<0.0001	1.4–2.2
Lower SES	0.36	1.4	0.001	1.2–1.8
Middle age	0.80	2.2	<0.0001	1.8–2.8

frequent intensive PA. In addition participants who had an intensive physical load less than once a week were at higher risk of anxiety and depression symptoms.

Sleep Quality, Anxiety, and Depression

All sleep problems analyzed in this study were tightly linked to anxiety and depression level (**Table 5**). Participants with sleep duration less than 6 h, with frequent difficulties in initiating and maintaining sleep, with daytime sleepiness and experience of sleep medication use have a significantly higher risk of having increased anxiety and depression scores in HADS.

DISCUSSION

The present study was aimed at elucidating the link between different levels and types of PA and sleep. We found that having a high physical load six or more times a week is a risk factor for having insomnia symptoms, in particularly, sleep-onset difficulties.

High and regular PA is traditionally considered an important factor for physical and psychological well-being and an essential component of healthy lifestyle (Penedo and Dahn, 2005; Samitz et al., 2011; Cunningham et al., 2020). The role of exercise for improving quality of sleep, especially in persons with sleep problems, was also documented in a number of studies (Banno et al., 2018). Nevertheless, there are some controversies concerning the effects of different types of PA, its regimen, and intensity (Soltani et al., 2012; Wennman et al., 2014; Skarpsno et al., 2018a; Cillekens et al., 2020). The results of our study are in agreement with findings that physically demanding work and a very frequent intensive PA may have a negative impact on sleep quality, especially in terms of sleep initiating.

A number of social, psychological and physical variables may be proposed as mediators of the relationship

TABLE 4 | Physical activity (PA), anxiety and depression.

Characteristics of PA		Anxiety		Depression	
		Normal	Increased	Normal	Increased
Type of PA at work, *n* (%)	sitting	1,129 (51.0)	1,083 (49.0)	1,594 (72.1)	618 (27.9)
	walking	676 (51.8)	628 (48.2)	915 (70.2)	389 (29.8)
	carrying loads	166 (47.0)	187 (53.0)	249 (70.5)	104 (29.5)
	heavy physical work	63 (45.0)	77 (55.0)	97 (69.3)	43 (30.7)
Chi-square/p-level		4.51/0.21		1.80/0.61	
Frequency of high PA, *n* (%)	<1 time a week	343 (46.7)	392 (53.3)	500 (68.0)	235 (32.0)
	1–2 times a week	575 (54.8)	475 (45.2)	822 (78.3)	228 (21.7)
	3–5 times a week	391 (53.4)	341 (46.6)	564 (77.0)	168 (23.0)
	>5 times a week	102 (44.3)	128 (55.7)	179 (77.8)	51 (22.2)
Chi-square/p-level		17.11/0.001		27.81/ < 0.0001	
Mean leisure-time walking, min., M ± m		73.1 ± 1.1	72.7 ± 1.1	73.5 ± 0.9	71.3 ± 1.4
t/p-level		0.26/0.79		1.28/0.20	

Additionally individuals with increased depression scores more frequently than participants with normal depression scores had leisure-time walking less than 1 h a day [571 (46.5%) vs. 1,198 (41.9%), Chi-square = 7.4, and p = 0.006].

TABLE 5 | Sleep characteristics, anxiety, and depression.

Sleep characteristics		Anxiety		Chi-square/p-level	Depression		Chi-square/p-level
		Normal	Increased		Normal	Increased	
Mean sleep duration during last month, *n* (%)	<6 h	82 (37.4)	137 (62.6)	12.18/ < 0.001	121 (55.3)	98 (44.7)	22.49/ < 0.0001
	≥6 h	2,268 (49.5)	2,313 (50.5)		3,222 (70.3)	1,359 (29.7)	
Difficulty falling asleep, *n* (%)	≥3 times a week	200 (30.3)	459 (69.7)	105.86/ < 0.0001	393 (59.6)	266 (40.4)	36.21/ < 0.0001
	no or <3 times a week	2,150 (51.9)	1,991 (48.1)		2,950 (71.2)	1,191 (28.8)	
Difficulty staying asleep, *n* (%)	≥3 times a week	147 (29.1)	358 (70.9)	88.98/ < 0.0001	274 (54.3)	231 (45.7)	63.22/ < 0.0001
	no or <3 times a week	2,203 (51.3)	2,092 (48.7)		3,069 (71.5)	1,226 (28.5)	
Sleepiness: episodes of daytime falling asleep, *n* (%)	≥3 times a week	71 (31.7)	153 (68.3)	28.02/ < 0.0001	137 (61.2)	87 (38.8)	8.0/0.005
	no or <3 times a week	2,279 (49.8)	2,297 (50.2)		3,206 (70.1)	1,370 (29.9)	
Sleep medication use, *n* (%)	at least once	224 (29.4)	539 (70.6)	139.47/ < 0.0001	435 (57.0)	328 (43.0)	68.50/ < 0.0001
	never	2,126 (52.7)	1,911 (47.3)		2,908 (72.0)	1,129 (28.0)	

between high physical load at work and sleep problems including musculoskeletal pain, physical exhaustion, social stress, social inequalities in physical and mental health, poor work hygiene, occupational stress and additional occupational hazards. These factors along with detailed information on physical well-being and chronic conditions should be taken into account in further research.

Our results indicate that the impact of very intensive PA on sleep quality is not limited to working conditions. We found that participants who practice very frequent (6 days a week or everyday) intensive PA are at higher risk of problems in initiating sleep irrespective of sociodemographic confounders. For adequate explanation this finding needs further investigation in terms of high PA, its causes and motivations. However, in general these results are in concordance with the evidence

that vigorous PA may not have such benefits as moderate PA (Myllymäki et al., 2011; Pengpid and Peltzer, 2018) and a very high regular PA is linked to insomnia (Hartescu and Morgan, 2019). Thus, a very intensive PA may have a detrimental effect on sleep. One of possible mechanisms underlying this effect is hyperarousal state that represents the main feature of insomnia (Riemann et al., 2010). On the other hand, there could be a more complex relationship, when sleep problems and very high PA are determined by a third factor, e.g., body dissatisfaction or some difficult life circumstances.

The association between PA and sleep problems in our study could not be fully explained by emotional factors such as anxiety and depression, because no significant association between PA and psychological well-being was identified. On the other hand, as expected (Baglioni et al., 2011; Krystal, 2012), a tight link between sleep complaints, anxiety, and depression scores was found.

Contrary to our expectations we did not find any significant association between leisure-time walking and sleep quality when controlling for sociodemographic factors. This may be attributable to a relatively small percentage of participants with very low leisure-time walking and the role of some additional factors that were not analyzed in this study, such as the availability of personal vehicle.

Limitations

Indeed, cross-sectional design of the study prevents definite conclusions about causal relationships between PA, sleep, anxiety and depression. As the study was screening and multidimensional, including a wide range of variables (Scientific Organizing Committee of the ESSE-RF. . ., 2013), no full standard questionnaires on sleep and PA were applied. We did not include in analysis compete data on chronic conditions and health behaviors that could be possible mediating variables and covariates.

In general the study emphasizes the necessity to consider the association between PA, sleep and psychological well-being as complex relationship. We found that excessively high PA is detrimental for sleep quality and poor sleep is linked to a wide range of emotional problems. Further research is needed to determine the role of social, psychosocial and physiological factors mediating these relationships as well as mechanisms underlying this association.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Local Ethical Committee (Almazov National Medical Research Centre), approval #193 dated by 8 October 2012. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

VA and ED: manuscript design, drafting manuscript, analysis and interpretation of data, and revising manuscript critically for important content. LK: manuscript design, drafting manuscript, analysis and interpretation of data, revising manuscript critically for important content, and approval for publication. OR: study concept and design, data collection and storage, data analysis, interpretation of data, revising manuscript critically for important content, and approval for publication. MaB: data collection and storage, data analysis, interpretation of data, and revising manuscript critically for important content. TS and MiB: interpretation of data and revising manuscript critically for important content. EB, RL, and DD: study concept and design, data collection and storage, data analysis, and interpretation of data. YS: manuscript design, drafting manuscript, analysis and interpretation of data, revising manuscript critically for important content, approval for publication, and accountable in ensuring that work-related questions are appropriately investigated/resolved. ES and AK: principal co-investigator, study concept and design, and approval for publication. All authors contributed to the article and approved the submitted version.

FUNDING

This study is partly supported by the Ministry of Science and Higher Education of the Russian Federation (Agreement No. 075-15-2020-901) and by the grant of the Russian Foundation for Basic Research (project No. 20-013-00874 A).

ACKNOWLEDGMENTS

The authors would like to thank Svetlana A. Shalnova (MD, Ph.D., DSc, Professor, Head, Department of Epidemiology of Chronic Non-communicable Diseases, National Research Center for Preventive Medicine, Moscow) for the design development, Alexander D. Deev (Ph.D. of physical and mathematical sciences, Head, Biostatistics Laboratory) for the sample development and raw data processing, and Sergey A. Boytsov (MD, Ph.D., DSc, Professor, Director, National Medical Research Center of Cardiology) for the advice on planning study and analyzing the results.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2021.705212/full#supplementary-material

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychology

REVIEW
published: 12 August 2021
doi: 10.3389/fpsyg.2021.705364

Improving CPAP Adherence in Adults With Obstructive Sleep Apnea Syndrome: A Scoping Review of Motivational Interventions

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Edited by:
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Reviewed by:
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Antonia Csillik, Université Paris Nanterre, France

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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *05 May 2021*
Accepted: *09 July 2021*
Published: *12 August 2021*

Citation:
Rapelli G, Pietrabissa G, Manzoni GM, Bastoni I, Scarpina F, Tovaglieri I, Perger E, Garbarino S, Fanari P, Lombardi C and Castelnuovo G (2021) Improving CPAP Adherence in Adults With Obstructive Sleep Apnea Syndrome: A Scoping Review of Motivational Interventions. Front. Psychol. 12:705364. doi: 10.3389/fpsyg.2021.705364

Objective: This scoping review aims to provide an accessible summary of available evidence on the efficacy of motivational interventions to increase adherence to Continuous Positive Airway Pressure (CPAP) among patients with Obstructive Sleep Apnea Syndrome (OSAS) and of their specific aspects and strategies by assessing adherence measures.

Methods: A literature search was performed in PubMed, Scopus, Medline, PsycINFO, and Web of Science databases using the concepts of "obstructive sleep apnea syndrome," "continuous positive airway pressure," "motivational intervention," and "adherence." Rigorous inclusion criteria and screening by at least two reviewers were applied. Data were extracted to address the review aims and were presented as a narrative synthesis.

Results: Search for databases produced 11 randomized controlled trials, all including naïve CPAP users. Findings showed that motivational interventions were more effective than usual care and educational programs in increasing adherence to CPAP, despite results were not always maintained over time across studies.

Discussion: To our knowledge, this is the first scoping review of the literature aimed to explore the characteristics and impact of motivational interventions to promote adherence to CPAP in patients with OSAS. More research providing a detailed description of motivational strategies, and testing of their association with positive treatment outcomes via both direct and indirect measures are needed to increase awareness on active mechanisms of change.

Keywords: sleep disorders, obstructive sleep apnea syndrome, continuous positive airway pressure, adherence, motivational intervention

INTRODUCTION

Obstructive Sleep Apnea Syndrome (OSAS) is a sleep-related breathing disorder characterized by transient interruption of ventilation during sleep caused by complete or partial occlusion of the upper airway (McNicholas et al., 2007). Consequent oxygen desaturation, increased inspiratory effort, sleep fragmentation, and arousal from sleep (Lévy et al., 2015; Jennum et al., 2021) lead to excessive daytime sleepiness, cardiovascular, and metabolic diseases (Pépin et al., 2019; Visniauskas et al., 2021), cognitive and memory impairments (Alomri et al., 2021; Huang et al., 2021; Legault et al., 2021), and mood disorders (Garbarino et al., 2020).

Continuous Positive Airway Pressure (CPAP) is the treatment of choice for moderate to severe OSAS (Zhang et al., 2015; Chen et al., 2021; Sugiyama et al., 2021). It involves the use of an airflow generator which provides a constant stream of pressurized air to splint open and maintain patency of the upper airways during the inspiratory and expiratory phases of breathing. However, its effectiveness is limited by poor acceptance and adherence (Bros et al., 2020). The literature suggests that 8 to 15% of patients with OSAS refuse CPAP treatment after the first night and that at least 50% of individuals discontinue its usage within 1 year from the treatment beginning (Rotenberg et al., 2016; Borker et al., 2021; Contal et al., 2021).

A dose-response relationship between CPAP adherence and improvements in health and quality of life has been highlighted in several studies, which show a substantial increase in memory, functional status, and blood pressure (Gay et al., 2006; Giles et al., 2006), as well as reduced rates of sleepiness and cardiovascular mortality (Marin et al., 2005; Martínez-García et al., 2012; Dong et al., 2013; Mashaqi and Gozal, 2020) among those who use the device for a greater number of hours per night. However, what remains unclear is the nightly duration of CPAP usage required to normalize functioning (Lewis et al., 2004), which ranges from a minimum of 4 h (Lewis et al., 2004; Richard et al., 2007) to 6–8 h per night (Zimmerman et al., 2006; Weaver et al., 2007) across studies.

Specific barriers to treatment include skin irritation, dry throat, nasal congestion, and mask leaks (Zozula and Rosen, 2001; Cayanan et al., 2019), but a reduction in side effects offered by technical solutions (i.e., air humidifiers and different types of devices) did not correlate with increased adherence to CPAP, and quality of life in several investigations (Zozula and Rosen, 2001; Weaver and Grunstein, 2008; Broström et al., 2009; Sawyer et al., 2011). Adherence to CPAP use might, therefore, depends on factors other than disease-specific characteristics or technological advancements in the delivery of positive airway pressure, including psychological, motivational, and environmental aspects. These encompass characteristics of negative affectivity and social inhibition associated with Type-D (distressed) personality (Broström et al., 2007; Copur et al., 2018), or symptoms of claustrophobia (Chasens et al., 2005), while research findings are inconclusive on the association between mood disorders, such as anxiety and depression, and adherence to CPAP (Stepnowsky et al., 2002; Garbarino et al., 2018; Yang et al., 2020; Scarpina et al., 2021). Additional factors include coping styles with challenging situations (active vs. passive), treatment expectations, and perceived self-efficacy (i.e., confidence in one's own ability to carry out a particular behavior) (Aloia et al., 2005; Olsen et al., 2008; Baron et al., 2011; Sawyer et al., 2011; Mehrtash et al., 2019), together with social support (Lewis et al., 2004; Xu et al., 2020), and marital satisfaction (i.e., problems with the bed partner) (Batool-Anwar et al., 2017; Luyster, 2017; Gentina et al., 2019).

Accordingly, findings from previous studies highlight that interventions focused on enhancing knowledge about OSAS and CPAP use, or on removing a potential barrier to device usage lead only to partial improvements in treatment adherence (Aloia et al., 2004; Minassian and Doran, 2020).

Indeed, behavioral change is a complex process involving three specific constructs: (a) readiness to change, (b) perceived importance of change, and (c) confidence in one's ability to change (Miller and Rollnick, 2002, 2013).

Several theoretically informed behavior change interventions targeting the individuals' motivation to change (Miller and Rollnick, 1991, 2002; Kreman et al., 2006; Pietrabissa et al., 2015) and self-efficacy (Miller et al., 1997; Pietrabissa et al., 2013) to improve adherence to treatment recommendations have been developed and successfully tested across chronic conditions (Burke et al., 2003; Pietrabissa et al., 2012, 2017; Soderlund, 2018), including pulmonary disease that requires the use of the CPAP (Aloia et al., 2005; Weaver and Grunstein, 2008; Shannon et al., 2017).

However, motivational interventions vary widely across studies due to different theoretical backgrounds and employed strategies, Moreover, adherence is operationalized and measured differently across studies—thus limiting the conceptualization of behavioral change interventions in clinical practice and the generalization of research findings (Martin et al., 2005).

To overcome this gap, this study was conducted to systematically review the research done in this area, as well as to provide an accessible summary of available evidence on motivational interventions to increase adherence to CPAP use among patients with OSAS by answering the following research questions: (1) Which are the characteristics of motivational interventions to increase CPAP use/acceptance/adherence in patients with OSAS? (2) Which motivational strategies are specifically used to enhance adherence to CPAP in patients with OSAS? (3) Which theoretical model underlines the interventions? (4) Who provides the intervention? (5) How adherence to CPAP is operationalized and measured, and what are the reported effects (primary and secondary outcomes) of motivational interventions in the short- and long-term?

METHODS

This scoping review employed the five-stage framework as outlined by Arksey and O'Malley (2005) as follow: (1) identifying the research question, (2) identifying relevant studies, (3) selecting the studies, (4) charting the data (data extraction), and (5) collating, summarizing, and reporting the results. Furthermore, the PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses

extension for Scoping Reviews; Tricco et al., 2018) was used (**Supplementary Material 1**).

Search Strategy

Searches were conducted in the PubMed, Scopus, Medline, PsycINFO, and Web of Science databases from October 2020 to March 2021.

The search strategies combined key terms and Medical Search Headings (MESH) terms based on the patient problem (or population), intervention, comparison, or control, and outcome (PICO) framework as follows: ("OSAS" OR "Obstructive Sleep Apnea Syndrome") AND ("CPAP" OR "Continuous Positive Airway Pressure") AND ("Motivational intervention" OR "Motivational treatment" OR "Motivational interviewing") AND ("Adherence" OR "Compliance" OR "CPAP use") (Huang et al., 2006). Boolean and truncation operators were used to systematically combine searched terms and to list documents containing variations on search terms, respectively. The search syntax was modified as appropriate for each database.

Inclusion and Exclusion Criteria

Only original articles that (1) employed randomized controlled trials (RCTs), non-randomized trials, or non-controlled trials study designs, (2) were published in English, and (3) examined the impact of motivational interventions on adherence (primary outcome) to CPAP use in adult (4) with a primary diagnosis of OSAS (5) were included. Records were excluded if they (1) considered only biomedical outcome variables, (2) were review articles, single-case studies, qualitative studies, mixed-method studies, protocol studies, or workplace interventions.

Unpublished works were not considered. No restrictions were set for the date of publication.

Study Selection

Following the search and exclusion of duplicates, two reviewers (authors 1 and 2) independently assessed the eligibility of the articles first on the title and the abstract, and the full-text according to the inclusion criteria. Author 3 resolved disagreements. The reference lists of all selected articles and relevant systematic reviews (Weaver, 2019) were manually screened to identify any further references for possible inclusion—but none was found.

RESULTS

Study Selection

A search of electronic databases identified 115 reports, of which 98 were excluded based on information from the title and abstract. The remaining 17 articles were evaluated for inclusion by reviewing their full text and resulted in the exclusion of 6 records for the following reasons: (1) focused on motivational App development and testing ($n = 1$; Alismail and Olfman, 2020), (2) aimed at validating a screening questionnaire ($n = 1$; Sawyer et al., 2014), (3) was a review ($n = 1$; Weaver, 2019) or (4) a protocol study ($n = 1$; Williams et al., 2014), (5) OSAS was not reported as the primary diagnosis ($n = 1$; Whittington et al., 2020) and (6) employed a mixed-method study design ($n = 1$; Broström et al., 2013). Eleven records finally were included in this review (Roecklein et al., 2010; Sparrow et al., 2010; Olsen et al., 2012; Aloia et al., 2013; Lai et al., 2014; Lo Bue et al., 2014; Dantas et al., 2015; Bakker et al., 2016; Jean-Louis et al., 2017; Pengo et al., 2018; Rudilla et al., 2021).

The flowchart presented in **Figure 1** provides step-by-step details of the study selection.

Study Characteristics

Details of the 11 included papers are provided in **Table 1**.

The selected articles were published from 2010 (Roecklein et al., 2010; Sparrow et al., 2010) to 2021 (Rudilla et al., 2021), and were conducted in the USA (Roecklein et al., 2010; Sparrow et al., 2010; Aloia et al., 2013; Bakker et al., 2016; Jean-Louis et al., 2017; $n = 5$), China ($n = 1$; Lai et al., 2014), Australia ($n = 1$; Olsen et al., 2012), UK ($n = 1$; Pengo et al., 2018), Portugal ($n = 1$; Dantas et al., 2015), Spain ($n = 1$; Rudilla et al., 2021) and Italy ($n = 1$; Lo Bue et al., 2014). All studies employed a randomized parallel-group trial design.

Description of Participants

Selected contributions included a total of 1472 adult participants of both genders (age range: 34-75; mean age = 54.66 years) with a diagnosis of OSAS at their first use of a recognized sleep diagnostic tool with an Oxygen Desaturation Index (ODI) of ≥ 5 per hour or an Apnea-Hypopnea Index (AHI) ≥ 5 per hour.

Description of Intervention

The main characteristics of the interventions are reported in **Supplementary Material 2** using the CONsolidated Standards of Reporting Trials 2010 (Consort10) checklist (Schulz et al., 2010) and **Supplementary Material 3** using the Template for Intervention Description and Replication (TIDieR) checklist (Hoffmann et al., 2014). **Figure 2** showed substantial differences in reporting frequency occurred between TIDieR items in each of the 11 trial reports.

Intervention Group

Intervention groups were based on the principles and techniques of Motivational Interviewing (MI) (Olsen et al., 2012; Dantas et al., 2015; Rudilla et al., 2021) and Motivational Enhancement Therapy (MET) (Roecklein et al., 2010; Sparrow et al., 2010; Aloia et al., 2013; Lai et al., 2014; Lo Bue et al., 2014; Bakker et al., 2016), which combines MI with personalized assessments, feedback, and change plans (Miller, 1992).

The number of intervention sessions ranged from one (Roecklein et al., 2010; Lai et al., 2014; Lo Bue et al., 2014; Dantas et al., 2015) to 16 (Sparrow et al., 2010), and the length of each session varied from 2 (Pengo et al., 2018) to 90 min (Rudilla et al., 2021).

In all the selected studies, the treatment consisted of providing OSAS-related information, addressing treatment expectations, and ambivalence toward the use of the CPAP, as well as in defining goals and motivating treatment adherence. The individual's understanding of the health risks associated with untreated OSAS and the extent to which they believed that

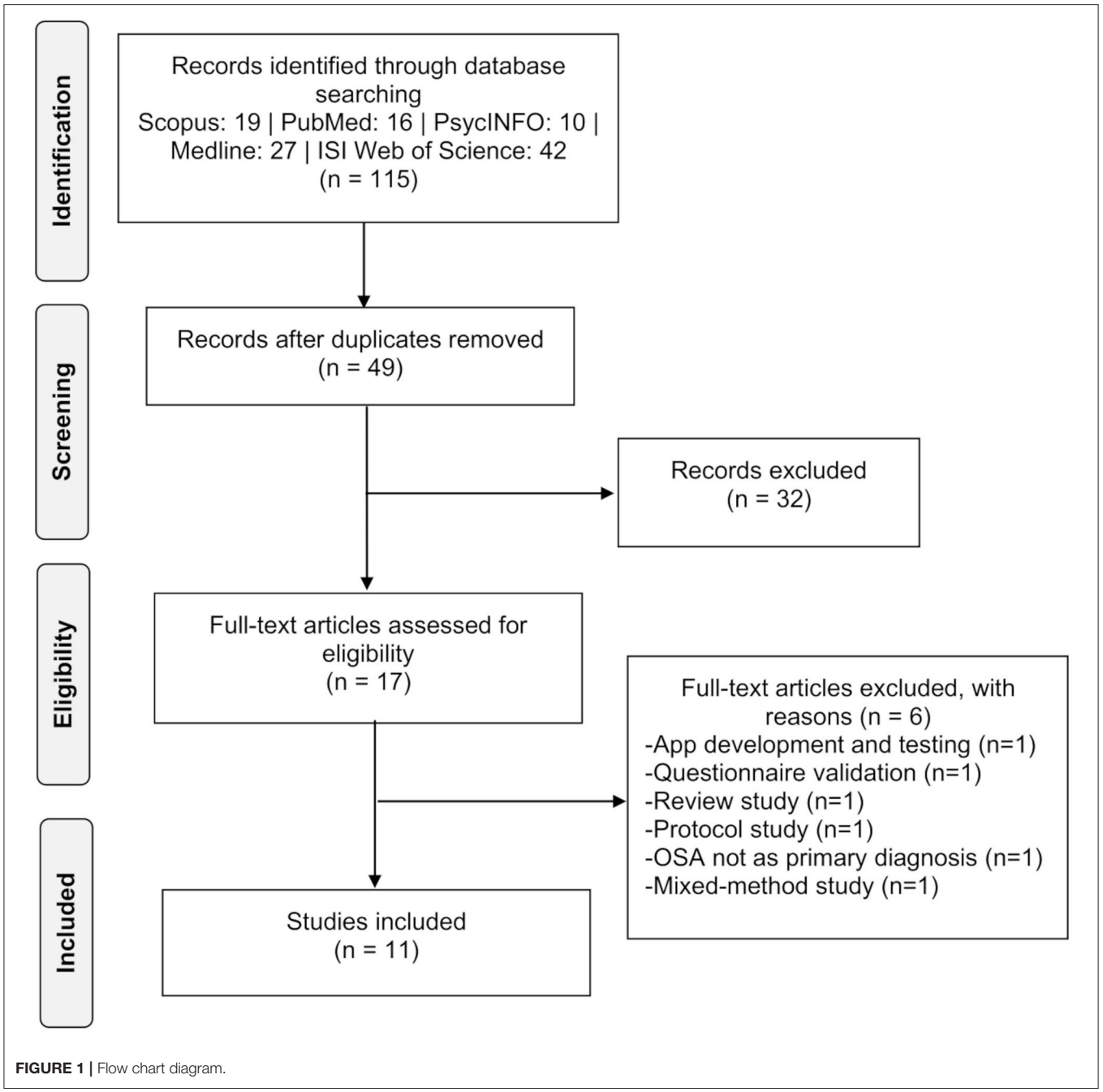

FIGURE 1 | Flow chart diagram.

consistent CPAP use would lead to symptoms improvement were also discussed during treatment.

