

Interventions for Disrupted Sleep Patterns and Insomnia in Pediatric and Adolescent Populations Diagnosed with ASD

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Abstract – The objective of this study is to develop a set of recommendations for effectively addressing sleep disturbance in adolescents and children with autism spectrum disorder (ASD). This will be achieved through a comprehensive evaluation of both pharmacological and non-pharmacological approaches utilised in the treatment of sleep disruptions in this specific population. Healthcare professionals who are providing care for adolescents and children with ASD and experiencing sleep disturbances should actively investigate potential underlying factors contributing to the disruption, such as medication usage or the presence of comorbid conditions. Subsequently, it is crucial for clinicians to address these identified causes in order to effectively manage the sleep disturbances. When managing sleep disturbance, it is advisable for clinicians to first suggest behavioural interventions, either independently or in combination with pharmacological or nutraceutical treatments, in order to facilitate improved sleep for children and their families. In cases where behavioural interventions prove ineffective and comorbid conditions and concurrent drug usage have been appropriately managed, healthcare professionals may contemplate the administration of melatonin, commencing with a conservative dosage. It is advisable to recommend melatonin of pharmaceutical grade if it is readily available for clinical use. It is incumbent upon healthcare professionals to engage in comprehensive discussions regarding the potential advantages and drawbacks associated with the utilisation of melatonin among paediatric patients, adolescents, and their guardians.

Keywords – Autism Spectrum Disorder, Total Sleep Time, Sleep Onset Latency, Bedtime Resistance, Sleep Continuity, Daytime Behavior.

I. INTRODUCTION

Autism spectrum disorder (ASD) [1], a developmental impairment, can be attributed to variations in brain structure and function. Certain individuals with ASD exhibit a clearly discernible differentiation, such as a genetic abnormality. No additional elucidations have been discovered. It is postulated by researchers that a confluence of factors contributes to the modification of customary developmental trajectories, thereby resulting in ASD. The impact of these factors on individuals with ASD, as well as their recognition, remains largely unexplored. Individuals diagnosed with ASD exhibit a range of atypical behaviours, communication patterns, social interactions, and learning styles. There are no discernible physical attributes that set them apart from the general population. Individuals who fall within the autism spectrum exhibit a diverse array of aptitudes and abilities. Individuals with ASD can exhibit a wide range of conversational abilities, varying from above-average proficiency to complete nonverbal communication skills.

While it is true that certain persons diagnosed with ASD necessitate significant support, there are also those who exhibit the capability to navigate the realms of employment and daily activities autonomously. ASD is a chronic condition that typically presents in early childhood, although there is potential for amelioration over time. From the onset of infancy, certain children display indications of autism spectrum disorder. Certain individuals may not exhibit any

symptoms until they reach the age of 24 months. Certain individuals diagnosed with ASD demonstrate ongoing acquisition of new skills and attainment of developmental milestones until approximately 18 to 24 months of age. However, subsequent to this period, these individuals may experience a decline in their abilities or fail to achieve developmental progress at the same rate as their typically developing peers.

Sleep disturbances are commonly observed in individuals with ASD, encompassing difficulties in initiating and maintaining sleep, frequent awakenings and prolonged periods of wakefulness during the night, experiencing insufficient sleep duration, early morning awakenings, and disrupted sleep-wake patterns. The presence of concurrent sleep disorders significantly impacts the daily functioning of a substantial proportion, ranging from 44 to 83 percent, of adolescents and children diagnosed with ASD. Approximately 40% of children and adolescents who exhibit typical developmental patterns experience sleep disturbances, although a majority of these individuals tend to show improvement as they progress in age. Sleep disturbances are frequently observed in adolescents and children diagnosed with ASD. There exists a significant association between severe disturbances in sleep patterns and adverse effects on both physical and mental well-being, as well as a diminished overall quality of life. Insufficient sleep during the night and substandard sleep quality can potentially yield noteworthy repercussions on mood and the regulation of emotions, behaviour, and cognitive functioning.

These outcomes are closely associated with the core symptoms of ASD. Sleep difficulties are frequently observed in children and adolescents who have intellectual impairments and exhibit severe signs and symptoms of ASD. There exists a correlation between sleep disturbances and symptoms associated with ASD, such as challenges in communication and participation in restricted and repetitive behaviours. The presence of a sleep disorder can negatively impact an individual's sleep patterns and subsequently affect the overall quality of life for both the individual and their family.¹⁰ Sleep disruptions are frequently associated with daytime behaviour problems. There is an increased likelihood of injury among individuals with obesity, particularly within the age range of 11 to 13. The academic performance of children as a whole exhibits a decline during the ages of 14, 15, and 16, followed by a slight improvement from 17 to 19.

Possible contributors to the circadian rhythm misalignments integrate altered melatonin secretion and dysregulated melatonin synthesis patterns, a deficiency in awareness concerning environmental and social cues and irregularities in the circadian clock genes cues, which determine the cycle of sleep-wake. Aberrations in the glutamatergic, GABAergic, dopaminergic, and serotonergic systems are among the potential contributing factors associated with Autism Spectrum Disorder (ASD). Several coexisting medical disorders, such as attention deficit hyperactivity disorder (ADHD), psychosis, depression, nocturnal gastroesophageal reflux disease (GERD), bipolar disorder, anxiety, and epilepsy, can exacerbate the challenges associated with initiating and maintaining sleep. The occurrence of difficulties in initiating or maintaining sleep may be further compounded by underlying or concurrent factors. ASD is characterised by a range of symptoms, which encompass cognitive impairments, challenges in sensory integration, engagement in repetitive or self-harming behaviours, deficits in communication abilities, and difficulties in interpreting social cues.