However, only 4 out of 11 contributions detailed the motivational strategies employed in the intervention (Olsen et al., 2012; Aloia et al., 2013; Jean-Louis et al., 2017; Rudilla et al., 2021).

In the study by Aloia et al. (2013) and Jean-Louis et al. (2017), the practitioners first discussed with the patients what they already knew or were interested in learning about the impact that sleep apneas and the use of the CPAP have on health and asked the patients for permission to provide information. Information was given in a neutral, non-judgmental fashion to elicit the patient's interpretation (the elicit-provide-elicit technique). The goal-setting technique was then used to identify and set realistic goals that align with the patients' values (Aloia et al., 2013; Jean-Louis et al., 2017). Moreover, in the study by Jean-Louis et al. (2017), coaching and role-playing techniques were applied. In the final phase of the intervention, the practitioners also complimented the patients for the achieved results and offered further education on the benefits of CPAP therapy in case resistance to change was encounter.

Instead, in the study by Olsen et al. (2012), the first session focused on increasing readiness to change by exploring the patients' motivation to treatment, assessing discrepancies

TABLE 1 | Characteristics of the included studies.

Author, year	Country	Study aim*	Sample size (*n*)	Age (yrs): *Mean (SD), range*	Male gender: *n(%)*	BMI (kg/m²): *Mean (SD); range*	ESS	AHI: *events/h (SD)*	Follow-up points**	Primary outcomes: *measure*	Secondary outcomes: *measure*	Drop-out *N (%)*	Results (primary outcomes)†	Results (secondary outcomes)†
Aloia et al. (2013)	US	To compare motivational enhancement intervention (*IG*) vs. *TAU* vs. educational group (*ED*) in improving **adherence** to CPAP, and **self-efficacy** and **decisional balance**	*N* = 227 *TAU* = 74 *ED* = 80 *IG* = 73	*TAU* = 52.4 (11.8) *ED* = 47.0 (11.4) *IG* = 51.7 (10.0)	*TAU* = 57 (77) *ED* = 48 (60) *IG* = 45 (62)	*TAU* = 35.8 (8.4) *ED* = 35.0 (7.3) *IG* = 35.1 (7.3)	*TAU* = 11.9 (5.1) *ED* = 12.6 (4.9) *IG* = 11.6 (5.2)	*TAU* = 48.2 (26.2) *ED* = 46.1 (23.2) *IG* = 45.7 (23.8)	**T0–**T1–T2–**T3–T6–T12**	Adherence to CPAP: Machine usage (h/night)	Self-efficacy and decisional balance: *ad hoc* measure	*TAU*: 25 (33) *ED*: 27 (33) *IG*: 26 (36)	Adherence declined over time for all three groups. Among moderate users (≥2 but <6 h/night) in the first week, average adherence at T12 in the *IG* was significantly higher (*M* = 4.12 h/night, *SE* = 0.42) than the average adherence in the other two control groups (*TAU*: *M* = 2.46 h/night, *SE* = 0.40; *ED*: *M* = 3.21 h/night, *SE* = 0.40; *p* = 0.002).	For self-efficacy at T12 *IG* had the highest mean confidence score for moderate PAP users and *ED* had the highest mean confidence score for high users, but there were no significant group differences. *TAU*: T0 = 20.96 (2.88); T3 = 20.61 (4.49); T6 = 21.00 (5.06); T12 = 19.83 (6.29) *ED*: T0: 21.11 (3.21); T3 = 21.05 (4.50); T6 = 21.04 (5.03); T12 = 20.98 (5.19) *IG*: T0 = 20.63 (3.26); T3 = 22.48 (3.08); T620.96 (4.23); T12 = 21.25 (4.84) For decisional balance the moderate user group (≥ 2 but < 6 h/night) of *IG* demonstrated a higher index score at T12 when compared to the average of other two groups for moderate users (*p* = 0.04). *TAU*: T0 = 47.11 (6.02); T3 = 45.51 (7.67); T6 = 45.51 (7.90); T12 = 45.08 (10.55) *ED*: T0 = 46.32 (5.70); T3 = 46.33 (7.69); T6 = 44.66 (9.14); T12 = 45.76 (8.38) *IG*: T0 = 45.28 (6.94); T3 = 46.13 (6.23); T6 = 45.91 (6.95); T12 = 46.61 (7.47)
Bakker et al. (2016)	US	To compare motivational enhancement intervention (*IG*) vs. *TAU* in improving **adherence** to CPAP and **sleep duration**	*N* = 83 *TAU* = 42 *IG* = 41	*TAU* = 63.9 (7.4) *IG* = 63.8 (8.3)	*TAU* = 28 (66.7) *IG* = 27 (65.9)	*TAU* = 30.6 (4.5) *IG* =31.6 (5.9)	*TAU* = 7.7 (4.2) *IG* = 8.4 (4.8)	*TAU* = 23.7 (15.9, 31.4) *IG* = 21.8 (17.4, 31.0)	**T0**–T6–**T12**	Adherence to CPAP: Machine usage (h/night); % days of CPAP use	Sleep duration	*TAU*: 16 (38%) *IG*: 15(36%)	At T6, average nightly adherence was 99.0 min/night higher in *IG* compared with *TAU* (*p* = 0.003). At T12 a consistent difference in adherence between arms of 97 min/night (*p* = 0.006) favoring *IG*.	There were no significant differences in sleep duration, either over time within arms.
Dantas et al. (2015)	PT	To compare motivational interviewing (*IG*) vs. *TAU* vs. educational group (*ED*) in improving **adherence** to CPAP, **conviction, and confidence,** and **daytime sleepiness**	*N* = 61 *ED* = 20 *TAU* = 20 *IG* = 21	*ED* = 56.4 (8.5) *TAU* = 57.1 (10.6) *IG* = 56.2 (11.2)	*ED* = 18 (86) *TAU* = 16 (80) *IG* = 13 (65)	*ED* = 32.5 (5.0) *TAU* = 31.3 (4.6) *IG* = 34.8 (7.2)	NR	*ED* = Moderate ≥15: 5 (24); Severe > 30: 16 (76) *TAU* = Moderate ≥15: 5 (25); Severe >30: 15 (75) *IG* = Moderate ≥15: 6 (30); Severe >30: 14 (70)	T0–**T1–T2**	Adherence to CPAP: Machine usage (h/night); % days of CPAP use	AHI Daytime sleepiness: ESS Conviction: VAS 0–10 Confidence: VAS 0–10	*ED*: 1	The *IG* presented higher adherence to CPAP—percentage of days of use >4 h (89.8% *p* = 0.013), mean effective use per effective day (6.2; *p* = 0.000) at T2, compared with *TAU* and IN groups.	*IG* showed lower AHI (2.7; *p* = 0.019) at T2 when compared with the other two groups. For conviction, no differences were detected. Confidence was higher in the *IG* group at T2 than at T1 (*p* = 0.000). The ESS presented a significant reduction (*p* = 0.000) in the *IG* and the IN (*p* = 0.008) but was higher in the *TAU* (*p* = 0.015).

(Continued)

TABLE 1 | Continued

Author, year	Country	Study aim*	Sample size (*n*)	Age (yrs): *Mean (SD), range*	Male gender: *n(%)*	BMI (kg/m^2): *Mean (SD); range*	ESS	AHI: *events/h (SD)*	Follow-up points**	Primary outcomes: *measure*	Secondary outcomes: *measure*	Drop-out *N (%)*	Results (primary outcomes)†	Results (secondary outcomes)†
Jean-Louis et al. (2017)	US	To compare motivational-based intervention (*IG*) vs. *ED* in improving **adherence** to physician-recommended assessment	*N* = 380 *ED* = 143 *IG* = 160	*ED*: 57.9 (13.0) *IG*: 60.2 (13.6)	*ED* = 28.7% *IG* = 28.8%	*ED*: <25 = 14.9%; 25-30 = 21.3%; >30 = 63.8% *IG*: <25 = 10%; 25-30 = 21.2%; >30 = 68.8%	NR	NR	**T0 -** T6	Adherence to recommended OSAS evaluations: directly asked	NR	*ED*: 47 (25%) *IG*: 30 (16%)	No significant differences between the two arms regarding adherence to OSAS evaluation or treatment.	NR
Lai et al. (2014)	CH	To compare motivational enhancement intervention (*IG*) vs. *TAU* in improving adherence to CPAP, **self-efficacy, risk perception, outcome expectancies, daytime sleepiness,** and **quality of life**	*N* = 100 *TAU* = 51 *IG* = 49	*TAU*: 51 (10.0) *IG*: 53 (10.0)	*TAU* = 42 (82) *IG* = 41 (84),	*TAU* = 29.3 (5.4) *IG* = 28.6 (5.5)	*TAU* = 9 (5.0) *IG* = 9.5 (5.8)	*TAU* = 28.2 (20.3, 53.6) *IG* = 30.7 (20.6, 52.2)	T1w**–T1–T3**	Adherence to CPAP: Machine usage (h/night)	Risk perception and Expectancies: *ad hoc* measure Daytime sleepiness: ESS Self-efficacy: SEMSA Quality of life: FOSQ, CSAQLI, SF-36	*TAU*: 1 *IG*:1	The *IG* had better CPAP use (higher daily CPAP usage by 2 h/d) [Cohen $d = 1.33$, $p < 0.001$], a four-fold increase in the number using CPAP for ≥70% of days with ≥4 h/d ($p < 0.001$) compared with *TAU* at T3. *TAU*: T1w = 2.9 (2.5); T1 = 2.6 (2.3); T3 = 2.4 (2.3) *IG*: T1w = 5.5 (1.8); T1 = 4.8 (1.6); T3 = 4.4 (1.8)	No between-group differences on Risk perception, Outcome expectancies and in any score of the three health-related quality-of-life scales. The *IG* had greater improvements in ESS by 2.2 units ($p < 0.001$) and SEMSA by 0.2 units ($p < 0.012$) compared with *TAU*.
Lo Bue et al. (2014)	IT	To compare motivational enhancement intervention (*IG*) vs. *TAU* in improving adherence to CPAP and **daytime sleepiness**	*N* = 40 *TAU* = 20 *IG* = 20	*TAU*: 55.65(8.25) *IG*: 58.55 (13.2)	27	*TAU*: 34 (5.99) *IG*: 33.93 (5.44)	*TAU*: 10.55 (6.21) *IG*: 8.95 (5.74)	*TAU*: 44.45 (25.18) *IG*: 44.05 (16.90)	T0–T1–T3–T6–T12	Adherence to CPAP: Machine usage (h/night); % days of CPAP use	Daytime sleepiness: ESS	*TAU*: 2 *IG*: 1	During the first month, intervention group patients showed a higher number of nights with a device use ≥4 h. Average treatment adherence in the T1 (days of therapy with at least 4 h per night on the total number of days from device delivery) was 77.5% in *IG* and 55.7% in *TAU* ($p = 0.022$). No significant differences in other follow-up points.	Both in the *IG* and *TAU*, ESS was lower at the 3rd, 6th, and 12th month than at baseline with no significant differences between the two groups
Olsen et al. (2012)	AU	To compare motivational interviewing (*IG*) vs. educational intervention (*ED*) in improving acceptance and adherence to CPAP, **daytime sleepiness, risk perception, health-related quality of life, self-efficacy,** and **satisfaction with therapy**	*N* = 106 *ED* = 53 *IG* = 53	*ED*: 57.74 (9.51) *IG*: 55.14 (12.58)	*ED*: 38 (76) *IG*: 31 (62)	*ED*: 34.65 (7.07) *IG*: 34.28 (6.71)	*ED*: 11.14 (5.32) *IG*: 10.82 (4.41)	*ED*: 32.39 (20.32) *IG*: 36.23 (27.76)	**T1–T2–T3**–T12	Adherence to CPAP: Machine usage (h/night) Acceptance of CPAP: rejection rate	Daytime sleepiness: ESS Self-efficacy: SMSA Benefits: SMSA Risk perception: SMSA Health-related quality of life: FOSC Satisfaction with Therapy and Therapist: STTS-R	NR	Adherence declined over time in the two groups. The number of hours of CPAP use per night in the *IG* at T1, T2, and T3 was significantly higher compared with *TAU* ($p < 0.005$). No significant between-group difference at T12. *TAU*: T1 = 3.25 (2.83); T2 = 3.22 (2.76); T3 = 3.16 (2.69); T12 = 3.00 (3.18) *IG*: T1= 4.85 (2.55); T2 = 4.73 (2.62); T3 = 4.63 (2.69); T12 = 4.21 (3.25) Significantly more participants in the *IG*	For ESS, no between-group differences, but the main effect for time emerged (TI–T3 mean ESS: 10.04 vs. 6.73, $p < 0.01$; T2–T3 mean ESS: 8.90 vs. 6.73, $p < 0.01$). For SMSA, *IG* showed greater self-efficacy than *TAU* but not significantly (3.42 vs. 3.11). A significant main effect for time is reported for the reduction in risk perception between T1 and T3 ($p < 0.05$) in all patients. A significant main effect for time is reported for better health-related quality of life from T1 to T2, from T2 to T3, and from T1 to T3 (all $p < 0.01$).

(Continued)

TABLE 1 | Continued

Author, year	Country	Study aim*	Sample size (*n*)	Age (yrs): *Mean (SD), range*	Male gender: *n(%)*	BMI (kg/m²): *Mean (SD); range*	ESS	AHI: *events/h (SD)*	Follow-up points**	Primary outcomes: *measure*	Secondary outcomes: *measure*	Drop-out *N (%)*	Results (primary outcomes)†	Results (secondary outcomes)†
													commenced on CPAP at T3 (6% rejection rate) compared to *ED* (28% rejection rate) ($p = 0.004$). At T12, the difference between CPAP commencement in the *IG* (4% rejection rate) compared to the *ED* (26% rejection rate) was still significant, ($p = 0.002$).	The STTS-R was not correlated with adherence at any of the three follow-up points.
Pengo et al. (2018)	UK	To compare positive (*IG*+) and negative framed messages (*IG*–) based on motivational strategies and *TAU* in improving **adherence** to CPAP and **daytime sleepiness**	$N = 112$ *TAU* = 36 *IG*(+) = 36 *IG*(–) = 37	*TAU*: 53.5 (12.5) *IG*(+): 46.7 (12.2) *IG*(–): 47.1 (11.7)	*TAU*: 31 *IG*(+):25 *IG*(–):28	*TAU*: 37.3 (11.7) *IG*(+):36.0 (8.3) *IG*(–):36.3 (7.6)	*TAU*: 11.9 (6.1) *IG*(+): 10.8 (5.3) *IG*(–): 11.2 (6.2)	NR	T2w–T6w	Adherence to CPAP: Machine usage (total hours)	Daytime sleepiness: ESS	*TAU*: 11 (30.5) *IG*(+): 5 (14%) *IG*(–): 8 (21.63%)	The *IG*(+) showed significantly greater CPAP usage after 2 weeks (total use 53.7 ± 31.4 h) compared to the *IG*(–) (35.6 ± 27.4) and *TAU* (40.8 ± 33.5 h, $p < 0.05$); however, no differences were seen at 6 weeks.	ESS improved in all patients (baseline 11.0 (6.0) vs. ESS at 2 weeks 9.2 (5.9) points, $p < 0.0001$) with no significant differences among groups. There was no difference between 2 and 6 weeks.
Roecklein et al. (2010)	US	To compare motivational enhancement intervention (*IG*) vs. *TAU* in improving **adherence to CPAP**, apnea, **side effects of CPAP use, daytime sleepiness**	$N = 30$ *TAU* = 16 *IG* = 14	*TAU*: 46.10 (11.50) *IG*: 46.60 (11.30)	*TAU*: 25% *IG*: 30%	*TAU*: 42.18 (7.61) *IG*: 42.06 (8.91)	*TAU*: 11.25 (4.15) *IG*: 11.92 (5.50)	*TAU*: 45.82 (42.38) *IG*: 42.69 (34.34)	**T2w**–T3	Adherence to CPAP: Machine usage (h/night) Self-reported CPAP usage: CPAP/BiPAP Questionnaire	Side effects of CPAP use: SEQ Apnea: CSAQLI Daytime sleepiness: ESS Readiness, Motivation, Knowledge and Social support: *ad hoc* measure	*TAU*:1 *IG*:1	There was no difference in objective average daily use or total hours between-group at T2w and T3, but in both groups, the daily use of CPAP decreased. Individuals in the *IG* with self-report measure reported using CPAP longer than controls in both time points, but at T3 the adherence-reported level is significantly higher in *IG* [$F_{(1,22)} = 7.13$, $p < 0.05$] *TAU*: T2w = 7.11 (8.45); T3 = 66.43 (32.07) *IG*: T2w = 11.26 (7.89); T3 = 93.75 (15.83)	Groups did not differ in rates of CPAP side effects, daytime sleepiness, or symptoms between time points. There was a main effect of time on symptoms due to the expected decrease in symptoms over time [$F_{(1,25)} = 15.49$, $p < 0.01$]. Readiness at T2w predicted total therapy hours at T3 ($\beta = -207.97$, $Se\beta = 94.60$, $p < 0.05$), readiness improved significantly over time [$F_{(1,25)} = 49.44$, $p < 0.05$].
Rudilla et al. (2021)	SP	To compare motivational interviewing (*IG*) vs. *TAU* in improving **adherence** to CPAP, **motivation, perceived competence, quality of life, daytime sleepiness, emotional state,** and **social relations**	$N = 83$ *TAU* = 42 *IG* = 41	*TAU*: 57.51 (12.19) *IG*: 61.35 (13.11)	*TAU*: 28 *IG*: 32	NR	*TAU*: 13.02 (4.29) *IG*: 10.35 (4.53)	*TAU*: 49.95 (17.85) *IG*: 46.30 (18.80)	**T1–T3**	Adherence to CPAP: Machine usage (h/night)	Motivation: open-ended questions Perceived competence: CEPCA Quality of life: VAWBS-A Daytime sleepiness: ESS Emotional state, Activities, and social relations: *ad hoc* measure	*TAU*: 2 *IG*: 1	For CPAP adherence, statistically significant results were obtained in favor of *IG* ($p < 0.01$), with a mean difference of 1.60 h (95% CI, 0.60–2.61).	CEPCA was significantly higher in *IG* at T3 with a mean difference of 4.61 (95% CI, 3.49 to 5.72) ($p < 0.001$). VAWBS-A was significantly higher in *IG* at T3 ($p < 0.001$.). No statistically significant differences were observed for ESS when comparing the before-after change between the treatment arms at T3, but there were statistically significant differences found when comparing the outcomes between the two study groups.

(Continued)

TABLE 1 | Continued

Author, year	Country	Study aim*	Sample size (*n*)	Age (yrs): *Mean (SD), range*	Male gender: *n(%)*	BMI (kg/m²): *Mean (SD); range*	ESS	AHI: *events/h (SD)*	Follow-up points**	Primary outcomes: *measure*	Secondary outcomes: *measure*	Drop-out *N (%)*	Results (primary outcomes)†	Results (secondary outcomes)†
Sparrow et al. (2010)	US	To compare motivational enhancement intervention (*IG*) vs. educational group (*ED*) in improving **adherence** to CPAP, **daytime sleepiness, sleep-related symptoms, depression, behavioral alertness, CPAP self-efficacy,** and **decisional balance**	*N* = 250 *ED* = 126 *IG* = 124	*ED*: 54.0 (45.0-62.0) *IG*: 56.0 (48.0-63.0)	*ED*: 105 (83.3) *IG*: 100 (80.7)	*ED*: 35.9; 31.9-42.1 *IG*: 34.4; 30.1-40.1	*ED*: 11.0 (8.0-15.0) *IG*: 10.0 (6.0-15.0)	*ED*: 40.5 (21.0-64.0) *IG*: 36.0 (22.0-63.0)	T0**–T6–T12**	Adherence to CPAP: Machine usage (h/night)	Daytime sleepiness: FOSQ Sleep-related symptoms: SSC Depression: CES-D Behavioral alertness: PVT CPAP Self-Efficacy: *ad hoc* measure CPAP Decisional Balance: *ad hoc* measure	*ED*: 14 *IG*: 12	The intervention had a significant effect on CPAP adherence: median observed CPAP use in patients in *IG* was approximately 1 h/night higher than in subjects of *TAU* at 6 months ($p = 0.006$) and 2 h/night higher at 12 months ($p = 0.004$)	CPAP adherence was significantly associated with a greater reduction in sleep apnea symptoms and depressive symptoms and a greater improvement in functional status. At T6 and T12 *IG* scored significantly higher than *TAU* on self-efficacy and decisional balance *TAU*(self-efficacy): T6 = 4.2, 3.0–4.8; T12 = 4.2, 3.0–5.0 *IG*(self-efficacy): T6 =4.4, 3.8–5.0; T12 = 4.6, 3.6–5.0 *TAU*(decisional balance): T6 = −3.0, −10.5–4.0; T12 = −2.0, −11.0–4.0 *IG*(decisional balance): T6 = 1.2, −6.0–7.0; T12 = 0.0, −6.0–6.0

AHI, Apnea-Hypopnea index; AU, Australia; CEPCA, Questionnaire of Evaluation of Perceived Competence in Adherence to CPAP in OSAS; CES-D, the Center for Epidemiological Studies Depression; CH, China; CSAQLI, Calgary Sleep Apnea Quality of Life Index; ESS, Epworth Sleepiness Scale; FOSQ, Functional Outcomes of Sleep Questionnaire; IT, Italy; PT, Portugal; PVT, Psychomotor Vigilance Task; SEMSA, Self-Efficacy Measures Of Sleep Apnea; SEQ, The Side Effects Questionnaire; SF-36, Short Form-36 Health Survey Questionnaire; SMSA, Self-Efficacy Measure for Sleep Apnea; SP, Spain; SSC, Sleep Symptoms Checklist; STTS-R, The Satisfaction with Therapy and Therapist Scale–Revised; UK, The United Kingdom; US, The United States; VAS, Visual Analog Scale; VAWBS-A, Visual Analogical Well-Being Scale for Apnoea.

**Patient-Reported Outcomes in bold; **Psychological data measurements in bold. Where not otherwise specified, times are expressed in months.*

† Only significant p-values were reported. NR, not reported.

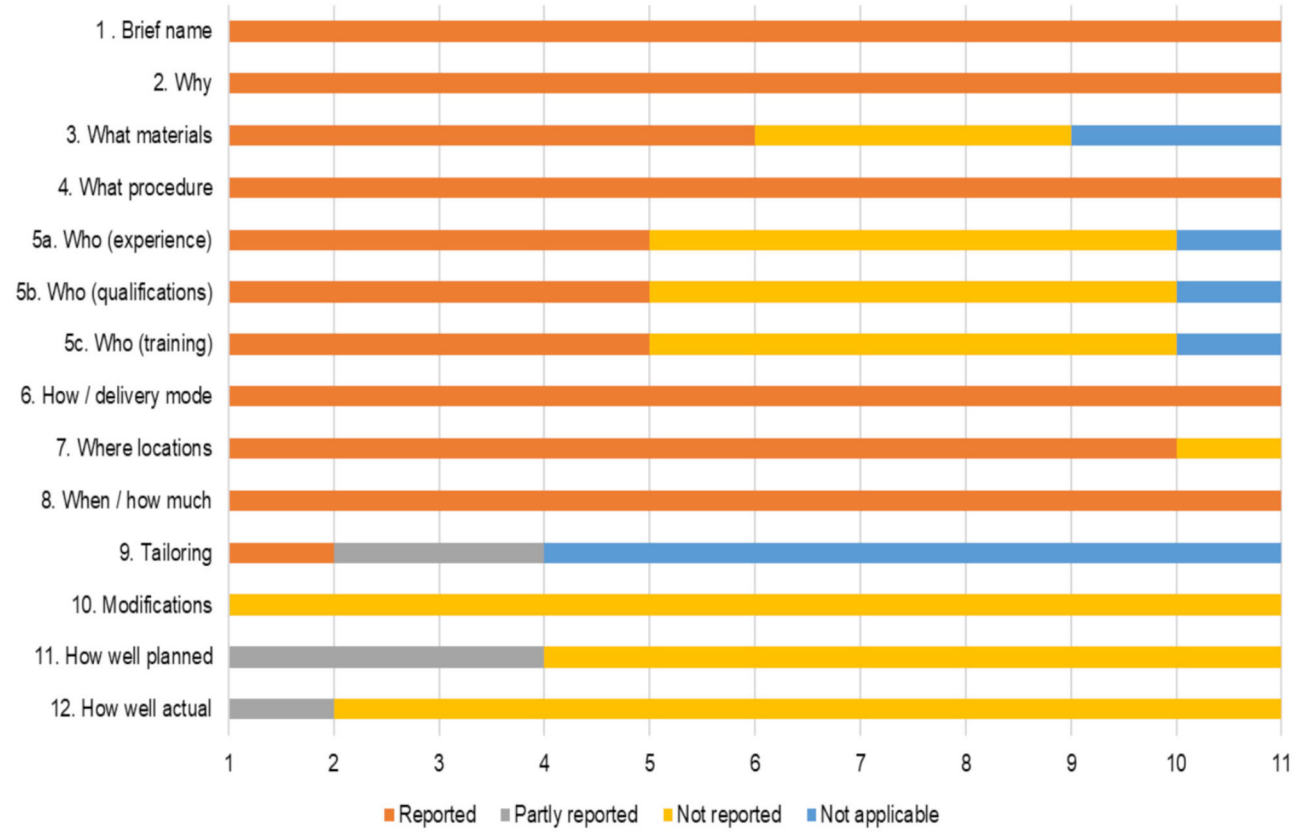

FIGURE 2 | Proportion of TIDieR items not/partly or fully included in each of the 11 trial reports.

between their ideal and current behavior (decisional balance technique), and eliciting self-motivational statements (change talk). The importance of CPAP use was also discussed, and emphasis was placed on the patients' autonomy. The second session was aimed at strengthening the patient's commitment to change, summarizing the pros and cons of the use of CPAP, and setting realistic goals to achieve. Following, the patient's improvements were reviewed and reinforced, while key barriers to CPAP use were identified and addressed. In the study by Rudilla et al. (2021), motivational strategies were adapted to the patient's stage of change (Prochaska and DiClemente, 1983). When in the pre-contemplation phase, information was provided while dealing with resistance to change and supporting the patients' self-efficacy. In the contemplation phase, the pros and cons of change were discussed to support goal setting. In the determination phase, emphasis was made on setting a change plan. In the maintenance phase, strategies to deal with risk situations were provided. In case of relapses, the patients were helped to understand their reason causes, while confidence in their ability to make behavioral changes and related action plans were further supported. Further, in the study by Pengo et al. (2018), health-related information was offered in terms of either risk or benefits framed via positive or negative message.

Notably, only 4 out of 11 studies (Aloia et al., 2013; Dantas et al., 2015; Jean-Louis et al., 2017; Rudilla et al., 2021) tailored motivational intervention strategies according to the patient's initial degree of readiness to change and confidence in their ability to succeed.

In four studies the treatment was conducted by a motivational-trained-nurse (Olsen et al., 2012; Aloia et al., 2013; Lai et al., 2014; Rudilla et al., 2021), in two studies by a sleep doctor/sleep technician (Lo Bue et al., 2014; Pengo et al., 2018), and in one record by a psychologist (Bakker et al., 2016) and by a trained health educator (Jean-Louis et al., 2017), respectively. A multidisciplinary intervention involving a pulmonologist, psychologist, and physiotherapist was employed in one study (Dantas et al., 2015), while Sparrow et al. (2010) implemented the intervention with the use of an automated telephone-linked communication system. Only Roecklein et al. (2010) did not mention who conducted the intervention.

The treatment was conducted through regular in-person meetings in four studies (Roecklein et al., 2010; Olsen et al., 2012; Aloia et al., 2013; Rudilla et al., 2021), while in five contributions (Sparrow et al., 2010; Lo Bue et al., 2014; Jean-Louis et al., 2017) motivational interventions were entirely provided via remote interactions, and in three studies the interventions began in-person followed by telephone-based follow-ups sessions

(Lai et al., 2014; Bakker et al., 2016; Pengo et al., 2018) or the use of an App motivating and assisting the use of the CPAP.

Ad hoc video education offering real-life experiences with the CPAP was also used in 2 out of 11 studies in addition to the motivational intervention (Lai et al., 2014; Bakker et al., 2016). Moreover, a single motivational group-format intervention with 20 participants was employed in one contribution (Dantas et al., 2015).

The theoretical background of the intervention was reported in 5 out of 11 studies (Roecklein et al., 2010; Sparrow et al., 2010; Olsen et al., 2012; Aloia et al., 2013; Rudilla et al., 2021). Aloia et al. (2013) and Roecklein et al. (2010) referred both to the Social Cognitive Theory (SCT; Bandura et al., 1999) and the Transtheoretical Model of Change (TTM; Prochaska and DiClemente, 1983). In Rudilla et al. (2021) and Sparrow et al. (2010), the interventions were respectively based on the TTM and SCT, while in Olsen et al. (2012) on the Health Belief Model (HBM; Becker, 1974).

Control Group

Six studies compared the intervention group with a standard care condition only (treatment as usual; *TAU*) (Roecklein et al., 2010; Lai et al., 2014; Lo Bue et al., 2014; Bakker et al., 2016; Pengo et al., 2018; Rudilla et al., 2021). Educational sessions focused on increasing awareness on the benefits of a healthy lifestyle and of the use of the CPAP were, instead, used as controls in two contributions (Sparrow et al., 2010; Olsen et al., 2012; Aloia et al., 2013; Jean-Louis et al., 2017), while two records included both *TAU* and educational controls (Aloia et al., 2013; Dantas et al., 2015).

Effects of the Intervention Across Time-Points

Primary Outcomes

Study duration ranged from 2 weeks (Pengo et al., 2018) to 12 months (Sparrow et al., 2010; Olsen et al., 2012; Aloia et al., 2013; Lo Bue et al., 2014; Bakker et al., 2016). In one study, the intervention had a duration of 2 months (Dantas et al., 2015), 3 months (Roecklein et al., 2010; Lai et al., 2014; Rudilla et al., 2021), or 6 months (Jean-Louis et al., 2017), respectively.

In 10 studies data related to hourly CPAP usage were used to measure adherence to treatment as a primary outcome (Roecklein et al., 2010; Sparrow et al., 2010; Olsen et al., 2012; Aloia et al., 2013; Lai et al., 2014; Lo Bue et al., 2014; Dantas et al., 2015; Bakker et al., 2016; Pengo et al., 2018; Rudilla et al., 2021), and in 1 study patients were directly asked if they were following the indications (Jean-Louis et al., 2017). Only Roecklein et al. (2010) used both objective (CPAP usage data) and subjective (self-report *ad-hoc* questionnaire) measures of adherence.

Nine out of 11 studies showed that motivational interventions were effective in increasing the average hours of CPAP use (Sparrow et al., 2010; Olsen et al., 2012; Aloia et al., 2013; Lai et al., 2014; Lo Bue et al., 2014; Dantas et al., 2015; Bakker et al., 2016; Pengo et al., 2018; Rudilla et al., 2021). In particular, significantly higher CPAP adherence was found after 2 weeks (Pengo et al., 2018) and 1 month (Lo Bue et al., 2014) from CPAP titration among participants in the motivational group compared with those receiving usual care, despite in Lo Bue et al. (2014) results were not maintained over time. Similarly, in the study by Dantas et al. (2015), patients assigned to the experimental condition presented significantly higher adherence to CPAP after 2-month from CPAP titration than those in the *TAU* and educational controls. Moreover, three studies assessed adherence to CPAP after 3 months from the beginning of the treatment and showed that motivational interventions were significantly more effective than *TAU* (Olsen et al., 2012; Lai et al., 2014; Rudilla et al., 2021) and educational controls (Olsen et al., 2012), respectively. Participants in the motivational interventions also revealed a significantly higher CPAP adherence compared with *TAU* (Bakker et al., 2016) and the educational control group (Sparrow et al., 2010) at 6- and 12-month follow-ups in 2 records and another study showed significant between-group differences at 12 months in favor of those participants in the motivational group who displayed moderate levels of adherence during their first week of CPAP use compared to both *TAU* and educational controls (Aloia et al., 2013). Instead, no significant between-group differences were found by Jean-Louis et al. (2017) and by Roecklein et al. (2010)—but a greater likelihood of adhering to CPAP was detected among patients receiving the motivational intervention compared to those participating in the educational group. Specifically, in Roecklein et al. (2010), significantly higher self-reported adherence was reported in the intervention group at 2-week and 3-month follow-ups.

The figures below show the mean daily usage of CPAP (h/night) across conditions at different time-points as reported in the selected studies (**Figure 3**) and provide a summary of motivational interventions by type of intervention format that has been shown effective in increasing adherence to CPAP in the short- and long-term, according to Webb et al.' taxonomy (Webb et al., 2010) (**Figure 4**). The studies by Jean-Louis et al. (2017) and by Roecklein et al. (2010) were, therefore, excluded despite showing that patients in the intervention group had a greater likelihood of adhering to recommended CPAP compared with the educational group, and indicated significantly higher—but self-reported—adherence to CPAP than *TAU* and educational controls, respectively.

Secondary Outcomes

Seven out of the 11 selected studies made use of the Epworth Sleepiness Scale (ESS) to report the presence and intensity of daytime sleepiness (Roecklein et al., 2010; Olsen et al., 2012; Lai et al., 2014; Lo Bue et al., 2014; Dantas et al., 2015; Pengo et al., 2018; Rudilla et al., 2021).

In one study, after 3 months among participants in the motivational group compared with *TAU*. the ESS scores decreased significantly in the intervention group compared with *TAU* and educational controls at 1 and 2 months after CPAP titration (Dantas et al., 2015), while in another record (Lai et al., 2014) daytime sleepiness reduced significantly.

Instead, five studies failed to detect significant between-group differences in the ESS scores across conditions (Roecklein et al., 2010; Olsen et al., 2012; Lo Bue et al., 2014; Pengo et al., 2018; Rudilla et al., 2021), but an overall improvement of ESS among

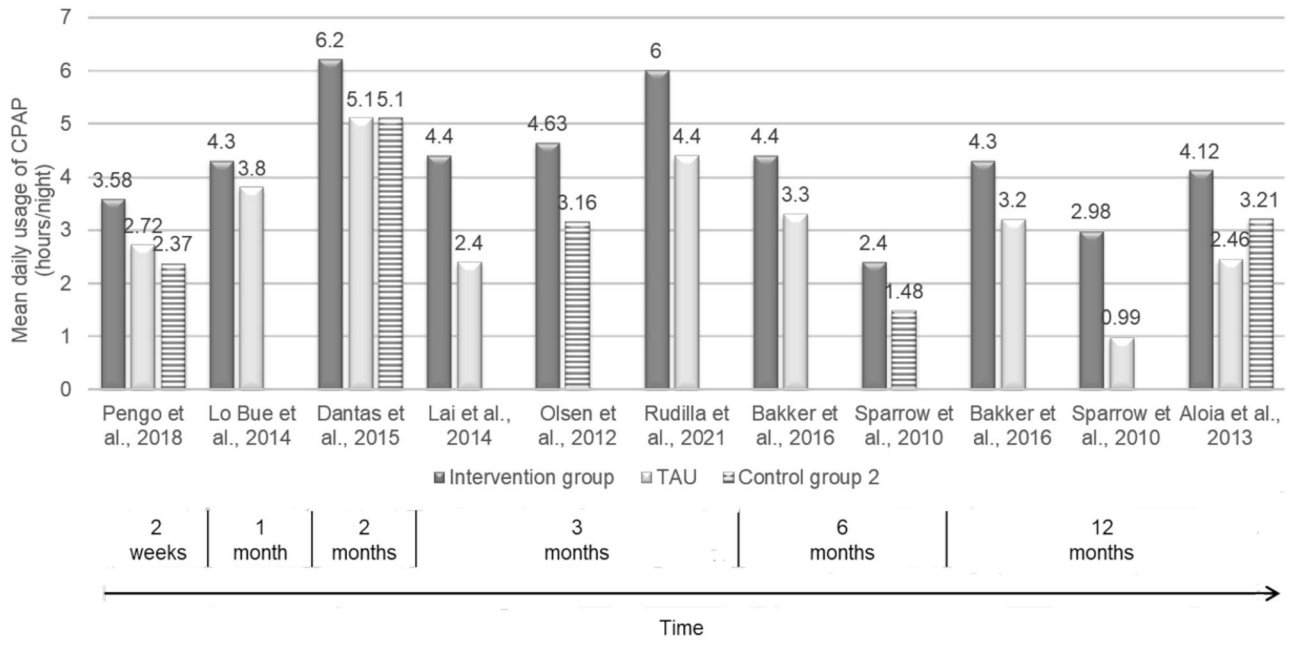

FIGURE 3 | Mean daily usage of CPAP (hours/night) across conditions at different time-points.

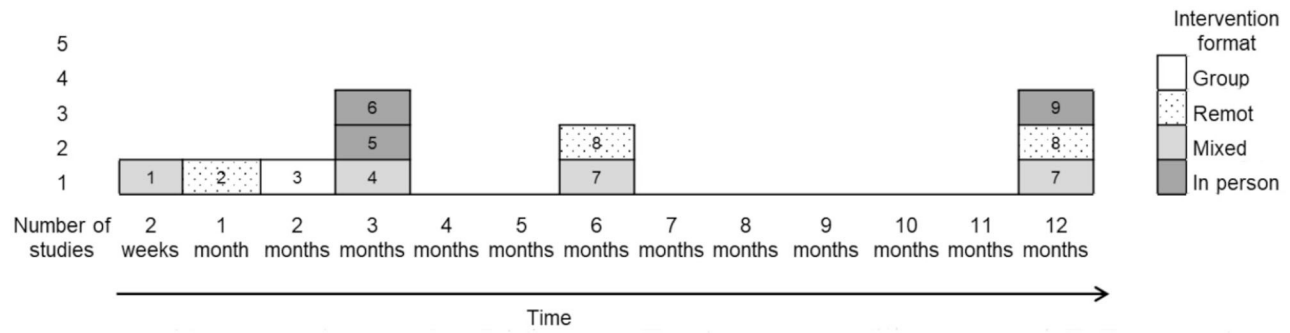

FIGURE 4 | Efficacy of motivational interventions by type of intervention format. 1, Pengo et al., 2018; 2, Lo Bue et al., 2014; 3, Dantas et al., 2015; 4, Lai et al., 2014; 5, Olsen et al., 2012; 6, Rudilla et al., 2021; 7, Bakker et al., 2016; 8, Sparrow et al., 2010; 9, Aloia et al., 2013.

all the respondents was found in three studies (Olsen et al., 2012; Lo Bue et al., 2014; Pengo et al., 2018).

Moreover, one contribution showed over time an AHI improvement across conditions, and significantly lower AHI scores were registered after 2 months from CPAP titration in the motivational group compared with the educational and *TAU* controls (Dantas et al., 2015).

Two records (Olsen et al., 2012; Lai et al., 2014) also assessed OSAS risk perception. Although no significant between-group difference was found, it reduced significantly between 1 and 3-month follow-ups in one contribution (Olsen et al., 2012), while no significant improvement was shown by Lai et al. (2014).

Self-efficacy was assessed in six studies (Sparrow et al., 2010; Olsen et al., 2012; Aloia et al., 2013; Lai et al., 2014; Dantas et al., 2015; Rudilla et al., 2021) using: self-statements investigating the participants' confidence in their ability to follow the treatment recommendations (Sparrow et al., 2010; Aloia et al., 2013), the Self-efficacy Measure for Sleep Apnea (SMSA) (Olsen et al., 2012; Lai et al., 2014) the Questionnaire of Evaluation of Perceived Competence in Adherence to CPAP in OSA (Rudilla et al., 2021) or a Visual Analog Scale (VAS) (Dantas et al., 2015).

No between-group differences were detected with the first measure. However, self-efficacy levels decreased over time in the control conditions, while improving among participants in the motivational intervention in one study (Aloia et al., 2013). Moreover, Sparrow et al. (2010) observed a significant increase in self-efficacy at 6- and 12-month follow-ups in favor of the motivational group compared with *TAU*.

Significantly higher rates of self-efficacy were also found by Dantas et al. (2015) at 2-month follow-up among patients

assigned to the motivational intervention compared with those receiving education. Self-efficacy increased in the motivational group and decreased in the control conditions.

Instead, even though higher SMSA scores were detected at 3-month follow-up in the motivational group compared with *TAU*, statistical between-group differences were found only in one contribution (Lai et al., 2014). These results were parallel to those by Rudilla et al. (2021), which showed that competence increased significantly at 3-month follow-up in the motivational group compared with *TAU* (Rudilla et al., 2021).

The construct of health-related quality was measured with the Functional Outcomes of Sleep Questionnaire (FOSC) in two contributions (Olsen et al., 2012; Lai et al., 2014). No between-group differences were observed in both studies, but in Olsen et al. (2012), increased scores were observed at 3-month follow-up across conditions. Instead, in the study by Rudilla et al. (2021) patients assigned to the motivational intervention showed better quality of life measured by the Visual Analogical Well-being Scale for apnoea than *TAU* after 3 months from CPAP titration.

Notably, the patients' readiness to change was investigated only in one study (Roecklein et al., 2010) using the SCT and the TTM Questionnaires adapted for CPAP. Results showed that motivation improved significantly over time both in the experimental and the educational control groups, and that baseline levels of readiness to change were negatively associated with CPAP use (h/night) at 3-month follow-up.

Potential side effects associated with the use of the CPAP were also explored by Roecklein et al. (2010), but no between-group differences were found across time points in both the motivational intervention and the educational control.

No significant between-group differences were also observed in the emotional state, daily activities, and social relationships of the participants in one study (Rudilla et al., 2021). Moreover, satisfaction with the therapy and the therapist did not appear to be related to CPAP adherence in another contribution (Olsen et al., 2012).

DISCUSSION

To our knowledge, this is the first scoping review of the literature aimed to explore the characteristics and impact of motivational interventions to promote adherence to CPAP therapy in patients with OSAS, commonly operationalized as increased daily hours of CPAP usage.

Results from 9 out of the 11 included studies showed that motivational interventions were more effective than usual care and/or educational programs in increasing adherence to CPAP. However, significant between-group differences favoring motivational interventions were mostly observed in the short term, and results were not always maintained over time. Moreover, adherence declined over time in both the motivational and control groups in six studies (Roecklein et al., 2010; Olsen et al., 2012; Aloia et al., 2013; Lai et al., 2014; Lo Bue et al., 2014; Bakker et al., 2016).

This outcome variability may to some extent be explained by the characteristics of the intervention, as some contributions reported on the effect of only one encounter, some of them had follow-up periods shorter than 3 months, and the treatment was delivered in different ways (i.e., in-person meetings or remote interactions; individual or group format).

Still, positive outcomes were observed even in brief motivational encounters of only 2 min (Pengo et al., 2018), and more than one encounter with a patient seems to increase the likelihood of an effect.

It should also be considered that aspects such as different types of healthcare professionals delivering the treatment, and their training and experience in the use of motivational strategies may have influenced the magnitude of the treatment, even if this cannot be shown in this review. Six out of 11 studies (Olsen et al., 2012; Aloia et al., 2013; Lai et al., 2014; Bakker et al., 2016; Jean-Louis et al., 2017; Rudilla et al., 2021) reported on how practitioners were trained, but only two of them (Lai et al., 2014; Bakker et al., 2016) assessed the treatment fidelity.

Most of the contributions also lack adequate details on the training of professionals, the contents of the interventions, and the theoretical models on which they were based.

Motivational interventions are of proven efficacy in improving adherence to treatment in patients suffering from various chronic conditions (Burke et al., 2003; Van Nes and Sawatzky, 2010; Maissi et al., 2011; Pietrabissa et al., 2012, 2015, 2017; Bonde et al., 2014; Soderlund, 2018)—but for the development of advanced intervention protocols, studies should include a more comprehensive description and assessment of the communicational strategies employed in the intervention. In fact, evidence exists for the correlation between poor compliance and health care providers' lack of communication skills. Often, patients deliberately ignore professionals' recommendations, even when change is needed, but this paradoxical behavior cannot be overcome with rational explanations. Therefore, mastering communication abilities in the medical setting is essential to promote low-cost interventions with a positive cost/benefit ratio.

Since motivational interventions largely depend on "listening" to the patients and accommodating their ambivalence and resistance to change—rather than "telling" and educating—the use of respectful, and compassionate communication may play a crucial role during the process of ending risk behaviors and/or adopting positive health behaviors in the clinical context.

In all the selected studies, the motivational strategies employed in the interventions were largely aimed to address treatment expectations and ambivalence toward the use of the CPAP, to define goals, and increase patients' confidence in their ability to make enduring behavioral change.

However, a relevant consideration is that only a few contributions targeted the interventions on the individuals' initial level of readiness and confidence to change, thus preventing from drawing valid conclusions over their outcomes.

Well-established theories of change (Prochaska and DiClemente, 1983; Miller and Rollnick, 1991) postulates that patients who are less motivated are expected to be more responsive to an intervention focused on increasing and maintaining motivation to change and that lower levels of self-efficacy reflect the number of previous failed attempts to make

a change. Moreover, studies show that how patients with OSAS experience their first month of CPAP therapy may influence their long-term adherence to the device (Budhiraja et al., 2007; Collen et al., 2009; Perger et al., 2019).

In the selected contributions, participants were all first-time CPAP users. It is, therefore, reasonable to believe that the patients did not fall in the "resistant to change" category—for which motivational approaches are proven to be most effective. Accordingly, the only record that assessed the individuals' readiness to change over time (Roecklein et al., 2010) revealed a negative association between self-reported motivation to change and actual use of the CPAP in patients with OSAS. The reduced superiority of the motivational interventions in increasing adherence to CPAP among naïve uses might, therefore, also depend on the patients' level of motivation. These findings support the assumption that motivational intervention might even be counterproductive for highly motivated individuals (Resnicow and McMaster, 2012). Behavioral change is a complex phenomenon with multiple determinants that also includes psychological, motivational, and socio-environmental aspects. Therefore, assessing the individuals' adherence to a treatment regimen also means considering their level of problem awareness (reasons for change), willingness to change, and perceived ability to do so (Ceccarini et al., 2015). Subjective measures of adherence had relatively little representation in the reviewed studies. Yet, self-report indices of motivation to change do not necessarily equate to actual change in response to treatment, and they should be recognized as the patient's intent at that moment to change rather than a predictor for any real change in behavior.

Findings from this review also reveal that research testing the impact of motivational interventions on adherence to CPAP use among people suffering from OSAS is only recent—as selected studies were published between 2010 and 2021. Further studies need to be re-examined by including both objective and subjective measures of adherence, and longer follow-up periods that make sure the absence of any dissonance between the patients' intention to change and their current status.

Strengths and Limitations

The results of the present scoping review should be interpreted with the following limitations in mind. First, the search of electronic databases was limited to trials published in the English language, and this may have led to the exclusion of relevant records. Second, there are limitations inherent in the decision not to include the gray literature, which may have further impacted the selection of studies and results. Third, this review investigated treatment components in isolation. As more trials are published, it may be useful to explore whether different effects are obtaining by combining treatment strategies, rather than investigating components in isolation. Fourth, inconsistent operationalizations and considerable variability in measures of adherence to treatment, the short-term assessment of outcomes, and the need for well-trained providers of motivational interventions were identified as major barriers to research progress in this area. As a result—despite the strengths of its well-defined methodology, careful selection of participants, extensive measures of psychological profile, and outcomes—this review has limited ability to project the likelihood of any adherence to CPAP being maintained over time following motivational interventions.

Future Research and Practical Directions

Although motivational interventions are strongly recommended in clinical settings (Lim et al., 2019) to facilitate health behavior change in patients with pulmonary diseases (Minassian and Doran, 2020), the present findings suggest that several aspects may impact the intervention efficacy. More research providing a detailed description of motivational strategies and testing of their association with positive treatment outcomes is therefore needed. It would make adherence assessment more straightforward and increase knowledge on effective mechanisms of change.

Future research may also wish to apply both direct and indirect measures of adherence and to examine whether the duration of motivational intervention and frequency of sessions are associated with treatment effects. Moreover, qualitative investigations into the type of information or strategy patients with OSAS find most meaningful may aid in optimizing the content of the interventions.

Motivational interventions appear to be a useful strategy and that can easily be broadly disseminated, but more longitudinal study should test their longer-term effects.

Research also shows that motivational interventions can effectively be provided digitally to patients with OSAS using CPAP (Hu et al., 2021), with proven advantages and reduced costs (Appel et al., 2011; Bus et al., 2018). Further investigations should focus on the use of the different format of delivering motivational interventions including the use of new technologies, or the provision of motivational interventions in group settings (Velasquez et al., 2006; Channon et al., 2007; Tucker et al., 2017)—as the group format requires specific competence and additional tasks, and the motivational strategies are far more complex to operate than in individual sessions (Major and Palmer, 2001; Britt et al., 2004; Pietrabissa, 2018). This further supports the need for studies assessing treatment fidelity, and that also carefully describe the training offered to providers and the processes of supervision of motivational sessions (Lim et al., 2019). The feasibility of implementing MI in the clinical setting also warrants attention to the patients' perceived social support and quality of family relationships, as the interventions may differ depending on the level of involvement of significant others in the process of change.

CONCLUSION

This scoping review leads to the conclusion that motivational strategies outperform traditional advice-giving in increasing adherence to CPAP use in patients with OSAS. However, a proper evaluation of the individuals' motivation to change and the provision of the corresponding motivational strategy in a clinical setting deserve further attention. Future trials providing more detailed information on the mechanisms of behavioral changes would help optimizing the effectiveness of motivational interventions in adults with OSAS. The cost-effectiveness of

motivational intervention—alone or in combination with other interventions—might be a worthwhile endeavor to pursue.

AUTHOR CONTRIBUTIONS

GR and GP designed the study, conducted extensive literature searches, analyzed the data, and wrote the first draft of the paper. GM, IB, IT, EP, and CL revised the manuscript. GR, GP, GC, SG, FS, and PF reviewed methodological as well clinical issues and further edited the manuscript. All authors approved the final version of the manuscript.

ACKNOWLEDGMENTS

The authors would like to thank Alessandra Scarpa and Claudia Tarquinio for their precious assistance in the preparation of this manuscript.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2021.705364/full#supplementary-material

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frontiers in Psychology

ORIGINAL RESEARCH
published: 18 August 2021
doi: 10.3389/fpsyg.2021.703089

Short-Term Effects of a Multidisciplinary Residential Rehabilitation Program on Perceived Risks, Confidence Toward Continuous Positive Airway Pressure Treatment, and Self-Efficacy in a Sample of Individuals Affected by Obstructive Sleep Apnea Syndrome

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OPEN ACCESS

Edited by:
Luigi De Gennaro, Sapienza University of Rome, Italy

Reviewed by:
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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *30 April 2021*
Accepted: *21 July 2021*
Published: *18 August 2021*

Citation:
Scarpina F, Bastoni I, Cappelli S, Priano L, Giacomotti E, Castelnuovo G, Molinari E, Tovaglieri IMA, Cornacchia M, Fanari P and Mauro A (2021) Short-Term Effects of a Multidisciplinary Residential Rehabilitation Program on Perceived Risks, Confidence Toward Continuous Positive Airway Pressure Treatment, and Self-Efficacy in a Sample of Individuals Affected by Obstructive Sleep Apnea Syndrome. Front. Psychol. 12:703089. doi: 10.3389/fpsyg.2021.703089

Continuous positive airway pressure (CPAP) therapy is the standard treatment for obstructive sleep apnea (OSA) syndrome. However, optimizing adherence to CPAP therapy of individuals remains very challenging for clinicians because of the role played by the psychological components. In this study, we verified the changes in cognitions and beliefs of individuals after a four-week multidisciplinary residential rehabilitation program targeting the adaptation to CPAP therapy for OSA syndrome. We assessed the components of perceived risks, confidence toward the treatment, and self-efficacy through the self-report questionnaire, namely the Self-Efficacy Measure for Sleep Apnea (SEMSA) questionnaire. We also explored the role played by the temperamental traits on the changes registered in these components after the treatment. Forty-five participants completed the rehabilitation program, showing a higher level of adherence to the treatment. Significant changes were observed in terms of confidence toward the treatment, although no change was reported in terms of perceived risks and self-efficacy. Moreover, those individuals with a higher persistent temperamental trait reported a significant improvement in perceived risks, in the absence of other significant results. After the rehabilitation treatment, our participants were more prone to consider the effect of

CPAP treatment on health outcomes. This was in line with the educational aim of the rehabilitation treatment. The temperament seemed to play only a marginal role in the global changes reported by our participants. We discussed the need for behavioral interventions, in addition to education, in improving self-efficacy.

Keywords: OSA syndrome, CPAP therapy, obesity, perceived risk, self-efficacy, temperament

INTRODUCTION

Continuous positive airway pressure (CPAP) therapy is the standard treatment for the obstructive sleep apnea (OSA) syndrome, a respiratory sleep disorder characterized by repeated episodes of partial or complete obstruction of the upper airway occurring during the inspiratory phase (American Academy of Sleep Medicine, 2014). The therapy consists of the use of a ventilator, which performs by blowing air into the throat *via* a mask, subtly increasing air pressure in the throat, and preventing the airway from narrowing. Despite its benefits, compliance of patients to CPAP therapy is not always satisfactory, and optimizing adherence of individuals to CPAP ventilator remains very challenging for clinicians. Dropout of patients is generally due to difficulties in using the ventilator and discomfort with the usage of the full-face mask. Moreover, it should be underlined that CPAP therapy requires a considerable alteration of the lifestyle and sleeping of an individual (Kribbs et al., 1993; Rosen et al., 2012). Crucially, non-adherence to the treatment emerges very early, within the first week of therapy (Weaver et al., 1997; Rosentha et al., 2000; Weaver and Grunstein, 2008). In fact, in this short time period, individuals develop personal cognitions and beliefs about CPAP therapy (i.e., outcome expectancies, risk perception, and self-efficacy), which shape the volition to use the ventilator (Aloia et al., 2005; Olsen et al., 2008; Weaver and Grunstein, 2008; Baron et al., 2011; Sawyer et al., 2011a,b) with the long-term effects on the level of adherence to treatment (Weaver and Grunstein, 2008; Sawyer et al., 2011a; Cayanan et al., 2019). Moreover, the subjective perception of the disease as well as its consequences on the health and psychological wellbeing of an individual do not necessarily reflect the objective severity of the illness and the need for treatment (Scarpina et al., 2020). This mismatch limits the efficacy of the treatment itself (Cayanan et al., 2019). Thus, the clinical procedures adopted in the earlier weeks to assist patients in their process of adaptation to ventilotherapy might play a significant role in increasing the long-term compliance of an individual to the use of CPAP.

In this study, we described an observational study with the aim to evaluate the short-term within-group effects of a four-week residential rehabilitation program in a sample of individuals affected by OSA syndrome. We focused on the changes in the cognitive components of perceived risks, confidence toward CPAP treatment, and self-efficacy, measured through the Self-Efficacy Measure for Sleep Apnea (SEMSA, Weaver et al., 2003) self-report questionnaire. The rehabilitation program was multidisciplinary: it targeted the adaptation to CPAP therapy for OSA syndrome (Budin et al., 2019); moreover, it regarded diet therapy, exercise training, and nutritional and psychological counseling.

Adherence to CPAP therapy is traditionally the main outcome of the process of adaptation, in which the psychological factors of individuals play a crucial role (Stepnowsky et al., 2002; Cayanan et al., 2019; Garbarino et al., 2020). In exploring which individual factors may enhance the subjective perception of positive outcomes associated with CPAP therapy in the case of OSA syndrome, in this study, we focused on the role of temperament. No previous study has been reported in the literature about the impact on the perceptions of individuals about CPAP therapy for OSA syndrome in the earlier weeks of treatment. Temperament is the inheritable and stable set of emotional and learning factors that underline the acquisition of the traits and attitudes of automatic emotional behavior of individuals (Cloninger et al., 1993; Cloninger, 1999). According to Maschauer et al. (2017), those individuals who show negative affectivity, social inhibition, and unhealthy lifestyle associated with reluctance to consult and/or follow medical advice (type D personality) have the long-term higher levels of non-compliance and poor treatment outcomes; conversely, individuals with a high internal locus of control and high self-efficacy, with self-refer for treatment, and having active coping skills are more likely to adhere to the CPAP treatment. However, in the previous literature, the role of temperament on the adherence to the treatment was verified as a long-term outcome (3 months and more after the beginning of the CPAP treatment), but not in short term (<3 months) (Maschauer et al., 2017). To provide the first evidence in this field, we explored if individual changes, specifically in terms of perceived risks, confidence toward CPAP treatment, and self-efficacy (Weaver et al., 2003) registered after a four-week residential program for OSA syndrome, might be related to the individual temperament.

METHODS

This observational study had a quasi-experimental pre–post design without the control group. This study was approved by the Ethics Committee of our Institution (Reference number: 21C924_2019). All participants were volunteers who gave informed written consent before participating in this study; they were free to withdraw at any time and were naïve to the rationale of this study. None of the participants were remunerated for their participation in this study; in fact, the National Sanitary System in Italy covers all hospital charges.

Participants

We included in-patients consecutively recruited at their admission to the hospital between February 2019 and February 2020 and between November 2020 and April 2021. The

recruitment was interrupted between February 2020 and November 2020 due to the COVID-19 pandemic worldwide.

Individuals were included in this study if: (i) they reported an Apnea–Hypopnea Index (AHI) higher than the value of 5 (Berry et al., 2012) at the full-night polysomnography (American Academy of Sleep Medicine, 2014) performed at their admission to our hospital, and (ii) they attended the rehabilitation program for the adaptation to CPAP therapy. We excluded individuals who used ventilotherapy in the past and who declared the regular use of hypnotic medications. Also, we excluded smokers; individuals with a history of alcohol abuse; and individuals with a history of cardiovascular, psychiatric, neurological disorders, or any concurrent medical condition that was not related to OSA syndrome.

Due to the negative side effects of OSA syndrome on cognition (Alomri et al., 2021; Legault et al., 2021), all participants performed a global assessment of the cognitive functioning through the Mini-Mental State Examination (Folstein et al., 1975; Italian version; Magni et al., 1996), the Clock-Drawing Test (Rouleau et al., 1992; Italian version: Siciliano et al., 2016), and the Frontal Assessment Battery (Dubois et al., 2000; Italian version: Appollonio et al., 2005).

Participants completed the Temperament and Character Inventory-Revised published by Martinotti et al. (2008). It is a 240-item self-administered questionnaire designed to assess four main temperamental traits as follows: (i) *novelty seeking*, associated with the emotion of anger, expresses the level of activation of exploratory activity; (ii) *harm avoidance*, related to fear, reflects the efficiency of the behavioral inhibition system; (iii) *reward dependence*, associated with attachment, refers to reward-based behavioral maintenance, and (iv) *persistence*, related to ambition, expresses the maintenance of behavior such as resistance to frustration. The questionnaire also measures three character dimensions, namely, self-directedness, cooperativeness, and self-transcendence, which denote self-concept and individual differences in goals and values and which influence choices and intentions.

The Rehabilitation Program

Individuals took part in a residential four-week multidisciplinary approach targeting the adaptation to CPAP therapy for OSA syndrome and the improvement of quality of life (Budin et al., 2019). The process of adaption to the use of CPAP starts after the polysomnography, and it is supervised by trained nurses. The nurses assist patients in using autonomously the CPAP and in increasing the level of awareness about the benefits associated with the ventilotherapy when used during sleeping. Before the first night of CPAP therapy, the nurse informs the patient about the procedure that will be followed during the four weeks; moreover, she/he illustrates the CPAP, its components, and its functioning. Together with the patient, the nurse choices the most suitable mask, taking into account the facial shape of patients. While the patient wears the mask, he/she sees him/herself in a mirror to verify the right position of the mask on the face. In addition, the nurse verifies the level of comfort. Then, the patient experiences the use of CPAP for 15/20 min. Later, the CPAP is delivered to the patient, who can start using it during sleeping. During night, the nursing staff supervises patients in ventilotherapy, assisting them in case of necessity. For example, if the patient removes the mask during night, the nursing staff wakes up and invites him/her to replace it in the right position. The next morning, the nursing staff verifies if the CPAP has been used correctly during night through the CPAP output.

The rehabilitation program includes individual and group-based psychological and educational sessions. The individual sessions consist of psychological consultation once a week (overall, four sessions), in which specialized psychologists provide support for psychological distress, such as depression and anxiety problems. Group sessions are scheduled every hour once a week (four sessions overall) and provide impersonal education about psychosocial risk factors and promotion of healthy habits.

The program entails daily sessions (six days a week) of aerobic activity that included 30 min/day of recreational activities at low intensity (walking) and 45 min of physical activities at high intensity (Lanzi et al., 2015).

All participants receive nutritional counseling, in which dietary assessment, evaluation of nutrient intake and adequacy, nutritional status, anthropometric measures, eating patterns, and history of overweight are performed. Thus, a personalized diet (i.e., 50% of energy from carbohydrates, 30% from lipids, and 20% from proteins) is furnished to each patient, in which the caloric intake is set at approximately 80% of resting energy expenditure. Every week, the diet is checked and adapted (Panasini et al., 2015). Participants also receive hourly group impersonal nutritional counseling twice a week relative to healthy eating, general nutrition, and core food groups.

Main Outcome: The SEMSA Questionnaire

At T0 (at the beginning of the treatment) and T1 (after 4 weeks, at the end of the rehabilitation program), participants filled out the Italian version (Manni and Palagini, 2016) of the SEMSA questionnaire (Weaver et al., 2003). This questionnaire assesses the following: (i) risk perception—the perceived vulnerability of patients to health risks (i.e., that untreated OSA syndrome would result in a negative outcome); (ii) outcome expectancy—perceived expectations regarding the potential of the behavior to reduce those risks (i.e., the perception that the use of CPAP would result in positive consequences in the life of patients); and (iii) treatment self-efficacy—perceived ability to perform the behavior (i.e., the perception that the patient has the wherewithal to use the CPAP effectively under a wide range of circumstances). The internal consistency coefficient of the total scale was 0.92 with item-to-total correlations ranging from 0.26 to 0.66 (Manni and Palagini, 2016). The Cronbach's α statistic for each of the three subscales was >0.85. Test–retest reliability coefficients ($N = 20$) were 0.68, $p = 0.001$ for perceived risk; 0.77, $p < 0.0001$ for outcome expectancies; and 0.71, $p = 0.0005$ for the treatment self-efficacy subscales.

Secondary Outcomes

All the following measures were collected twice, at T0 and T1. We assessed the effect of rehabilitation treatment on the psychological wellbeing of participants through the Italian

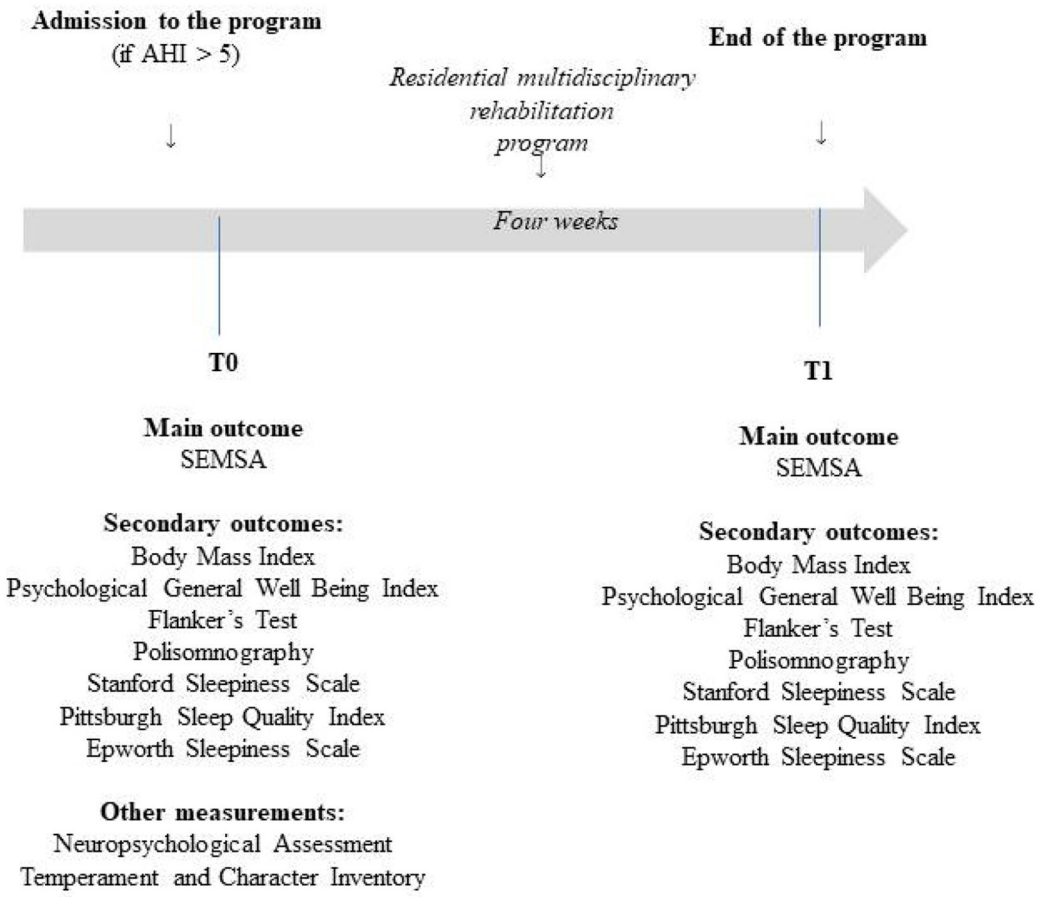

FIGURE 1 | Schematic representation of the procedure.

version (Grossi et al., 2006) of the Psychological General Well Being Index (PGWBI) (Dupuy, 1984). The questionnaire measures the domains of anxiety, depressed mood, positive wellbeing, self-control, general health, and vitality. We also measured the subjective perception of sleeping efficacy through three questionnaires: the Epworth Sleepiness Scale (Johns, 1991; Italian version: Vignatelli et al., 2003), which focuses on the pathological daily sleepiness (the higher the score the worse the sleepiness); the Pittsburgh Sleep Quality Index (Buysse et al., 2005; Italian version: Curcio et al., 2013), which assesses the sleep quality (the higher the score, the worse the quality); and the Stanford Sleepiness Scale (Hoddes, 1972), which quantifies the subjective level of alertness throughout the day (the higher the score the better the level of alertness).

To verify the effect of rehabilitation treatment on the attentional abilities, our participants performed the Flanker's test from the Psychology Experiment Building Language (PEBL)—Psychological Test Battery (Mueller and Piper, 2014) and as described in the study by Scarpina et al. (2020). This computerized attentional test measures the response inhibition. Participants were asked to detect visual stimuli (i.e., the targets) presented centrally while ignoring stimuli (i.e., the flankers) presented spatially close to them. The flankers correspond either to the same directional (right vs. left) response as the target (congruent condition), to the opposite response (incongruent condition), or to neither (neutral condition). There is also an experimental condition in which no flanker is shown. The flankers affect the behavioral responses to the central target positively (increasing the level of accuracy and the detection velocity), when they are consistent with the target response, or negatively (decreasing the level of accuracy and the detection velocity), when they are incompatible with the target. Overall, in the version used in this study, 160 trials were tested, 40 for each condition. Before the task, participants performed eight run-in trials to familiarize themselves with it. Further technical details can be found online (http://pebl.sourceforge.net) and in the study by Mueller and Piper (2014). For each trial, we registered the reaction time in milliseconds and the level of accuracy expressed in percentage (Scarpina et al., 2020).

Finally, after the four-week adaptation program, the standard full-night polysomnography was performed and compared with the measurement performed during admission.

The timeline of our study is shown in **Figure 1**.

ANALYSES

Adherence to CPAP

Adherence to CPAP was measured in terms of the number of nights of use and number of hours of use per night (Bravata et al., 2012). Adherence was classified into the following three groups: "good" if the usage was at least four hours per night for at least 70% of nights; "some" if the patient had used the device at least 10% of nights but less than the threshold for "good;" and "none/poor" if the patient used the device <10% of nights (Miech et al., 2019).

Primary Outcome

We investigated the changes in the three components measured through the SEMSA questionnaire, comparing the scores reported at the baseline (T0) and after the treatment (T1) within our sample using the Wilcoxon signed-rank test. Successively, we investigated if the changes observed between the baseline (T0) and after the four-week rehabilitation program (T1) in the SEMSA questionnaire scores were explained by the level of OSA syndrome severity and level of obesity of participants registered at their admission to the rehabilitation (T0) using the linear regression analysis (Myers et al., 2012). In detail, for each component of SEMSA, we computed the difference between the score reported at T0 and the score reported at T1 (i.e., Δ score). The Δ scores were used in the linear regression model, in which the AHI, indicating the level of OSA syndrome severity, and the body mass index (BMI), as the index of obesity severity, were used as statistical predictors. We reported the *R*-squared as a goodness-of-fit measure. We also evaluated the significance of the model through *F*-value and *p*-value. The relative contribution of the two predictors (i.e., AHI and BMI) with the independent variable (i.e., Δ SEMSA score for each component of the questionnaire) was analyzed. The variance inflation factor (VIF) was used as a measure of multicollinearity.

Secondary Outcomes

We investigated the changes associated with the four-week treatment in the PGWBI questionnaire and the three questionnaires assessing the subjective sleeping quality, comparing the scores reported at the baseline (T0) and after the treatment (T1) within our sample, using the Wilcoxon signed-rank test. We used the related-sample *t*-test to assess the changes in the BMI and the objective measurements of sleeping from polysomnography. To explore the changes in attentional abilities measured using the Flanker's test after the four-week treatment, we performed a repeated measure ANOVA with the factor *Condition* (i.e., neutral, congruent, incongruent, and single) and the factor *Time* (i.e., T0 vs. T1), independently for the reaction time in milliseconds and the level of accuracy expressed in percentage, as done in the study by Scarpina et al. (2020).

The Role of Temperament

We compared the scores of our participants reported at the Temperament and Character Inventory-Revised with those reported by the normative sample (Martinotti et al., 2008). Successively, the scores were converted into *T*-scores (which have a normal distribution with a mean of 50 and an SD of 10) as done in the study by Cloninger et al. (1994). We aimed to verify if changes observed between the baseline (T0) and after the four-week rehabilitation program (T1) in the scores relative to the SEMSA questionnaire were explained by the temperamental traits of participants. To respond to this aim, we used a linear regression analysis (Myers et al., 2012), as previously done. Specifically, we computed the difference between the score reported at T0 and the score reported at T1 (i.e., Δ score). Successively, we analyzed the correlation and directionality of the data to formulate the statistical model as follows: the Spearman's correlation coefficient was computed between the Δ scores relative to the SEMSA subscales and the *T*-scores relative to the four temperamental traits from the Temperament and Character Inventory-Revised. Those Δ scores that were significantly associated with one or more *T*-scores of the temperamental traits ($p \leq 0.05$) were used in the linear regression model. We reported the *R*-squared as a goodness-of-fit measure, the significance of the model through *F*-value and *p*-value, the relative contribution of the temperamental trait(s) included in the statistical model with the independent variable (i.e., Δ SEMSA scores), and the VIF as the measure of multicollinearity.

RESULTS

Fifty-two individuals (i.e., 32 women; 20 men; mean age in years = 54.61; SD = 9.52; range = 34–75; mean education in years = 11.88; SD = 3.82; range = 5–23) were enrolled. However, only 45 individuals (i.e., 27 women and 18 men) were included in this study, since 7 participants did not complete the rehabilitation program. The mean age in years was 53.6 (SD = 9.85; min–max = 34–72); the mean education in years was 12.26 (SD = 3.97; min–max = 5–23). At their admission to the rehabilitation program, 80% of our participants reported a severe apnea, with the AHI higher than 30, 4.44% of our participants reported a mild sleep apnea ($5 \leq$ AHI < 15), and 15.55% of our participants reported a moderate apnea ($15 \leq$ AHI < 30). Moreover, 91.11% of participants suffered from class III (high risk) obesity, since the BMI was equal to or >40, 6.66% of participants suffered from class II (moderate risk; BMI between 35.0 and 39), and 2.22% of participants suffered from class 1 (low risk; BMI between 30.0 and 34.9). The observed pattern was in line with the observation that OSA syndrome occurs frequently in obesity, as well as obesity is a high-risk factor for the development and progression of sleep apnea (Schwartz et al., 2008). The mean score relative to the Mini-Mental State Examination (Folstein et al., 1975) was 28.84 (SD = 1.06; min–max = 26–30), the Clock-Drawing Test (Rouleau et al., 1992) was 8.94 (SD = 1.73; min–max = 0–10), and the Frontal Assessment Battery (Dubois et al., 2000) was 16.95 (SD = 1.16; min–max = 12–18).

Adherence to CPAP

When we assessed the level of adherence to CPAP therapy, the majority of our participants (94.87%) had good use of CPAP after the four-week rehabilitation treatment, although only 5.4% of participants reported some good use of CPAP. The mean number of night of CPAP used was 24.91 (SD = 3.09; range 15–29), and

TABLE 1 | Mean, SD, and minimum (min) and maximum (max) for each scale relative to the Self-Efficacy Measure for Sleep Apnea (SEMSA) questionnaire registered at T0 (i.e., before the treatment) and T1 (i.e., after the four-week rehabilitation program).

	T0	T1	Statistical results
Perceived Risk (range score 1–4)	M = 1.91 SD = 1.24 min-max = 0–4	M = 2.28 SD = 1.47 min-max = 0–4	W (44) = 542; p = 0.07; d' = 0.27
Outcome Expectancies (range score 1–4)	M = 2.43 SD = 0.93 min-max = 0–4	M = 2.78 SD = 0.96 min-max = 0–4	W(44) = 597; **p = 0.004**; d' = 0.37
Treatment Self-Efficacy (range score 1–4)	M = 1.28 SD = 0.79 min-max = 0–3.11	M = 1.14 SD = 0.81 min-max = 0–3.7	W(44) = 249; p = 0.78; d' = 0.17

We reported statistical difference, and the significant difference between T0 and T1 scores is given in bold. For each scale, we reported the range score, according to the seminal article.

the mean time of CPAP was 6 h and 4 min for night (SD = 0.05; range 3 h and 26 min−9 h and 3 min).

Main Outcome

The scores registered at T0 and T1 as well as the statistical results for the three components investigated through the SEMSA questionnaire are reported in **Table 1**.

We observed that the level of individual perceived vulnerability to health risks and the level of perceived self-efficacy did not change after the rehabilitation; instead, our participants reported higher perceived expectations about the positive outcome of CPAP therapy on quality of life after the treatment. We successively verified the predictive role of the level of OSA syndrome severity (i.e., AHI) and the level of obesity (i.e., BMI) registered during admission on the changes in the SEMSA questionnaire scores. The VIF value relative to the AHI was 1.047; for the BMI, it was 1.047. Neither the AHI [$\beta = -0.005$, $t_{(41)} = -0.83$, $p = 0.5$] nor the BMI [$\beta = 0.03$, $t_{(41)} = 1.08$, $p = 0.28$] predicted the changes in the perceived risk score [$R^2 = 0.03$; $F_{(1,41)} = 0.78$; $p = 0.64$]. Changes in the outcome expectancies score were not predicted by AHI [$\beta = -0.004$, $t_{(41)} = -0.8$, $p = 042$] or by BMI [$\beta = 0.002$, $t_{(41)} = 0.1$, $p = 0.91$] [$R^2 = 0.01$; $F_{(1,41)} = 0.31$; $p = 0.72$]. Similarly, no effect was registered relative to the AHI [$\beta = -0.007$, $t_{(41)} = -0.8$, $p = 0.42$] and the BMI [$\beta = -0.07$, $t_{(41)} = -1.91$, $p = 0.06$] [$R^2 = 0.11$; $F_{(1,41)} = 2.59$; $p = 0.08$] when we focused on the treatment self-efficacy score. These results suggested that the level of obesity as well as the level of OSA syndrome severity did not explain the changes registered in the SEMSA scores after the rehabilitation treatment.

Secondary Outcomes

Mean, SD, and range registered at T0 and T1 for all the assessed factors (except for the Flanker's test) are reported in **Table 2**.

After the four-week program, participants reported a significantly lower BMI in comparison with the baseline. They also reported an overall increase in the psychological wellbeing, as shown by the results relative to the PGWBI scores. Considering the subjective sleeping quality, participants reported a significantly reduced level of daily sleepiness, measured through the Epworth Sleepiness Scale (Johns, 1991), as well as they reported a significantly higher level of alertness throughout the day (Stanford Sleepiness Scale, Hoddes, 1972) and a higher level of sleep quality (Pittsburgh Sleep Quality Index, Buysse et al., 2005). Finally, in all indexes measured through the polysomnography, we registered a significant improvement.

We used the Flanker's test to verify the changes in attentional abilities in our sample. When we considered the reaction time, we observed the significant main effect of *Condition* [$F_{(3,126)} = 259.132$; $p < 0.001$; partial eta-squared $p = 0.86$]; according to the *post hoc* estimated marginal means comparisons Bonferroni-corrected, the presence of the incongruent or congruent flanker affected the detection velocity in comparison with the conditions in which the flanker was not shown or it was neutral; all the comparisons were significant [$p < 0.001$], except between the congruent and the incongruent conditions [$p = 0.35$] (**Figure 2A**). Crucially, we observed the significant main effect of *Time* [$F_{(1,42)} = 19.07$; $p < 0.001$; partial eta-squared $p = 0.31$], in which participants showed significant lower reaction time in T1 ($M = 496$; SD = 71) in comparison with T0 ($M = 514$; SD = 73). Finally, the interaction *Condition* × *Time* was not significant $F_{(3,126)} = 2.21$; $p = 0.09$; partial eta-squared $p < 0.001$] (**Figure 2B**). When we considered the level of accuracy, we observed the significant main effect of *Condition* [$F_{(3,126)} = 15.34$; $p < 0.001$; partial eta-squared $p = 0.26$]; according to the *post hoc* estimated marginal means comparisons Bonferroni-corrected, the presence of an incongruent or congruent flanker affected the level of accuracy in comparison with the conditions in which the flanker was not shown or it was neutral; all the comparisons were significant ($p < 0.001$), except between the congruent and the incongruent conditions ($p = 1$) and the neutral and no flanker conditions ($p = 1$) (**Figure 2C**). No significant main effect of *Time* [$F_{(1,42)} = 3.34$; $p = 0.07$; partial eta-squared $p = 0.07$] emerged, where the level of accuracy observed at T1 ($M = 92.99$; SD = 7.48) and T0 ($M = 90.77$; SD = 8.21) overlapped. Finally, the interaction *Condition* × *Time* was not significant [$F_{(3,126)} = 1.38$; $p = 0.25$; partial eta-squared $p = 0.03$] (**Figure 2D**). This pattern of results suggested that the performance of our participants was in agreement with the Flanker's effect, mirroring the results reported by Scarpina et al. (2021). Crucially, after the rehabilitation, participants were faster in detecting the visual targets, suggesting an improvement of their attentional abilities. No significant change emerged in the level of accuracy; however, it should be considered that the percentage of accuracy was very high, suggesting a ceiling effect in our data.

The Role of Temperament

As shown in **Table 3**, our participants showed significantly higher scores in the novelty seeking and persistent temperamental traits, when compared with the normative data, with no other significant difference. The *T*-score of each participant at the four temperamental traits is shown in **Figure 3**.

We observed the following scores relative to the three character dimensions as follows: self-directedness ($M = 82.92$, SD = 49.12, and range = 25–176); cooperativeness ($M = 93.25$,

TABLE 2 | Mean, SD, and minimum (min) and maximum (max) for the secondary outcomes measured in this study at T0 (i.e., before the treatment) and T1 (i.e., after the four-week rehabilitation program).

	T0	T1	Statistical results
Body mass index	M = 46.69 SD = 7.08 min-max = 33.35–69.18	M = 44.59 SD = 6.65 min-max = 31.34–65.66	t(44) = 10.84; **p = 0.003**; d' = 0.3
Psychological well-being: Psychological General Well Being Index			
Anxiety (range score 0–25)	M = 16.11 SD = 4.66 min-max = 5–24	M = 20.93 SD = 3.76 min-max = 8–25	W(45) = 960.5; **p < 0.001**; d' = 1.13
Depression (range score 0–15)	M = 11.86 SD = 2.65 min-max = 2–15	M = 13.64 SD = 1.69 min-max = 8–15	W(45) = 587; **p < 0.001**; d' = 0.8
Positive well-being (range score 0–20)	M = 10.24 SD = 4.33 min-max = 3–19	M = 14.62 SD = 3.73 min-max = 6–20	W(45) = 952; **p < 0.001**; d' = 1.84
Self-control (range score 0–15)	M = 10.66 SD = 5.99 min-max = 3–15	M = 12.95 SD = 2.44 min-max = 6–15	W(45) = 622.5; ***p* < 0.001**; d' = 0.5
General healthy (range score 0–15)	M = 8.11 SD = 3.07 min-max = 3–13	M = 10.66 SD = 2.73 min-max = 5–15	W(45) = 669; **p < 0.001**; d' = 0.87
Vitality (range score 0–20)	M = 9.62 SD = 4.8 min-max = 1–20	M = 15.13 SD = 4.15 min-max = 0–20	W(45) = 869; **p < 0.001**; d' = 1.22
Total score (range score 0–110)	M = 66.62 SD = 19.03 min-max = 28–105	M = 87.95 SD = 15.14 min-max = 53–110	W(45) = 1024; **p < 0.001**; d' = 1.22
Sleep—quantitative measurement: polysomnography			
Number of apnea/hypopnea events per hour of sleep (Apnea/Hypopnea Index—AHI)	M = 59.84 SD = 34.91 min-max = 11–150.5	M = 2.85 SD = 2.88 min-max= 0.1–15.4	t(38) = 10.53; **p < 0.001;** d' = 2.3
Number of hypopnea events per hour of sleep (Hypopnea Index—HI)	M = 44.74 SD = 35.65 min-max = 0.8–127.8	M = 2.53 SD = 2.66 min-max = 0.1–14	t(38) = 7.73 **p < 0.001;** d' = 1.67
Number of apnea events per hour of sleep (Apnea Index—AI)	M = 29.43 SD = 20.78 min-max = 0.4–87.8	M = 0.35 SD = 0.62 min-max = 0–2.5	t(38) = 8.62; **p < 0.001;** d' = 1.97
Number of blood oxygen desaturation events per hour of sleep	M = 54.48 SD = 30.79 min-max = 10.9–136.5	M = 2.27 SD = 2.25 min-max = 0-9.4	t(38) = 10.64; **p = 0.019;** d' = 2.39
Time with SaO_2 < 90% (% of total sleep time)	M = 65.81 SD = 81.15 min-max = 3.5–100	M = 8.87 SD = 21.62 min-max = 0–100	t(38) = 4.03; **p < 0.001;** d' = 0.95
Average minimum SaO_2 during desaturations (%)	M = 82.42 SD = 4.82 min-max = 69 −89	M = 88.27 SD = 14.45 min-max = 0–95	t(38) = 2.45; **p < 0.001;** d' = 0.54
Minimum oxygen saturation (%)	M = 65.82 SD = 10.28 min-max = 49–87.4	M = 86.8 SD = 3.56 min-max = 80–95	t(38) = 13.58; **p < 0.001;** d' = 2.27
Average sleeping time in hour	M = 7.26 SD = 0.74 min-max = 4–8	M = 6.24 SD = 0.74 min-max = 5.1–8.1	t(38) = 6.87; **p < 0.001;** d' = 1.37
Sleep—subjective evaluation			
Stanford sleepiness scale (range score 0–7)	M = 2.84 SD = 1.06 min-max = 1.11–5.33	M = 1.96 SD = 0.63 min-max = 1.05–3.94	W(45) = 82; **p < 0.001;** d' = 1
Pittsburgh sleep quality index (range score 0–21)	M = 7 SD = 3.14 min-max = 1–13	M = 4.97 SD = 2.61 min-max = 1–13	W(45) = 165; **p < 0.001;** d' = 0.7
Epworth sleepiness scale (range score 0–24)	M = 8.82 SD = 5.27 min-max = 0–22	M = 3.73 SD = 3.5 min-max = 0–12	W(45) = 24; **p < 0.001;** d' = 1.13

We reported statistical results, and the significant difference between T0 and T1 scores is given in bold.

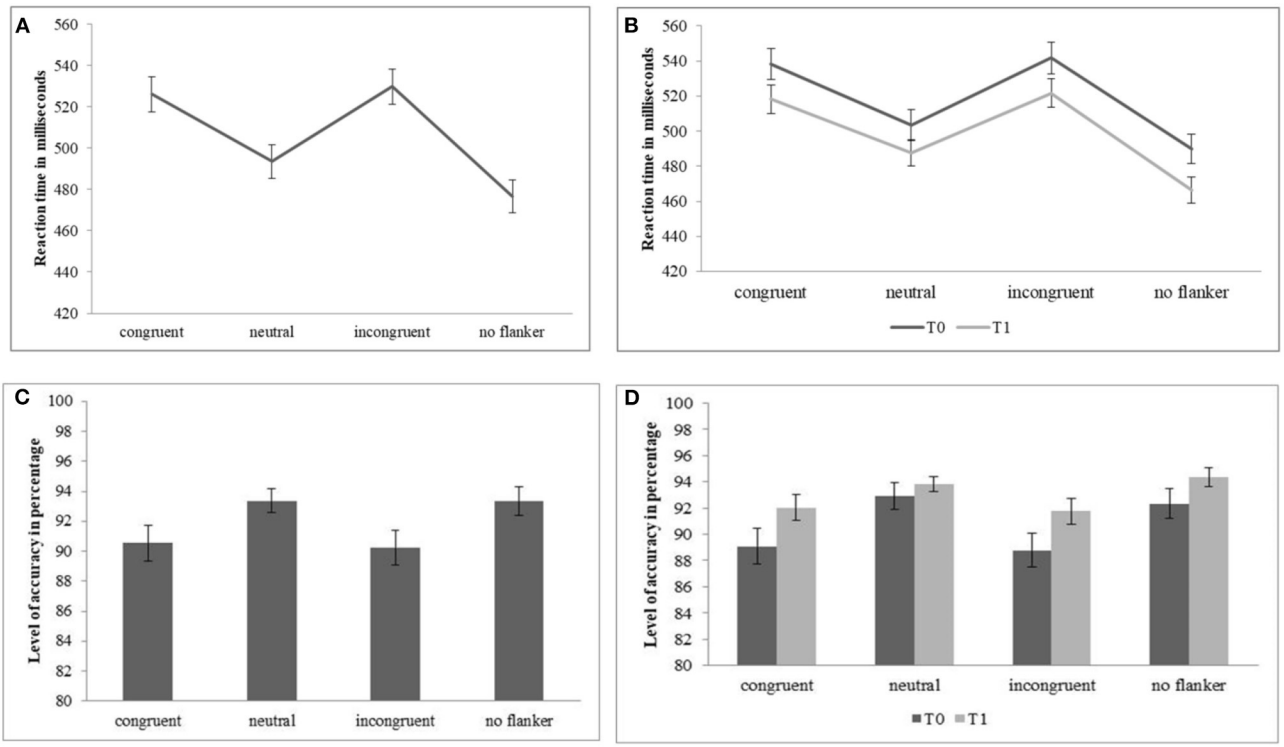

FIGURE 2 | Mean and SD (vertical lines) relative to the reaction time in milliseconds and the level of accuracy in percentage registered at the Flanker's test. Specifically, in panels **(A,C)**, the data in relation to the four experimental conditions are shown; in panels **(B,D)**, the data in relation to the four experimental conditions split for the two measurements (T0 vs. T1) are shown.

TABLE 3 | Mean, SD, and minimum (min) and maximum (max) for each scale of the Temperament and Character Inventory-Revised by Martinotti et al. (2008).

	M	SD	min-max	Normative data		Statistical comparison
				M	SD	
Novelty seeking (range score 0–175)	102.31	12.09	78–126	98.5	12.9	$t_{(50)} = 2.04$ **$p = 0.04$** d'= 0.3
Harm avoidance (range score 0–165)	93.75	16.06	68–125	96.4	14.4	$t_{(48)} = 1.08$ $p = 0.28$; d' = 0.17;
Reward dependence (range score 0–150)	103.53	11.57	75–125	101.4	13	$t_{(50)} = 1.19$ $p = 0.23$; d' = 0.17
Persistence (range score 0–175)	121.93	18.01	90–160	116.3	14.4	$t_{(47)} = 2.05$; **$p = 0.04$;** d' = 0.34;

We reported mean and SD relative to the Italian normative sample (N = 740; Martinotti et al., 2008) as well as the statistical comparison; bold values denote the significant results. For each scale, we reported the range score, according to the seminal article.

SD = 37.46, and range = 36–153); and self-transcendence ($M = 71.27$, SD = 14.38, and range = 39–97).

In **Table 4**, we reported the Spearman's correlation coefficient computed between the *T*-scores relative to the four temperamental traits from the Temperament and Character Inventory and the Δ scores (i.e., the changes between T0 and T1) relative to three components measured through the SEMSA questionnaire.

A significant positive relationship emerged relative to the changes observed in the perceived risk and the persistent temperamental trait, with no other significant results (**Table 4**). According to the linear regression model, the persistent

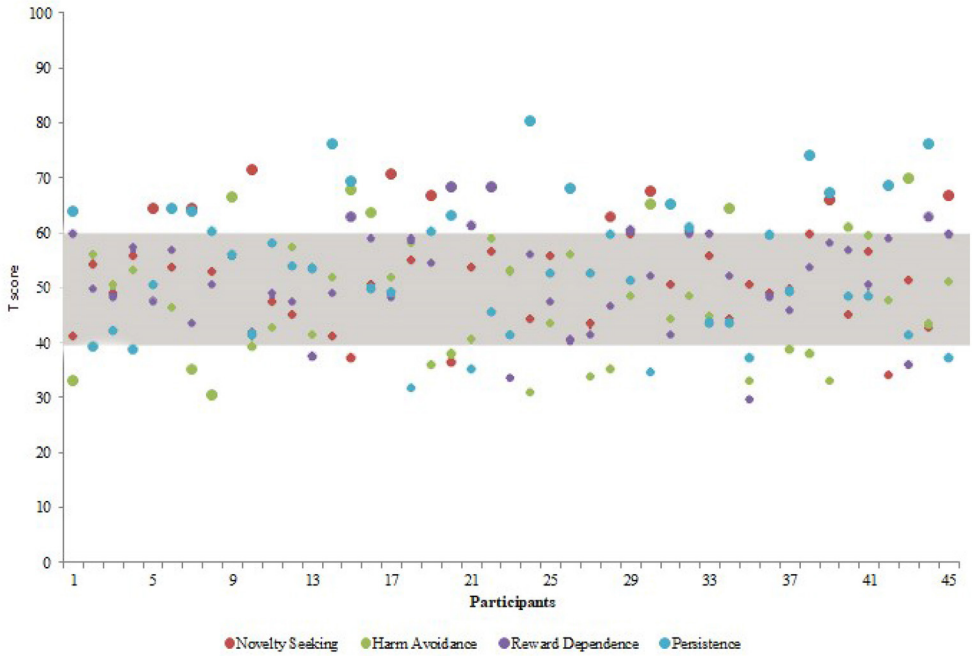

FIGURE 3 | *T*-score (*y*-axis) relative to each temperamental trait (novelty seeking in red, harm avoidance in green, reward dependence in purple, and persistent in green) measured through the Temperament and Character Inventory-Revised for each participants (*x*-axis). The gray area represents the medium range according to Martinotti et al. (2008).

TABLE 4 | Spearman's correlation (ρ score and p value) between the Δ score (i.e., the difference between T1 and T0 scores) relative to the SEMSA questionnaire scores and the *T*-scores for the temperamental traits, measured through the Temperament and Character Inventory-Revised.

	SEMSA questionnaire		
	Perceived risk	**Outcome expectancies**	**Treatment self-Efficacy**
Novelty seeking	$\rho = -0.06$ $p = 0.66$	$\rho = 0.04$ $p = 0.75$	$\rho = 0.05$ $p = 0.74$
Harm avoidance	$\rho = -0.11$ $p = 0.45$	$\rho = 0.04$ $p = 0.77$	$\rho = 0.12$ $p = 0.42$
Reward dependence	$\rho = 0.11$ $p = 0.94$	$\rho = 0.16$ $p = 0.28$	$\rho = 0.14$ $p = 0.35$
Persistent	**$\rho = 0.29$** **$p = 0.050$**	$\rho = -0.01$ $p = 0.94$	$\rho = -0.29$ $p = 0.055$

N = 45.
Bold values denote the significant results.

temperamental trait significantly predicted the changes in the perceived risk score [$\beta = 0.03$, $t_{(44)} = 2.02$, $p = 0.05$; VIF = 1] [$R^2 = 0.29$; $F_{(1, 43)} = 4.09$; $p = 0.05$].

DISCUSSION

In this study, we aimed to verify the changes in the cognitive components of risk perception, outcome expectancy, and self-efficacy relative to CPAP therapy (SEMSA, Weaver et al., 2003) after a multidisciplinary residential four-week rehabilitation program, in individuals affected by OSA syndrome. After our intervention, individuals reported significantly higher perceived expectations about the positive outcome of CPAP therapy on quality of life. However, no change was observed in the other two components measured by the questionnaire, that is, the level of perceived vulnerability of patients to health risks (i.e., risk perception) and the perceived level of self-efficacy. These results were not explained by the level of obesity as well as the level of OSA syndrome severity during admission to the rehabilitation treatment. Thus, after the rehabilitation treatment, our participants were more prone to consider the effect of CPAP therapy on health outcome, meaning how much they expected that the CPAP therapy potentially decreased the health risks and increased their quality of life (i.e., outcome expectancies) (Weaver et al., 2003). This result was strictly related to the aim of our rehabilitation treatment, which was to provide participants with detailed information about CPAP therapy. For its nature, this intervention could be defined as informative and educational. However, because of this peculiar characteristic, it might not be entirely efficient in changing the level of self-efficacy after four weeks in which individuals were involved in a residential program. In fact, the most powerful source of self-efficacy information is the personal experience of individuals (Bandura, 1997). In this clinical context, Weaver et al. (2003) defined self-efficacy as the perception that the individual has about the wherewithal to use the ventilator effectively under a wide range of daily life circumstances. However, during our rehabilitation, participants were highly supported by clinicians,

perhaps with an effect on the perception of self-experience of being actively and independently involved in the use of CPAP. We also observed no changes in the risk perception, meaning how much our participants perceived themselves as vulnerable to health risks and how much they were aware of the negative outcome associated with untreated OSA syndrome (Weaver et al., 2003). This result was surprising since individual and in-group activities proposed in our rehabilitation program were designed to decrease health-risk behaviors, such as eating habits and physical activities. This represents a very crucial point; in fact, if participants do not perceive the role of some negative behaviors in enhancing the OSA syndrome, they would not avoid them. Once again, the fact of being in a residential program, in which all participants were involved in activities chosen by the multidisciplinary team, might play a considerable role in the perception of the effect of activities on the health outcomes.

Interestingly, after our rehabilitation intervention, the level of adherence to CPAP was very high in our group, and the changes were observed in all the rehabilitation outcomes. According to the polysomnographic indexes, the objective sleep quality increased after the treatment; also, the sleep quality was subjectively perceived as higher (i.e., Pittsburgh Sleep Quality Index) (Buysse et al., 2005 Italian version: Curcio et al., 2013); our participants reported reduced sleepiness (i.e., Epworth Sleepiness Scale) (Johns, 1991; Vignatelli et al., 2003) and conversely, higher levels of alertness (i.e., Stanford Sleepiness Scale) (Hoddes, 1972) throughout the day. These results were in agreement with the decreased reaction time observed in the Flanker's test from the PEBL—Psychological Test Battery (Mueller and Piper, 2014; Scarpina et al., 2020) after the rehabilitation, and our participants were faster in recognizing the visual stimuli, suggesting an amelioration of their attentional abilities. Overall, participants described a better global quality of life (i.e., PGWBI, Dupuy, 1984). Thus, overall, our rehabilitation approach showed the potential to change several health components in our participants. Nevertheless, it seemed to be the only partially efficient in changing the cognitions of participants. Weaver (2019) recently underlined the importance to adopt behavioral interventions (i.e., cognitive behavioral therapy and motivational enhancement therapy), in addition to education, improving the adherence and the self-efficacy of patients, as reported in some previous studies (Aloia et al., 2001, 2013; Richards et al., 2007; Stepnowsky et al., 2007; Weaver and Grunstein, 2008; Shannon et al., 2017). Moreover, considering the role played by vicarious experience or modeling in shaping self-efficacy (Bandura, 1997), group activities in which information can be obtained through the performance and experience of others might be adopted. Moreover, in assigning participants to the groups, the clinicians could not strictly take into account the level of obesity and OSA disease severity, since in our sample, both components did not play a significant role in changes registered after the treatment.

In this study, we also verified the role of the temperamental traits (Cloninger et al., 1993, 1994; Cloninger, 1999) on the cognitive components measured through the SEMSA questionnaire (Weaver et al., 2003). To the best of our knowledge, no previous study investigated this relationship in the case of short-term outcomes registered after rehabilitation programs. Those individuals with a higher persistent temperamental trait reported a significant improvement in perceived risks, although the other temperamental traits were not implicated in the changes of individuals. According to Cloninger et al. (2012), individuals with a higher expression of the persistent temperamental trait can be described as determined and ambitious; moreover, they tend to persevere in their behaviors despite fatigue or frustration, even though in the absence of an immediate reward. In the clinical setting, those individuals who are highly persistent seem to be more prone to pro-health activities. In addition, a high level of persistence plays a protective effect on emotional functioning, reducing negative emotions and increasing positive ones (Cloninger et al., 2012). In this study, we observed that those individuals with a persistent temperamental trait were more prone to link their commitment to CPAP therapy to health-positive outcomes, even though the difficulties they might experience in the adaptation process. However, solely changes in risk perception, but not in the other cognitive components of outcome expectancies and the treatment self-efficacy, were related to the persistent temperamental trait in this study. It might be hypothesized that the role of temperament was not entirely crucial in shaping outcome expectancies because of the informative and educational nature of the proposed intervention. Instead, the absence of any effect of temperament on the third component, namely self-efficacy, measured through the SEMSA questionnaire seems to be more surprising. In fact, there is a tight relationship between self-efficacy and personality (Bandura, 1997), and it was also confirmed in the case of OSA syndrome and adherence to CPAP therapy in the long term (Maschauer et al., 2017). However, according to our results, the temperamental traits might not play a significant prominent role in self-efficacy when they are measured as a short-term outcome, as in our study. Future longitudinal studies should clarify this point. From a clinical perspective, our results might justify a multidisciplinary approach that does not take *a-priori* into account the temperamental traits of participants. This might be a piece of very crucial information because profiling the individual temperament through the questionnaires is a time-consuming activity. Such questionnaires, which consist of a very large number of items, might not be completely suitable in the case of individuals affected by OSA syndrome, who generally experience a higher level of mental fatigue, as well as attentional difficulties and a lower level of alertness (Llewellyn et al., 2008; Wilson et al., 2013; Alomri et al., 2021; Legault et al., 2021; Scarpina et al., 2021).

Some final considerations can be done about our study. The first one regards the scores registered at the temperament and Character Inventory-Revised (Martinotti et al., 2008), according to which our participants showed higher expressions of novelty seeking temperamental trait in comparison with the normative data (Martinotti et al., 2008), in agreement with recently published results provided by our group (Scarpina et al., 2021). We also reported that our participants showed higher expressions of the persistent temperamental trait. In this study, we enrolled individuals who participated and completed the residential four-week rehabilitation program. As reported by our group (Scarpina et al., 2021), this choice might be likely to be done by highly persistent individuals. As mentioned in the "Methods" section, a large percentage of our participants was affected by

high-risk obesity, as well as OSA syndrome occurs frequently in obesity (Schwartz et al., 2008). In our residential treatment, participants were supported in increasing the amount of physical activity as well as in increasing their knowledge about good diet habits; in fact, we registered a significant decrease in BMI after the treatment. Weight reduction may be used as a secondary outcome in the treatment of OSA syndrome (Cayanan et al., 2019). Nevertheless, the benefits associated with CPAP therapy are not related to the baseline degree of obesity (Weaver et al., 2007). Previous studies investigating the temperamental traits according to Cloninger et al. (1993, 1994) in individuals affected by OSA syndrome with low-risk obesity reported heterogeneous results. Sforza et al. (2002) observed that individuals with OSA syndrome mostly showed higher expressions of novelty seeking temperamental traits in comparison with healthy individuals. This result was in agreement with the data reported in this study as well as in the study by Scarpina et al. (2021) relative to individuals with OSA syndrome and severe obesity. In contrast, Fìdan et al. (2013) registered no difference in the expression of the four temperamental traits between individuals affected by OSA syndrome and healthy individuals. Thus, we would suggest some cautions in interpreting our results, since the role of obesity and OSA syndrome on subjective psychological functioning is not clear-cut.

We concluded our discussion underlining the major limitation of our study, which was the absence of a control group of participants (i.e., individuals who did not follow the rehabilitation program). We described an observational study with a quasi-experimental pre–post design. However, since this study was done during hospitalization (which guarantees the treatments to every patient), it was not possible to randomize patients to a control group for ethical reasons (Bjarnason-Wehrens et al., 2007; Manzoni et al., 2011).

Understanding the primal beliefs and cognition of individuals about CPAP therapy in the case of OSA syndrome may provide insight into who might be likely to show a higher level of adherence. To summarize our results, the multidisciplinary residential four-week intervention described in this study seemed to positively change the level of risk perceptions, but not the components of perceived risks related to the disease and the self-efficacy about CPAP therapy. Nevertheless, the temperamental traits might play only a marginal role in the global changes reported by our participants after the intervention.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Istituto Auxologico Italiano. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

FS and AM conceived the study. FS supervised the entire study, performed the statistical analyses, and wrote the manuscript. IB and SC performed the data collection. LP, EG, IT, and MC selected the participants and performed the clinical assessment. GC and EM supervised the psychological assessment. PF and AM supervised the clinical assessment. All authors revised the manuscript.

ACKNOWLEDGMENTS

The authors gratefully thanks the corresponding author for having provided the Temperament and Character Inventory-Revised (Martinotti et al., 2008).

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2021.703089/full#supplementary-material

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychology

ORIGINAL RESEARCH
published: 09 September 2021
doi: 10.3389/fpsyg.2021.705112

"Thinking About Thinking" in Insomnia Disorder: The Effect of Cognitive-Behavioral Therapy for Insomnia on Sleep-Related Metacognition

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OPEN ACCESS

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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: 04 May 2021
Accepted: 13 August 2021
Published: 09 September 2021

Citation:
Galbiati A, Sforza M, Scarpellino A, Salibba A, Leitner C, D'Este G, Mombelli S, Ferini-Strambi L and Castronovo V (2021) "Thinking About Thinking" in Insomnia Disorder: The Effect of Cognitive-Behavioral Therapy for Insomnia on Sleep-Related Metacognition. Front. Psychol. 12:705112. doi: 10.3389/fpsyg.2021.705112

Metacognition is defined as the ability to reflect on one's mental state and to govern thoughts and beliefs. Metacognitive dysfunctions are typical of several psychopathologic conditions, and also a feature of insomnia disorder, possibly playing a crucial role in its genesis and maintenance. In the context of insomnia, metacognition describes how individuals react to their own sleep-related thoughts and beliefs, boosting the hyperarousal state experienced by these patients. Up to now, no studies evaluated the effect of cognitive behavioral therapy for insomnia (CBT-I) on metacognitive functioning. Therefore, the aim of our study was to evaluate the effect of CBT-I administered in group format in patients with insomnia disorder. As expected, all patients showed significant improvements in both insomnia and sleep diary parameters after treatment. Furthermore, an improvement was observed also in dysfunctional metacognitive levels, assessed by means of the Metacognitions Questionnaire-Insomnia (MCQ-I). However, 63% of patients still showed a MCQ-I score above the clinical cutoff after treatment. Dividing the sample on the basis of MCQ-I questionnaire scores after CBT-I, we found that patients, who still presented metacognitive impairment, received significant beneficial effects from CBT-I both on insomnia symptoms and on dysfunctional beliefs, but not on dysfunctional metacognitive functioning. These findings suggest that metacognition should be carefully evaluated in insomnia patients and further studies are needed to evaluate long-term implications of this remaining dysfunction.

Keywords: insomnia, cognitive-behavioral therapy for insomnia, metacognition, dysfunctional beliefs, worry

INTRODUCTION

Insomnia disorder is a highly prevalent disorder, as it is the most common sleep disorder encountered in clinical practice and the second most prevalent mental disorder in the European countries (Wittchen et al., 2011; Sateia, 2014). It is characterized by difficulties in initiating and maintaining sleep and early morning awakenings associated with a complaint of sleep

dissatisfaction and important daytime consequences that interfere with working and social functioning (American Psychiatric Association, 2013; Sateia, 2014). Moreover, insomnia represents a risk factor for the development of mental disorders (depression, anxiety, alcohol abuse and psychosis; Hertenstein et al., 2019) as well as medical condition (Vgontzas et al., 2013). Importantly, although naively considered a nighttime disorder, insomnia is now universally deemed a daytime 24-h disorder (Ferini-Strambi et al., 2021). Indeed, one of the most accredited hypothesis for the genesis and the maintenance of the disorder is the hyperarousal model. This model described insomnia patients as characterized by increased neurophysiological and cognitive activities that impede relaxation and physiological drive to sleep resulting in prolonged sleep latencies and increased nocturnal awakenings (Riemann et al., 2010).

In this context, a refinement of different models regarding cognitive activity in insomnia is of utmost importance for developing new etiopathogenetic hypotheses but also for fine tuning therapy. Accordingly, a metacognitive model for insomnia has been proposed (Ong et al., 2012). Metacognition can be defined as a form of awareness or knowledge regarding one's own mental state and cognitive processes, such as the ability of governing or regulating thoughts and beliefs (Flavell, 1976). The striking relevance of metacognitive theory is to shift the focus from thoughts' contents to the processes that govern such cognition, such as repetitiveness and intrusiveness, in order to manage the unhelpful thinking styles. In other words, we could define metacognitive level as a form of "thoughts on thoughts," or beliefs regarding the usefulness of specific cognitive processes (Wells, 2009b). In the field of insomnia, Ong et al. (2012) differentiates between cognitions and metacognitions, defined two specific levels of cognitive arousal. "Primary arousal" refers to cognitive activity and contents directly interfering with sleep. This category comprises thoughts and beliefs affecting sleep or related to daytime consequence of disrupted sleep. "Secondary arousal" concerns how individuals react to sleep-related thoughts and beliefs. This category includes the interpretative value related to cognitive activity, such as emotional response associated with thoughts, the levels of attachment to these and their meaning. This secondary component magnifies the negative emotional evaluation biasing the attentional system of the subject toward sleep-related cognition generated at the former level. As an example, the thought/belief "I need 8 h of sleep to function well the next day" might generate a form of primary arousal interfering with sleep drive when the subject is trying to sleep. In addition, cognitive rumination and worry caused by the attentional bias to this belief amplify negative emotion, boosting secondary arousal, and impeding the automatic regulation of sleep–wake patterns typical of good sleepers (Espie et al., 2006). According to this view, "secondary arousal" represents the core feature for the maintenance of insomnia, impeding subjects to create alternative coping strategies.

Previous research on this topic showed that metacognition represents a core feature of insomnia disorder confirming that dysfunctional metacognitive functioning is strictly associated to poor sleep quality in this disorder when compared to other sleep disorders such as obstructive sleep apnea (Palagini et al., 2014). Specifically, metacognitive sleep-related beliefs are strictly related to stress-related sleep reactivity, i.e., the vulnerability to sleep disturbance when exposed to stress (Palagini et al., 2016a). Remarkably, sleep-related metacognitive processes have stronger effect in modulating hyperarousal in comparison to sleep reactivity (Palagini et al., 2016b). Moreover, although both sleep-related cognitive and metacognitive processes are related to somatic and cognitive pre-sleep arousal, when considering insomnia disorder's duration, the association between metacognitive processes and pre-sleep arousal is more prominent, thus highlighting their role in the chronicization of the disease (Palagini et al., 2017). Interestingly, an interaction between metacognitive beliefs related to sleep difficulties and subjective sleep quality in older subjects has been described (Sella et al., 2019).

Taken together, these findings underscore the crucial role played by metacognition in the genesis and maintenance of insomnia disorder. However, up to now, no studies investigated the effect of cognitive-behavioral therapy for insomnia (CBT-I) on dysfunctional metacognition. Therefore, the aim of our study was to (i) confirm the presence of metacognitive impairment in patients with insomnia compared to healthy subjects and (ii) to evaluate the effect of a group CBT-I in patients with insomnia disorder on sleep-related metacognition. By means of two specific validated scale, Dysfunctional Beliefs and Attitudes about Sleep (DBAS; Morin et al., 2007) and Metacognitions Questionnaire – Insomnia (MCQ-I; Waine et al., 2009), we aimed to assess the effect of CBT-I both on -primary (DBAS) and -secondary (MCQ-I) arousal postulated in the metacognitive model of insomnia (Ong et al., 2012). Our hypothesis is that despite a robust effect in ameliorating sleep and sleep-related cognition, CBT-I might have a reduced effect on dysfunctional metacognition due to a lack of a specific treatment component incorporated in CBT-I protocol. CBT-I does not include a protocol aimed to treat metacognitive dysfunction; on the contrary it includes a session of cognitive therapy aimed to challenge and restructure dysfunctional beliefs and cognition regarding sleep. Therefore, treating only sleep-related dysfunctional beliefs and not targeting metacognitive functioning might not be sufficient. This could represent a limitation, not directly for therapy outcome, but for the occurrence of relapses in the long term. Indeed, the absence of a specific metacognitive treatment may not limit the effect of CBT-I on patients' sleep, that is strongly ascribable to treatment's behavioral component (Maurer et al., 2020), but may favor the re-emergence of uncontrollable maladaptive strategies (e.g., pre-sleep worry and rumination) thus leading to relapses.

MATERIALS AND METHODS

Participants

Between 2019 and 2020, 27 consecutive insomnia patients (52% females, mean age 46.37 ± 13.67 years, age range 18–71 years, disease duration of 10.04 ± 8.79 years) and 23 healthy controls (63% females, mean age 33.00 ± 13.77 years) were enrolled in

this study. Patients visiting the Sleep Disorders Center of San Raffaele Hospital, Milan, were recruited for the purposes of this study, after a clinical evaluation performed by physician experts in sleep medicine who diagnosed insomnia disorder according to diagnostic criteria of ICSD 3 (Sateia, 2014). Patients taking medications and/or with major psychiatric comorbidities and/or with untreated medical conditions were excluded from the study. Healthy subjects were recruited with the same exclusion criteria and on the basis of an Insomnia Severity Index (ISI) score <10 (Morin et al., 2011). All participants provided written informed consent to the experimental procedure, which was previously approved by the local ethical committee (protocol number of ethics approval: 188/INT/2020).

Procedures

CBT-I consisted of a multicomponent treatment of seven 90-min group sessions (Spielman et al., 1987; Lichstein, 1988; Espie, 1991; Hauri, 1991; Morin, 1993). A licensed psychotherapist certified in sleep medicine conducted group sessions. The sessions were held weekly or biweekly depending on session content. The first and second sessions concerned introduction and education on the principles of regulation of sleep–wake system. In particular, the aim of the first session was to provide a general overview and define treatment goals, based on each patient's insomnia characteristics. The second session consisted of psychoeducation on sleep hygiene with the aim of emphasizing the importance of sleep and developing awareness about the factors that maintain the disorder. In the third session, strategies for reducing cognitive and emotional arousal were provided through deep-breathing relaxation exercise and cognitive strategies to reduce excessive thinking in bed. In the fourth session, stimulus control and sleep restriction techniques were introduced followed by an individual treatment plan that each subject received from the therapist. Session five dealt with how to keep improving sleep efficiency. Session six concerned cognitive restructuring of dysfunctional beliefs about sleep and the last session concerned review and relapse prevention.

All patients completed a comprehensive questionnaires battery before and after CBT-I aimed to evaluate insomnia severity, chronotype, daytime sleepiness, sleep-related metacognitions, sleep-related dysfunctional beliefs, stress, global health, anxiety, and depression symptoms.

- ISI (Bastien, 2001; Morin et al., 2011; Castronovo et al., 2016): ISI is a self-report questionnaire that assesses impact and severity of insomnia. It consists of seven items evaluating: (1) the severity of sleep onset, sleep maintenance and early morning awakenings; (2) satisfaction level with current sleep pattern; (3) interference of sleep difficulties with daytime functioning; (6) noticeability of sleep problems by others; (7) distress caused by the sleep difficulties. Each item is rated on a five-point Likert scale (0–4) with a total score ranging from 0 to 28. Higher scores indicate greater insomnia severity. $\alpha = 0.75$.
- Morningness–Eveningness Questionnaire (MEQ; Horne and Ostberg, 1976; Natale et al., 2006): MEQ is a 19-item self-administered questionnaire which assesses morning- (59–86), intermediate- (42–58) and evening-chronotype (16–41) subjects. The total score ranges from 16 to 86. $\alpha = 0.68$.
- Epworth Sleepiness Scale (ESS; Johns, 1991; Vignatelli et al., 2003): ESS is a eight-item self-administered questionnaire that evaluates the subject's sleep propensity during everyday life, thus providing an index of daytime sleepiness. The total score ranges from 0 to 24, with higher scores indicating greater levels of daytime sleepiness. $\alpha = 0.88$.
- Metacognitions Questionnaire-Insomnia (MCQ-I; Waine et al., 2009; Sella et al., 2016): MCQ-I is self-report questionnaire that consists of 60 items evaluating metacognitive beliefs about sleep in insomnia patients. Each item is rated on a four-point Likert scale (from 0: "do not agree" to 4: "agree very much"). Waine et al. (2009) reported that a cut-off of 110 correctly differentiated insomnia patients from normal sleepers and the discriminant validity, scale sensitivity and specificity of the questionnaire have been demonstrated. $\alpha = 0.95$.
- Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-16; Coradeschi et al., 2000; Morin et al., 2007): DBAS-16 is a self-report scale which consists of 16 items assessing cognitions about sleep and it is composed of four factors: (1) consequences of insomnia; (2) worry about insomnia; (3) sleep expectations; and (4) beliefs about medication. Each item is rated on a visual analogue scale from 0 (strongly disagree) to 10 (strongly agree). The total score ranges from 0 to 160, with higher scores indicating greater presence of dysfunctional beliefs about sleep. $\alpha = 0.77$.
- Perceived Stress Scale (PSS; Cohen et al., 1983; Cohen, 1988; Mondo et al., 2019): PSS is a 10-item scale which assesses perceived stress during the past month. Each item is rated on a five-point Likert scale form 0 (never) to 4 (very often). The total score ranges from 0 to 40, with higher scores indicating greater perceived stress. $\alpha = 0.83$.
- General Health Questionnaire-12 (GHQ-12; Goldberg and Hillier, 1979; Goldberg, 1988; Giorgi et al., 2014): GHQ-12 is a 12-item self-administered questionnaire for the assessment of mental health and the detection of psychological distress. Each item is scored on a four-point Likert Scale (0–3). The total score ranges from 0 to 36, with higher scores indicating greater psychological distress. $\alpha = 0.85$
- Beck Depression Inventory (BDI-II): BDI-II is a self-administered questionnaire, composed of 21 items on a four-point Likert scale (Beck et al., 1996). This questionnaire is design for diagnosis of depression and to assess depression symptom severity. The scores are divided into two subscales: affective symptoms (eight items) and somatic symptoms (13 items). BDI-II scores range between 0 and 63, with "minimal range" of 0–13, "mild" 14–19, "moderate" 20–28, and "severe" 29–63. $\alpha = 0.89$.
- State–Trait Anxiety Inventory (STAI): STAY provides a measure of trait- and state- anxiety by means of two scales that can be used independently (Spielberger et al., 1970). The scale STAI-Y-1 evaluates how the subject feels "at this moment" while STAI-Y-2 assesses patient's trait. Both scales consist of 20 items with a total score that ranges from 20 to 80. Of note, higher values indicate higher level of anxiety. α = from 0.86 to 0.95.

A sleep diary was compiled by patients from the week before the first CBT-I session and throughout the whole period of the treatment following the guidelines provided by Carney et al. (2012) for the consensus sleep diary (Carney et al., 2012). Sleep parameters extracted from sleep diaries consist of time in bed (TIB), total sleep time (TST), sleep efficiency (SE), sleep latency (SL), number of awakenings (NAWK), wake after sleep onset (WASO).

Data Analyses

Statistical analyses were performed using SPSS 13.0 and JASP version 0.14.1. Since our data did not meet the assumption for parametric tests, in particular the assumption of normally distributed data, and due to small sample size, we used non-parametric tests. Mann–Whitney U test were employed to evaluate differences between insomnia patients and healthy controls for all the questionnaires evaluating insomnia severity, chronotype, daytime sleepiness, sleep-related metacognitions, sleep-related dysfunctional beliefs, stress, global health, anxiety and depression symptoms. Due to the difference in age between patients and controls, this variable was used as covariate for all the comparisons in a rank analysis of covariance (Quade, 1967). To test differences before and after treatment, we used Wilcoxon signed-rank test with questionnaires assessing insomnia severity, sleep-related cognition and metacognitions, and sleep diaries indices as dependent variables. We also divided patients with insomnia into two groups based on their MCQ-I scores after treatment in order to identify those patients who still presented sleep-related metacognitive impairment (high MCQ-I = MCQ-I total score >110) and those without sleep-related metacognitive impairment (low MCQ-I = MCQ-I total score ≤110) after CBT-I, and to test possible differences between these two groups. Moreover, we extracted DBAS and MCQ-I delta scores (difference between pre- and post-treatment scores) to further investigate the effects of CBT-I on sleep-related cognition and metacognition in patients with high and low MCQ-I after treatment. Correlations between variables were assessed by means of Spearman's correlation coefficient. Chi-Square Test was used to assess gender and chronotype differences between patients with insomnia and controls. Significance levels were set at $p < 0.05$.

RESULTS

Healthy Controls vs. Insomnia Patients

Comparisons between insomnia patients and healthy controls for demographic and clinical data are reported in **Table 1**.

A significant positive correlation was found between MCQ-I and ISI (spearman's rho = 0.577, $p < 0.001$; **Figure 1A**), and between DBAS and ISI (spearman's rho = 0.717, $p < 0.001$) scores in the whole sample (**Figure 1B**).

Effect of CBT-I on Insomnia Symptoms, Sleep Diaries, and Clinical Indices

The effects of CBT-I on insomnia symptoms, sleep diaries and clinical indices are reported in **Tables 2** and **3**. As expected, we observed a significant improvement of insomnia severity both on ISI score and sleep diaries.

Effect of CBT-I on Metacognition

Significant correlation was found between MCQI total score and DBAS subscale "worry/helplessness about sleep" (spearman's rho = 0.625, $p < 0.001$; **Figure 2**). No correlation between MCQI total score and DBAS total score was observed.

In spite of a significant effect of CBT-I in reducing both DBAS ($DBAS_{before\ CBT\text{-}I} = 91.73 \pm 17.21$ vs. $DBAS_{after\ CBT\text{-}I} = 52.09 \pm 22.64$; Sig = $p < 0.001$) and MCQI ($MCQ\text{-}I_{before\ CBT\text{-}I} = 138.11 \pm 26.23$ vs. $MCQ\text{-}I_{after\ CBT\text{-}I} = 123.70 \pm 28.62$; Sig = $p < 0.05$) total scores, 29.6% of patients maintained equal or worse MCQ-I score after treatment in comparison to baseline. Moreover, 63% of patients (17 out of 27) showed MCQ-I scores above the cutoff following CBT-I intervention.

Sub-dividing the insomnia sample in patients who still presented significant levels of metacognitive deficits after CBT-I and who did not, and evaluating delta score (difference between pre- and post-treatment scores) of DBAS and MCQI, we found a significant difference in MCQ-I delta scores. In other words, patients with severe metacognitive impairment at end of the treatment did not receive a beneficial effect of CBT-I on this dimension (**Figure 3B**; high MCQ-I). On the contrary, DBAS showed important and significant reduction in both groups (**Figure 3A**).

Interestingly, although patients who still presented metacognitive impairment received significant beneficial effects

TABLE 1 | Comparison (Mann–Whitney U test or Chi Square test for gender and chronotype) between healthy control and insomnia patients in scores' questionnaire.

Baseline indices (mean ± SD)	Healty controls	Insomnia patients	*Z* or χ^2	Sig.
Gender	*F* = 63% M = 37%	*F* = 51.9% M = 48.1%	0.68*	0.409
Age	33.00 ± 13.77	46.37 ± 13.67	−2.89	<0.001
ESS	6.44 ± 3.23	4.41 ± 3.17	−1.54	0.119
ISI	4.59 ± 2.86	14.67 ± 4.67	−5.88	<0.001
DBAS	51.52 ± 21.07	91.41 ± 17.25	−5.56	<0.001
Circadian typology (MEQ)	Morning-type: 3.7% Intermediate-type: 74.1% Evening-type: 22.2%	Morning-type: 14.8% Intermediate-type: 66.7% Evening-type: 18.5%	1.99*	0.368
BDI-I	8.37 ± 7.22	11.04 ± 5.20	−2.32	<0.05
PSS	17.19 ± 5.23	18.00 ± 4.72	−0.77	0.231
STAI Y-1	42.48 ± 8.28	43.48 ± 10.52	−0.29	0.605
STAI Y-2	42.37 ± 7.61	44.19 ± 8.59	−0.77	0.130
MCQ-I	105.63 ± 20.52	138.11 ± 26.23	−4.35	<0.001
GHQ	15.93 ± 3.06	17.22 ± 4.63	−0.93	0.171

SD, standard deviation; ESS, Epworth sleepiness scale; ISI, insomnia severity index; DBAS (16 item), dysfunctional beliefs and attitudes about sleep; MEQ-SA, morningness-eveningness questionnaire self-assessment; BDI-I, beck's depression inventory for insomnia; PSS, perceived stress scale; STAI (Form Y-1 and Y-2), state–trait anxiety inventory; MCQ-I, metacognition insomnia questionnaire; and GHQ, general health questionnaire. *χ^2.

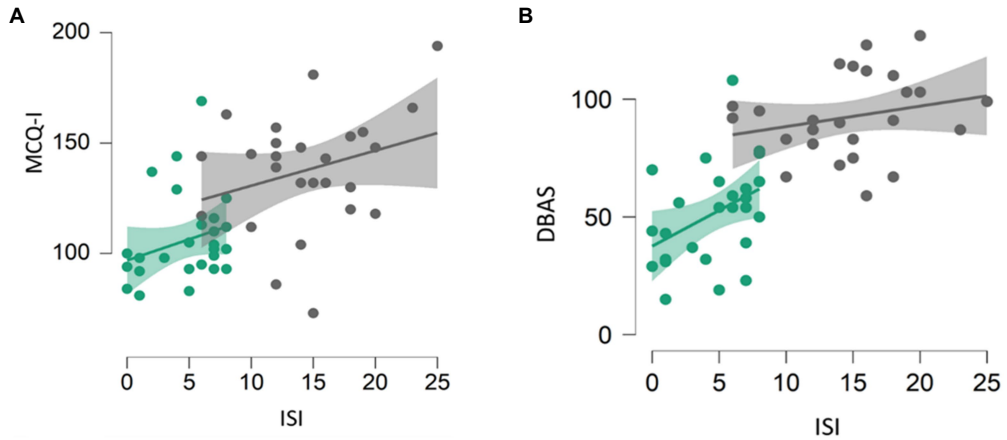

FIGURE 1 | Correlation between MCQ-I and insomnia severity **(A)** and DBAS and insomnia severity **(B)**. Healthy subjects are represented by green dots, patients by black dots. DBAS (16 item), dysfunctional beliefs and attitudes about sleep; MCQ-I, metacognition insomnia questionnaire; and ISI, insomnia severity index.

TABLE 2 | Comparison (Wilcoxon signed rank test) between pre- and post-treatment questionnaire's scores.

Questionnaire (mean ± SD)	Pre-treatment	Post-treatment	*Z*	Sig.
ESS	4.41 ± 3.17	4.74 ± 3	−0.50	NS
ISI	14.67 ± 4.67	7.48 ± 4.29	−4.32	<0.001
DBAS	92.41 ± 17.25	50.15 ± 24.35	−4.36	<0.001
BDI	11.04 ± 5.20	3.33 ± 3.32	−4.37	<0.001
PSS	18 ± 4.72	12.19 ± 4.68	−3.98	<0.001
STAY-1	43.48 ± 10.52	35.26 ± 12.24	−2.99	0.003
STAY-2	44.19 ± 8.59	34.82 ± 9.07	−4.29	<0.001
MCQ-I	138.11 ± 26.23	123.70 ± 28.62	−2.65	0.008
GHQ	17.22 ± 4.63	9.07 ± 5.58	−4.08	<0.001

ESS, Epworth sleepiness scale; ISI, insomnia severity index; DBAS (16 item), dysfunctional beliefs and attitudes about sleep; MEQ-SA, morningness-eveningness questionnaire self-assessment; BDI-I, beck's depression inventory for insomnia; PSS, perceived stress scale; STAI (Form Y-1 and Y-2), state– trait anxiety inventory; MCQ-I, metacognition insomnia questionnaire; and GHQ, general health questionnaire.

TABLE 3 | Comparison (Wilcoxon signed rank test) between pre- and post-treatment sleep diaries' data.

Sleep diaries data (mean ± SD)	Pre-treatment	Post-treatment	*Z*	Sig.
SL (min)	35.39 ± 36.94	16.76 ± 12.24	−3.48	<0.001
N awk	1.85 ± 1.31	1.09 ± 1.18	−3.62	<0.001
WASO (min)	34.21 ± 33.77	20.07 ± 24.67	−2.40	0.011
TIB (min)	481.96 ± 33.25	429.73 ± 50.72	−4.19	<0.001
TIB (h)	8.03 ± 0.55	7.16 ± 0.85	−4.19	<0.001
TST (min)	368.42 ± 77.94	382.55 ± 56.82	−1.21	N.S.
TST (h)	6.14 ± 1.3	6.38 ± 0.95	−1.23	N.S.
SE (%)	76.44 ± 14.61	88.88 ± 7.27	−3.79	<0.001

SL, sleep Latency; N awk, number of awakenings; WASO, wake after sleep onset; TIB, time in bed; TST, total sleep time; SE, sleep efficiency; and N.S., not significant.

of CBT-I on both insomnia symptoms and dysfunctional beliefs, they did not improve their MCQ-I after treatment in comparison to baseline ($p > 0.05$; **Figure 4**).

DISCUSSION

The aim of this study was to confirm the presence of impairment in sleep-related metacognition and to evaluate the effect of CBT-I on metacognitive functioning in patients with insomnia disorder. As expected, we confirmed the presence of dysfunctional metacognition in patients with insomnia in comparison to healthy controls. Regarding CBT-I, we found that metacognitive dysfunctions received beneficial effect from the treatment as measured by MCQ-I. These improvements were associated with a significant reduction in insomnia symptoms quantified both by sleep diaries' variables and by ISI scores. However, results concerning metacognition were not homogeneous. Indeed, we found a significant percentage of patients (63%) who did not present MCQ-I scores below the cut-off after CBT-I,

in spite of a significant amelioration of insomnia symptoms. In other words, it seems that for some patients CBT-I is not sufficient for treating their maladaptive metacognitive functioning, even if the treatment is successful, as underlined by ISI scores (**Figure 4**). Importantly, CBT-I is strongly effective in reducing dysfunctional beliefs and thoughts regarding sleep, as measured by DBAS, also in patients who still presented significant levels of impaired metacognition (**Figure 3**).

Metacognition is the ability to reflect on one's own mental states and cognitive processes, allowing subjects to regulate mental state, beliefs and processes (Flavell, 1976). A crucial aspect of metacognition in cognitive psychotherapy is to shift the focus from thought contents to cognitive processes (e.g., repetiveness and incontrollability). In the context of insomnia, a metacognitive model has been proposed by Ong et al. (2012). According to this model, the authors conceptualized two different levels of cognitive arousal that reflect a distinction between cognition and metacognition. "Primary arousal" refers to cognitive contents and beliefs regarding sleep that directly interfere with sleep. "Secondary arousal" instead consists of the cognitive process in response to thoughts and cognition, such as worry and rumination focused on beliefs that amplifies primary arousal. The dysfunctional response to cognition, represented for example by rumination and by implicit beliefs regarding its usefulness, clearly interferes with the automatic regulation of sleep throughout the generation and maintenance of hyperarousal. In our study, we considered DBAS scores, a scale developed to evaluate sleep-disruptive cognitions (Morin et al., 2007), as representative of "primary arousal," whereas MCQ-I referred to "secondary arousal." Confirming previous literature (Palagini et al., 2014), we found that patients showed significantly higher levels of MCQ-I and DBAS in comparison to controls. Importantly, these scales had significant strong correlations with insomnia symptoms when considering the whole sample, confirming the impact of these maladaptive cognitive beliefs and processes on the severity of the disorder.

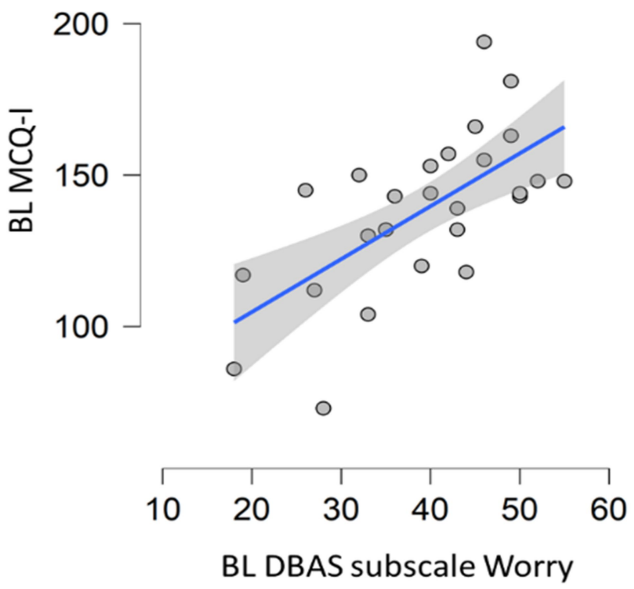

FIGURE 2 | Correlation between baseline metacognition scores and DBAS subscale assessing worrying. DBAS (16 item), dysfunctional beliefs and attitudes about sleep; MCQ-I, metacognition insomnia questionnaire; and BL, baseline.

Interestingly, when considering only the group of insomnia patients, the total scores of these two scales were not correlated. The only significant correlation was found between MCQ-I and DBAS subscale related to worry, confirming the latter as part of metacognitive functioning. Our results concerning CBT-I intervention suggest a dissociation between cognition and metacognition in treatment response. Indeed, despite we found significant global improvement in both DBAS and MCQ-I, more than a half of patients (63%) showed MCQ-I scores above the cut-off after intervention. Specific comparison analyses between patients with and without metacognitive impairment revealed that patients with MCQ-I scores above the cut-off after CBT-I received a significant improvement on insomnia symptoms but not on sleep-related metacognitive dysfunction, in comparison to patients with MCQ-I below the cut-off.

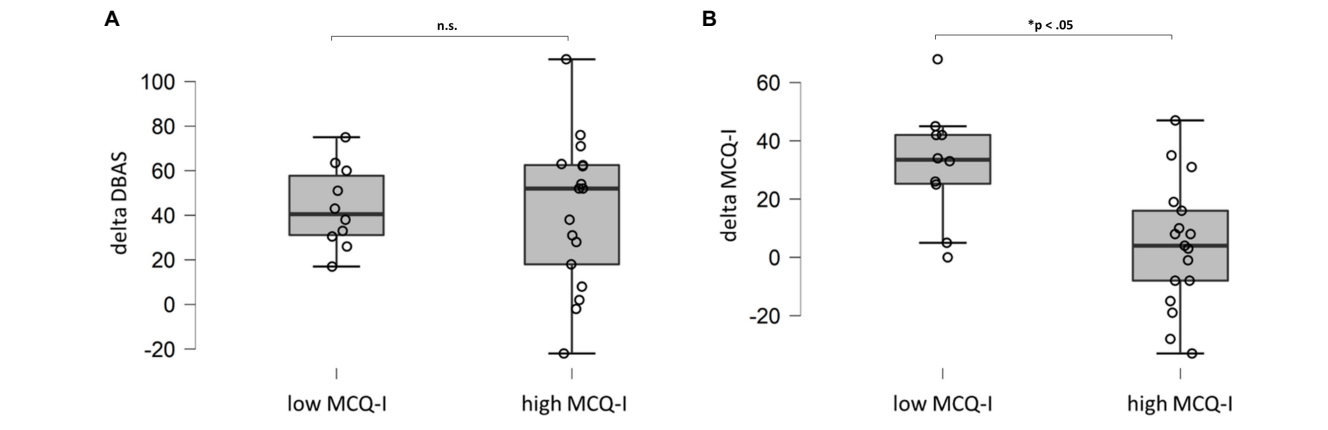

FIGURE 3 | Comparison (Mann–Whitney U test) for DBAS **(A)** and MCQ-I **(B)** delta scores for patients with MCQ-I score above or below the cut-off after treatment. DBAS (16 item), dysfunctional beliefs and attitudes about sleep; MCQ-I, metacognition insomnia questionnaire; and n.s., not significant.

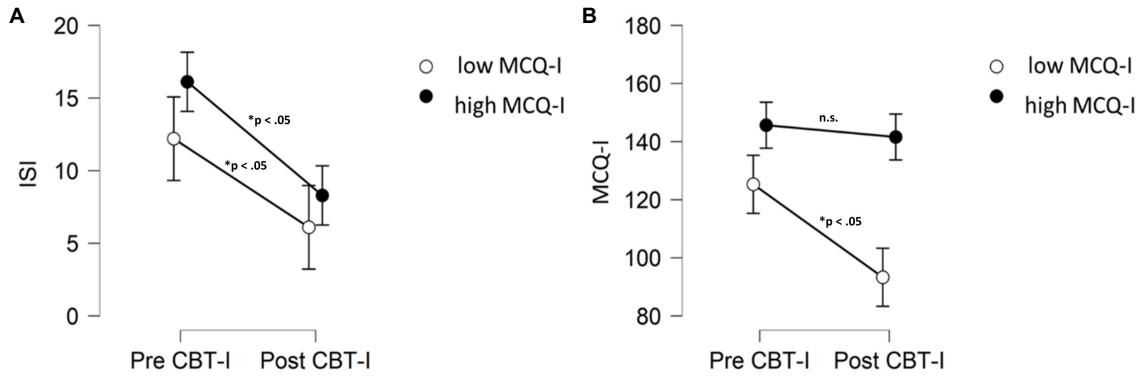

FIGURE 4 | Comparisons (Wilcoxon signed rank test) in ISI **(A)** and MCQ-I **(B)** scores before and after treatment for patients MCQ-I score above or below the cut-off after CBT-I. MCQ-I, metacognition insomnia questionnaire; ISI, insomnia severity index; and n.s., not significant.

Importantly, by further analysing delta DBAS and delta MCQ-I scores (difference between pre- and post-treatment scores), we found that the two groups specifically differ in terms of metacognition in response to treatment. Indeed, delta scores did not differ for DBAS but showed significant difference for MCQ-I (**Figure 3**). This finding might be interpreted on the basis of the specific cognitive intervention embedded in CBT-I package. Indeed, cognitive intervention associated to this therapy is thought to challenge dysfunctional sleep-related beliefs in order to decrease anxiety and arousal caused by these thoughts (Perlis et al., 2005). In other words, CBT-I might act specifically on "primary arousal" but not "secondary arousal," i.e., metacognition. However, we have to consider that also patients with significant metacognitive impairment after treatment (those patients who still present MCQ-I score above the cut-off of 110) showed a significant reduction of insomnia symptoms, hence it seems that this residual "secondary arousal" is not able to hinder the effect of CBT-I. One possible explanation in discussing this result, is that the behavioural core component of the intervention, such as sleep restriction, considered one of the most active element of CBT-I (Miller et al., 2014), might drive this improvement. Accordingly, a recent randomized controlled trial underlined the centrality of sleep restriction in improving insomnia symptoms throughout sleep consolidation (Maurer et al., 2020). Nevertheless, the presence of patients who still presented dysfunctional metacognition after treatment should be carefully considered. Indeed, this might result crucial to identify those patients at risk for relapses in the long term, thus providing fundamental prognostic information for clinicians. The presence of metacognitive dysfunction in insomnia patients after CBT-I may favor the re-emergence of uncontrollable maladaptive strategies, such as worry and rumination, thus leading to relapses. If this holds true, adding a specific component, addressing dysfunctional metacognition, might prevent relapses in those patients (Hjemdal et al., 2019).

Several works indicate that dysfunctional metacognitive functioning and related coping strategies are typical features of insomnia disorder. Patients with insomnia frequently employ thought control strategies, such as reappraisal, worry and thought suppression, at bedtime (Harvey, 2001; Ellis and Cropley, 2002). Furthermore, they also have more positive beliefs about worry. For example statements like "I will lose out in life if I do not use the time before falling asleep to think through things," "Helps me get things sorted out in my mind," "I need to use the time in bed before sleeping to think in order to remain organised," or "Helps me solve problems," regarding pre-sleep worry are more frequently endorsed by patients with insomnia in comparison to good sleepers (Harvey, 2003). These metacognitive beliefs and coping strategies are known to boost further thought intrusions (Wegner, 1994) maintaining sleep disturbances. Several techniques, such as attention training techniques, detached mindfulness and metacognitive-focused Socratic dialogue, are effective and well established in the context of metacognitive therapy (Wells, 2009a). The addition of these interventions in CBT-I protocol should be carefully evaluated in order to target a specific psychopathological functioning that is a hallmark of patients affected insomnia.

When interpreting the findings of our study several limitations should be considered. First, the small sample size and the lack of a control group does not allow us for a robust conclusion and generalization of our results. Secondly, the lack of a follow-up limits the possibility to evaluate the maintenance of improvements in insomnia symptoms and or amelioration of metacognitive functioning in the long term.

In conclusion, our study showed that patients, who still presented metacognitive impairment after treatment, received significant beneficial effects by CBT-I on both insomnia symptoms and dysfunctional beliefs, but not on metacognition, suggesting that this dimension should be carefully evaluated in insomnia patients, since it might have a prognostic valence. Indeed, although high levels of dysfunctional sleep-related metacognition do not seem to hinder the beneficial effect of CBT-I, they might represent a risk factor for relapses in the long term. Future studies should adopt a long term follow-up in order to test this hypothesis. Furthermore, the insertion of specific interventions focused on metacognition, such as attentional training, detached mindfulness as well as metacognitive-focused Socratic dialogue (Wells, 2009b), might be considered.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because the participants did not provide informed consent for sharing data. Requests to access the datasets should be directed to andrea.galbiati.unisr@gmail.com.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by San Raffaele Hospital (Milan, Italy) Ethics Committee. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

AG: study design, management, and manuscript writing and analysis. MS: study design, data collection, and manuscript drafting and analysis. ASc, ASa, CL, GD'E, and SM: study design, data collection, and manuscript drafting. LF-S: study design and management. VC: study design, management, and manuscript drafting. All authors contributed to the article and approved the submitted version.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychology

CASE REPORT
published: 25 October 2021
doi: 10.3389/fpsyg.2021.733911

Case Report: Why Sleep and Dream Related Psychological Treatments, Such as Sleepcoaching (According to Holzinger&Klösch) and CBT-I Should Be Implemented in Treatment Concepts in the Public Health System—Description of the Nightmare Treatment Process in the Context of PTSD

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In this case report, we explain the story of a woman diagnosed with severe PTSD, suffering from recurrent nightmares involving a traumatizing event. She participated in 6 week lucid dreaming training to help her reduce her nightmare frequency. Our descriptions include her dream reports as well as the results of the psychological assessment conducted. In only 6 weeks, she was able to begin to change her dream plots and to improve several of the psychological measures. In this case, we stated that paying more attention to sleep and, especially nightmares, not only in patients with PTSD, should be standard in treatment processes for psychiatric disorders. We, therefore, underpin our case with literature that explains the benefits of treatments, specifically for sleep problems that do not involve medication.

Keywords: nightmares, sleepcoaching, PTSD, lucid dreaming, sleep, dreams, CBT-I, public health

OPEN ACCESS

Edited by:
Christian Franceschini, University of Parma, Italy

Reviewed by:
Axel Steiger, Ludwig Maximilian University of Munich, Germany
Sérgio Arthuro Mota-Rolim, Federal University of Rio Grande do Norte, Brazil

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Specialty section:
This article was submitted to Psychology for Clinical Settings, a section of the journal Frontiers in Psychology

Received: *30 June 2021*
Accepted: *22 September 2021*
Published: *25 October 2021*

Citation:
Holzinger B, Nierwetberg F and Klösch G (2021) Case Report: Why Sleep and Dream Related Psychological Treatments, Such as Sleepcoaching (According to Holzinger&Klösch) and CBT-I Should Be Implemented in Treatment Concepts in the Public Health System—Description of the Nightmare Treatment Process in the Context of PTSD. Front. Psychol. 12:733911. doi: 10.3389/fpsyg.2021.733911

INTRODUCTION

This case study is a part of a sample of "cases" we had the honor to collect in the project "Cognitions in Sleep—Lucid Dreaming as an Intervention for Nightmares in Patients with PTSD," published 2020 in Frontiers of Psychology (Holzinger et al., 2020). In the context of a nightmare treatment evaluation research project in patients with posttraumatic stress disorder (PTSD) in 2009 at the inpatient rehabilitation clinic in Europe (we do not state specific countries in this article to provide additional protection of any identities), we had the opportunity to offer a lucid dreaming (LD) program, which we also call Cognition in Sleep (CIS) to inpatients with PTSD. LD is characterized by a person being aware that he/she is dreaming and by voluntary control over the dream plot (Holzinger, 2008). Lucid dreaming as a treatment for nightmares is part

of our holistic approach called sleepcoaching, which is based on Gestalt Therapy (Holzinger and Klösch, 2013; Holzinger et al., 2019a,b). Sleepcoaching consists of four elements: sleep education and sleep hygiene, cognitive behavioral therapy for insomnia (CBT-I), relaxation techniques, including medical hypnosis, and dream work, including LD techniques. During this program, our focus, of course, was on LD techniques. Nevertheless, it did incorporate aspects of sleep education and sleep hygiene.

In patients with PTSD, addiction problems and multiple comorbidities were treated in a 3 month psychotherapeutic program. Most of the patients were under excessive medication, as the risk of suicide was considered very high. PTSD is a psychiatric disorder emerging after a traumatic event or situation. Those events or situations evoke strong feelings of desperation in the affected person. Typical symptoms of PTSD are recurrent re-experiencing of an event, intruding memories of the event, dreams, nightmares, and a lingering feeling of numbness and emotional stupor. In addition, symptoms similar to depressive ones, like joylessness, reduced activity, and carelessness, may occur. If those feelings remain over a long time, this can also lead to suicidal thoughts (World Health Organization, 2017). The distress of reliving the traumatic events not only by flashbacks in the daytime but also in nightmares during sleep causes a great extent of psychological strain. Those disturbing dreams and nightmares are the core symptom of PTSD and are very common, as the prevalence of nightmares is 60%, which is the highest among mental health disturbances. The prevalence of PTSD is about 8–9% in the general population (Krakow et al., 2002). Nightmares among patients with PTSD tend to occur in two predominant forms:

1. Intrusive replicative nightmares that reenact parts of the trauma and cause difficulties initiating or maintaining sleep.
2. A form of nightmares corresponding to the re-experiencing and hyperarousal symptom cluster defining PTSD.

(Levin and Nielsen, 2007).

Nightmares, in general, are defined as dreams being "extended and extremely dysphoric," and that "usually involves efforts to avoid threats to survival, security, or physical integrity." They usually occur during REM sleep and tend to wake up the dreaming subject, remembering the dream vividly (American Academy of Sleep Medicine, 2014).

The case reported in the following sections displays how dream work, including LD training, was able to promote improvements concerning the nightmare and other symptoms in the reported PTSD case very quickly. Furthermore, it represents severe and multiple traumatizations, which conditioned a long history of PTSD with various sleep problems and other comorbidities in the patient.

CASE REPORT OF A FEMALE PARTICIPANT IN THE ADD-ON LUCID DREAMING TRAINING PROGRAM

The LD program was conducted as an add-on treatment to the regular trauma treatment. The program was offered weekly for 1 h in a group setting for a maximum of eight participants. All patients with PTSD of the rehabilitation center were informed about that service and voluntarily signed up. The ultimate goal of the program was to overcome nightmares by the use of LD techniques (cognition in sleep).

The program offered general information about sleep, sleep hygiene, and also on how to keep a sleep and dream diary, as this was the documentation method to keep track of the dreams of the patients. The core target of the program, to improve nightmare complaints by means of LD, was built on knowledge about dreams, nightmares, and LD and what they might do for us.

From the pool of patients participating in our program, one stuck out. We report the case of a female inpatient at a rehabilitation clinic; she experienced multiple traumas from childhood, for which she received treatment for PTSD. Her process is also described in *Lucid Dreaming: New Perspectives on Consciousness in Sleep* (Hurd and Bulkeley, 2014).

Mrs. L. (the initial of her name is altered) was traumatized multiple times throughout her life. She was sexually abused by her grandfather several times and was raped by a group of teenagers when she was 13 years old. She was unhappily married and divorced after 3 years. Her ex-husband did not accept this step and stalked her with a gun, and, by holding up the gun to her head, forced her to come back to him. During her marriage and, for some time after, she was living in a different country, but after those incidents, she moved back to where she was born. Shortly after moving, she got involved in a severe car accident, from which she had to recover for several months forcing her into sick leave for that time. After recovering, she started to work as a travel agent in a workspace separated by glass walls. Due to the hectic nature of this demanding job, she oversaw that glass wall and injuring herself severely by a craniocerebral trauma.

All those incidents reinforced insomnia symptoms, characterized by problems of falling and maintaining sleep associated with frequent nightmares. The nightmares, which occurred since childhood, were often recurrent, involving her ex-husband stalking and threatening her, occurring several times a week. As a consequence of these nightmares, Mrs. L. developed aversive feelings toward sleep, especially after nightmare episodes.

Mrs. L., as she had experienced several traumatizing situations in her life, developed a quite pronounced PTSD, which had been treated with psychopharmaceuticals (mornings: Duloxetine, 60 mg, evenings: Trazodone, 15 mg; Quetiapine, 25 mg). Additionally, as she was an inpatient at a rehabilitation clinic, she received the standard psychotherapeutic treatment for PTSD and traumatization in this clinic, which is single and group psychotherapy. She did not receive treatments targeting her sleep problems, except the medication listed.

Before entering the LD program, Mrs. L. had undergone excessive psychometric testing. The results of the *Symptom Checklist-90-R* (*SCL-90-R*: Derogatis, 1977) suggested that Mrs. L. had severe somatic complaints, high scores in anxiety, phobic fear, obsessive-compulsive disorder, and depression. The *Self-rating Anxiety Scale* (*SAS*: Zung, 1971) was conducted and confirmed an anxiety disorder; the Impact of Event Scale-assessed PTSD and the *Self-rating Depression Scale* (*SDS*: Zung, 1965) confirmed high scores in depression. In addition, sleep disorders

were also evaluated. The *Epworth Sleepiness Scale* (*ESS:* Johns, 1991) yielded pathological daytime sleepiness; the *International Restless Legs Syndrome Study Group rating scale for restless legs syndrome* (*IRLSSG*: Walters et al., 2003) revealed the presence of restless leg syndrome. This tool is assessing the severity of restless leg syndrome rather than diagnosing it, but, as it was the only measurement used and when looking at the results, we came to the conclusion that Mrs. L did, indeed, suffer from restless leg syndrome. Furthermore, the *Schlaffragebogen-B* (*Sf-B*: Görtelmeyer, 1986) indicated severe insomnia symptoms. Her overall sleep quality as measured by the *Pittsburgh Sleep Quality Index* (*PSQI*: Buysse et al., 1989) was 14, indicating chronic sleep disorders. Mrs. L also suffered from nightmares several times a week and thought about them often during the day. Consequently, her overall quality of life, measured by the *Quality of Life Index* (*QLI*: Ferrans and Powers, 1985), was very low (a total score of 3.7 in the QLI). The extent of her traumatization was measured by the *PTSD Symptom Scale* (*PSS*: Foa et al., 1993), containing three subscales, namely Intrusion, which measures the re-experience of the traumatic event; Avoidance; and Hyperarousal. Additionally, the *Impact of Event Scale* (*IES:* Horowitz et al., 1979) was conducted. Both measures indicated severe traumatization of Mrs. L. The measurements listed above and dream reports were collected at the end of the training program and 6 weeks after the end, as a follow-up assessment. Results of all time points are displayed in **Table 1**.

During the 6 week training program, Mrs. L reported two nightmares and two positive dreams in the first week. In the course of the LD-training program, she reported 13 dreams; 10 of them were nightmares, and, of those nightmares, four showed plot changes. In the second week, she reported three nightmares; in the third week, one positive dream; during the fourth week, one nightmare with a changed plot and one positive dream; during the fifth week, she reported three nightmares with changed plots; and during the sixth and final week of the program, there was no information about her dreams.

TABLE 1 | Mrs. L.'s scores of psychological measures.

	Begin	End	FU
PSQI	14	9	16
ESS	16	15	11
IRLSSG	18	12	13
SCL-90-R	71	73	80
SAS	53	49	Missing
SDS	56	57	62
QLI	3.7	3.5	2.7
IES	−3.69	−1.12	−0.93
PSS	41	26	37
Intrusion	3.75	3.5	2.375
Avoidance	2.75	1.625	2.25
Hyperarousal	3.67	3.17	2.83

Begin, beginning of training; End, end of the training; FU, follow-up.

We started the therapy by explaining to her how she can try to learn LD. Mrs. L. was very motivated to do so and followed the suggested steps. We also discussed several ways and options that she could choose from when dreaming her nightmare to try to change it. Those strategies were developed by asking the whole training group what they could suggest and discussing the ideas in the group. It is important in our approach that solutions are not predetermined by the therapist but developed together with the clients. Examples of the resulting options were searching for a safe place in the dream or looking directly at what is happening to see what is actually scary. After only 1 week, the first moderate changes in her dream were noticeable in her dream report:

Week 1: 02.02.2009 (rated as a nightmare):

> *I dreamt at around 2 am that my ex (former boyfriend whom she was separated 12 years ago) chases me by car through the city in which we used to live. He yelled: "I'll catch you and I'll kill you." Running away, I felt bad aches in my legs and couldn't move right. This all happened at night, nevertheless I saw him and his pointed gun. He tried to shoot at me but didn't hurt me. I woke up in my bed sitting [up].*

The next morning (week 1: 02/03/2009) she reported on the following dream:

> *A colleague of my ex had seen me and told him about that. He, again, chased me through the city in a car—never mind where I ran—he found me everywhere and grinned sadistically. Shortly before he ran me down with his car, I woke up. I fell back asleep and dreamed that dream again.*

This time she woke up before something really happened. Her dreams continued to change during the course of the group training, and her dreams started to become more masked and started to be situated in different settings. She reported dreams that she did not perceive as nightmares like the following:

Week 1: 02/05/2009:

> *I dreamt around 04.30 am that... I was at the dentist, he drilled a tooth, fixed it and said that I will live another 50 years with these teeth. The dental office was also a boutique for women's cloths where I wanted to buy some clothes. However, the dentist paid for everything. Another woman wanted to persuade me to start an affair with him. I refused. She said I should do that and loose my financial problems. I left laughing.*

The next week, dreams including her ex-boyfriend recurred:

Week 2: 02/09/2009:

> *I dreamt at 2.30 thatI was surrounded by many cabs. In each of them I saw the sadistic grin of my ex-boyfriend (who is a cab driver). Through a loudspeaker he yelled that he will catch me and kill me, wherever I ran to, he was everywhere. Woke up around 4 am, continued dreaming. He again was in many taxis, pushed me into a dead end street, I was able to disappear into a house and woke up sweating.*

Week 2: 02/10/09:

I dreamt at 2 am that… I was followed by me ex-boyfriend in his cab. Through the window he pointed his pistol towards me and yelled that he will kill me. After having been chased by him for a long time, I turned around and yelled that he should do it and stop torturing me. He shot at me, but didn't hit me and disappeared. I woke up sweating.

Week 2: 02/11/2009:

I dreamt at 2 am that … I was sitting in the cab of my ex-boyfriend, he drove at extreme high speed, I was nauseous and my head was spinning, he yelled at me that he would now kill me. Then we fell down a cliff and I woke up sweating.

All of these three nightmares during the 2nd week included the topic of her ex-husband stalking and threatened her. Even if those dreams cannot be considered to be changed in the plot, there is still a slight shift noticeable. One time, she did manage to escape into a house; the next time, she did escape the role of the victim for a short moment yelling at him, and another time, they both fell down the cliff.

During the 3rd week, she did have some dreams not considered being nightmares and off that topic surrounding her ex-husband.

The changes of the dream plots became more pronounced in dreams about her ex-husband in the 4th week:

Week 4: 02/26/2009:

At around 3 am I dream that my ex chases me, again by cab. I cried for help, many people came out of their houses and together we walked towards him. He disappeared.

Week 4: 02/28/2009:

I dreamt at 2.30 am that … I was driving through a wood with many people. We stopped at a restaurant. At once I was with a former colleague, much younger than I am and I had sex with him on a bench. The others, strangers to me did not notice apparently. Afterwards I yelled at him that I was afraid to catch an illness because his penis was deeply red. I ran away and woke up.

The most fundamental change was that she was now looking for help and did find help. Still, this dream is a nightmare, but her helplessness has disappeared. She gained new strength that allowed her to walk toward the stalker ready to confront him instead of only running away, and he disappeared. We had previously talked about this solution for her nightmare, and, even if she did not dream lucidly, she still incorporated this novel idea in her dream. The technique to find people a safe place or trying to acquire help during a nightmare may occur during PTSD treatment because helplessness is one factor hindering patients to let go of their traumatization. After 27 days of nightmare treatment, Mrs. L. reported the following dream:

Week 5: 03/02/2009:

At around 2:30 am I dreamt again that my ex chased me again in a cab. I ran and ran but was unable to cry for help; no sound came out; my voice had left me. He threatened me again with his gun. At some point, I was able to simply yell, "STOP." I woke up. After I had fallen asleep again, the dream continued, I ran, stumbled and woke up.

In this first dream, Mrs. L. was able to make a conscious decision to wake up and escape the situation, but she was not able to do the same in the subsequent dream. She kept having this dream, sometimes able to change it, sometimes not. This was her last dream report:

Week 5: 03/03/2009:

My ex chased me in a cab. This time the pointed gun was oversized. With a sadistic grin he yelled that he will kill me. I now yelled back that he should do it. I ran towards a downhill slope, he stumbled and fell down the hill. I looked but couldn't see him anymore. The cab and he had disappeared. I woke up, this time not frightened, but somewhat relieved.

In this dream, one could assume that she lost her fear to some extent. It was not necessary to seek help to confront her victimizer, and she did not choose to wake up. Even though this cannot be interpreted as healing, as the number of nightmares remained stable, it shows a significant change. Moreover, her anxiety and depressive symptoms had decreased. This outcome is very promising as no one expected those multiple traumas to be overcome in just 6 weeks.

Mrs. L. still reported dreams about her ex-husband, but it did not occur as often as before and it showed variations. In the 2 weeks, following the treatment, the contents of helplessness still dominated, maybe because she had to deal with her nightmares on her own again. After that, she was again able to make her ex-husband disappear, rescue herself, or could make herself wake up. Specifically, during the first week following the treatment, we got no information about her nightmares or dreams. In the second and third weeks after the program, she reported one nightmare each. During the fourth week, she reported two nightmares and, during the fifth week, one nightmare. In the sixth follow-up week, we got no information.

We believe that manipulating dreams directly is a more effective way of gaining inner strength than reframing waking fantasies in treatments.

At the end of the LD training, the diagnostic assessment had changed (**Table 1**). Her sleep quality improved, as, for example, she managed to shorten her sleep latency. However, she still had and remembered nightmares. Additionally, her overall quality of life improved slightly.

An LD training program for only 6 weeks is quite efficient and supportive but may have been too short to change traumatic experiences persistently. Between the end of the training program and the follow-up 6 weeks later, the dreams of the client suggest a form of relapse.

03/29/2009:

I dreamt at 2:30 am that … my ex followed me once more again in his cab, no people, no help! I ran and ran until I stumbled and fell. He drove over me and disappeared.

04/04/09:

I dreamt at 2.30 and 4 am that … my ex followed me in his cab and pointed with a pistol towards me. Yelled with a horrible laugh that he will get me and kill me. I was able to slip out of the dream twice, woke up, but fell asleep again and continued the dream. The 3rd time he shot around like a mad man and I woke up.

04/09/2009:

I dreamt at 2 am that … my ex drove in his cab towards me on the pedestrian zone and yelled hysterically that he will shoot me. He exited the car, pushed me toward the wall of a house and was about to shoot. I yelled, looked him straight in the eyes and he disappeared.

04/10/2009:

I dreamt around 2 am that… I drove with my ex in his cab, and he yelled that he will kill me, nevermind how. He threw me out of the car, turned and wanted to drive over me. I ran and ran and cried for help and woke up.

04/14/2009:

I dreamt at around 3 am that … my ex followed me again in his cab and yelled. I didn't see him much. When he pointed his pistol by the window towards me I yelled "Do it" and he disappeared.

DISCUSSION

The LD program was very well-received by all participants and was very informative for both sides. One of the most impressive observations on my part was that people with severe psychological problems, including PTSD and addiction problems, also often seem to additionally and substantially suffer from sleeping problems. This indicates that a treatment specifically targeting these problems should be implemented. People coming to a clinic are usually asked at the beginning of in-patient therapy about potential sleep impairment and are then given drugs for curing sleep problems. Pharmaceutics often cause various side effects, such as drowsiness and fatigue, during the day and lead to dependencies in patients with addictions, a common comorbidity of PTSD (Friedman, 2013).

In nightmares, a negative relationship between nightmares and poor sleep quality has frequently been reported (Schredl, 2003). Having frequent nightmares often results in trying to avoid sleeping, to begin with (Rosenberg and Van Hout, 2014), and the impacts of low sleep quality have been explored in the former section. The concern is also the fact that studies have already confirmed that having a nightmare induces behavioral consequences the next day, even in healthy subjects, namely higher anxiousness, mental instability, and even physical complaints (Köthe and Pietrowsky, 2001). Furthermore, having frequent nightmares was associated with declined mental health and sleep quality as well as increased suicide risk in patients suffering from mental disorders (Lemyre et al., 2019). Especially, that nightmares predict suicide risk that is found in several studies (Tanskanen et al., 2001; Sjöström et al., 2009; Nadorff et al., 2011, 2013, 2014) is concerning and further supports the demand to take frequent nightmares as an indicator for severe mental disorders, including suicidal risk (Nadorff et al., 2011), and their individual consequences on mental health, seriously. This notion gets further supported by results that nightmares predicted repeated suicide attempts, while no other sleep problem did so (Sjöström et al., 2009), and that they also predict self-harmful thoughts and behavior in a unidirectional way (meaning that nightmares predicted those thoughts and behaviors, but those thoughts and behaviors did not predict nightmares) (Hochard et al., 2015).

The treatment of nightmares by learning LD has been the topic in a recent review (de Macêdo et al., 2019), with some promising results: decreases in nightmare frequency and reduction in the intensity of psychological distress. But the literature on this topic is still inconclusive, and further studies are needed. The present case further highlights the potential that LD has to help with nightmares.

The aim of this therapeutic approach was to provide patients with the possibility to influence their dreaming, or even allow them to control nightmares while they occur. The aspect of having control is substantial as patients with PTSD often suffer from feelings of helplessness and makes this approach even more promising for this group of patients. Neurophysiologic studies suggest that brain regions associated with self-awareness and semantic understanding are significantly more active during LD as compared with non-lucid dreams (Holzinger et al., 2006). Implementing LD in Gestalt Therapy programs for the treatment of sleep problems was found to reduce symptoms more quickly, and positive effects were even found in patients not able to achieve LD (Holzinger et al., 2020). Own studies show that treating nightmares in patients with PTSD by LD has formerly decreased anxiety and depressive symptoms but did not improve sleep, including nightmares (Holzinger et al., 2020).

Mrs. L did not achieve to learn how to dream lucidly during this very short time period of the 6 week training. Still, it had a positive impact on the distress stemming from those nightmares. After the LD training, we observed that various measures improved. And even though the number of nightmares did not decrease, the nightmare plot changed, and the nightmares were less frightening. We, therefore, concluded that LD helped with nightmares, and, furthermore, that it improved psychological health and sleep quality in general.

The benefits of the training regressed to some extent after it ended. We suggest that had been the training continued, further progress would have been visible. This gets further support by the fact that, as we spoke to Mrs. L to get her consent for the present article, she mentioned the strategies she learned in our LD training are still helpful and her nightmare problems have further improved.

Based on these findings and the effectiveness of Cognitive Behavioral Treatment for Insomnia (CBT-I) (Morin, 2015; Ballesio et al., 2018; Baglioni et al., 2020), we defined our sleepcoaching concept: Its' theoretical background is Gestalt therapy and it involves CBT-I and relaxation techniques, but is

still addressing dreams and nightmares by implementing dream work and nightmare treatment (including LD training programs, particularly for PTSD patients). This inclusion of dream work and LD is the unique selling point, which distinguishes sleepcoaching from other psychotherapeutic approaches to sleep problems. We argue that sleepcoaching, as sleep problems are common comorbidity to various disorders, should be implemented in treatment plans in the public health system by default. Sleep problems and nightmares share a close relationship (Schredl et al., 2016), which gets also visible through the case of Mrs. L., as not only her nightmare symptoms but also other sleep and psychological health-related measures improved. These problems should, therefore, not be treated separately but in one holistic approach, like sleepcoaching. Patients would not only benefit from learning how to dream lucidly, which may improve their overall sleep quality but from sleepcoaching, which is a method to introduce knowledge that promotes healthy sleep habits and better sleep hygiene. Sleep hygiene education has often been proofed to improve sleep quality measures (de Sousa et al., 2007; Chen et al., 2010; O'Donnell and Driller, 2017). A review of the effectiveness of sleep hygiene education argued that sleep hygiene recommendations are most effective when individually fitted to the life of an individual, which is the case in the context of sleepcoaching (Irish et al., 2015). Another important benefit is that sleepcoaching has no unwanted side effects or interactions and, therefore, is applicable with any medication or disorder. Nevertheless, well-balanced drug treatment is sometimes supportive in combination with CBT-I and sleepcoaching by catalyzing additional improvement. Studies confirmed that several sleep measures improved after just a 2 day seminar on sleepcoaching (Holzinger et al., 2019a). This gets additional support as not only nightmares of Mrs. L. seemed to shift but other psychological problems as well. For example, her anxiety, depression, and quality of life score also improved. These changes already occurred over a time period of just 6 weeks.

As mentioned before, sleep problems are frequent comorbidity in various mental disorders and produce psychopathology and psychological distress to a high degree (Sateia, 2009). The urgency of treating sleep problems gets visible as they are present in affective, anxiety, eating, pervasive developmental, borderline and antisocial personality disorders, and schizophrenia (Baglioni et al., 2016). In PTSD, studies indicate that sleep mediates the relationship between rumination and more severe PTSD and depressive symptoms (Borders et al., 2015). That is in line with results suggesting that sleep problems hinder the recovery from PTSD (Babson and Feldner, 2010) and that remaining sleep problems after treating PTSD predicted worse treatment outcomes (López et al., 2017). Moreover, non-medical treatment of sleep problems can be as effective as the medical equivalent and can further elevate the effects of treatment for PTSD (Gilbert et al., 2015). Sleep seems to play a substantial role in not only the recovery from psychiatric disorders but also in the recovery from critical illnesses demanding ICU treatment (McKinley et al., 2013). Given that sleep is also correlated with quality of life, this further points to the direction that improving sleep quality could help any patient improve their overall mental state (Zeitlhofer et al., 2000; Košćec Bjelajac et al., 2020).

Limitations of the LD and sleepcoaching approach are that they need further empirical proof. Even though sleepcoaching has been proved useful in shift workers (Holzinger et al., 2019a) and healthy subjects (Holzinger et al., 2019a), it should be further researched in the context of other sleep and mental health problems. We suggest that patient groups with sleep problems like narcolepsy and obstructive sleep apnea would benefit from the program. Furthermore, it should be assessed in the context of other mental health problems involving nightmare and sleep symptoms, such as depression, borderline, and eating disorders. Another limitation to this technique is that LD is not always easy to induce, and empirical evaluations of the induction methods are sparse (Stumbrys et al., 2012). Nevertheless, cognitive techniques combined with wake-up-back-to-bed methods seem promising (Stumbrys et al., 2012), as well as portable devices (Mota-Rolim et al., 2019) and/or support through substances like glantamine (LaBerge et al., 2018).

In conclusion, since sleep problems trigger mental disorders and mental health in general, this may negatively affect recovery from traumas, such as PTSD and other physical illnesses. Nightmares, in turn, have an impact on sleep quality, and they are an indication of psychopathologic underpinnings, including suicide risk. The latter relationship is particularly of interest since this relationship seems to be unidirectional. There is evidence that treating nightmares by LD training programs is effective, as the dreamer might also gain insight into his/her psyche without the disadvantages of long-lasting drug treatments. Applying this approach by including the holistic approach of sleepcoaching into treatment concepts seems especially promising. Sleepcoaching targets various sleep problems; it enables the affected to make informed improvements in their sleep hygiene through education, uses concepts of CBT-I and relaxation techniques, including medical hypnosis, and incorporates dream work through LD techniques.

DATA AVAILABILITY STATEMENT

The data analyzed in this study is subject to the following licenses/restrictions: Psychtherapeutic Confidentiality. Requests to access these datasets should be directed to Brigitte Holzinger, info@schlafcoaching.org.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee MedUni Vienna. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

BH: conceptualization, manuscript, supervision, and LD-training. FN: manuscript, research, and formatting. GK: supervision. All authors contributed to the article and approved the submitted version.

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