The combination of medication, behavioural therapy, and complementary and alternative medicine (CAM) is frequently employed to address sleep disturbance in adolescents and children with ASD. Exogenous melatonin, which is artificially synthesised from the endogenous hormone melatonin present in the human body, is widely acknowledged as the most reliable marker of circadian sleep regulation. Melatonin is a hormone that exhibits hypnotic properties and is involved in regulating circadian rhythms, which follow a 24-hour cycle. The enforcement of purity standards for over-the-counter (OTC) products is not carried out by the US Food and Drug Administration (FDA) due to their classification as dietary supplements. Prescription pharmaceuticals are commonly prescribed in order to administer precise dosages. Examples of behavioural interventions for children under the age of five integrate unmodified progressive extinctions, bedtime fading, and pleasant routines. Cognitive-behavioral therapy (CBT), whenever modified from the paradigms of an adult, has demonstrated potential efficacy in addressing the needs of older children and adolescents. Insomnia interventions encompass brief, multifaceted, purpose-driven psychotherapeutic approaches aimed at altering cognitive patterns and behavioural tendencies that perpetuate the presence of insomnia.

This article aims to address the aforementioned issue/question. What are the most effective pharmacologic, behavioural, and complementary and alternative medicine (CAM) therapies for reducing total sleep time (TST), sleep onset latency (SOL), sleep continuity, bedtime resistance, and daytime behaviors in adolescents and children diagnosed with ASD? The subsequent sections of the article are systematized as follows: Section II presents the methodology employed in this research. Section III presents a detailed analysis and discussion of results concerning bedtime resistance, melatonin and CBT I and II, sleep onset latency, parent-based sleep education I, II, and III, and daytime behavior. Lastly, Section IV draws a conclusion to the article.

II. METHODOLOGY

The set of recommendations presented here was developed using the AAN (American Academy of Neurology) Guideline Manual, Version 1.1 (2011, as modified). The AAN GDDI (Guideline Development, Dissemination, and Implementation) committee granted authorization for the commencement of autism treatment recommendations in 2012 [2]. Following the guidelines outlined in the AAN Conflict of Interest (COI) policy, the leadership of the panel conducted an evaluation of the COI forms and resumes submitted by potential panel members. A multidisciplinary panel comprising developmental paediatricians, neurologists, psychiatrists, and neuropsychologists was established following the approval of the Global Developmental Delay Initiative (GDDI). The initiative is supported by proponents of evidence-based

medicine in [3]. Out of the total cohort of 26 scholars, six individuals encountered conflicts of interest (COIs); however, these conflicts were of a relatively insignificant nature, thereby not impeding their ability to make valuable contributions. The restricted capacities of the subject align with the regulations set forth by the AAN.²⁴ The principal author disclosed the absence of any conflicts of interest. Due to the existence of multiple studies conducted prior to the release of DSM-5, a diverse array of methodologies was employed in order to establish the definition of Autism Spectrum Disorder (ASD). Throughout this book, the term ASD, which is currently widely accepted, is utilised. To gain insight into the diagnostic methodologies employed by researchers in these studies, it is advisable to refer to the primary literature.

Initially, it was believed that fully conducted systematic reviews (SRs) would be adequate. Nevertheless, the evaluations that were deemed deficient in essential information were deemed inadequate for evaluating the credibility of the proof presented in individual studies. Consequently, the panel responsible for the guidelines assigned ratings to the studies included in each systematic review (SR) according to the established criteria set by the American Academy of Neurology (AAN). The panel reviewed a total of 900 article abstracts in the field of SR. An additional 1,087 abstracts were obtained through subsequent literature searches conducted by Lame [4]. Out of a total of 1,987 abstracts, a mere 139 exhibited potentials for practical applicability. A total of 12 articles were deemed appropriate for the purpose of data extraction. A total of eight participants were included in the analysis due to their classification as Class III or higher. The AAN technique was employed to categorise evidence, synthesise evidence, and generate recommendations. The panel formulated recommendations for practise by considering the weight of the evidence, axiomatic principles, substantial related evidence, and drawing appropriate conclusions. The responsibility levels were determined using the Modified Delphi voting method.

III. RESULTS AND DISCUSSION

There is a lack of clinically significant variations in the results of studies. In order to ascertain the parameters of a clinically significant change, particularly in relation to actigraphy, our study involved the solicitation of opinions from our panel of experts. The researchers employed three distinct questionnaires to evaluate children's behaviour in the integrated studies: the CSHQ (Children's Sleep Habits Questionnaire), consisting of 45 questions with ratings ranging from 1 to 3; the Developmental Behaviour Checklist (DBC), comprising 96 items with scores ranging from 0 to 2; and the Aberrant Behaviour Checklist (ABC), consisting of 58 items with grades ranging from 0 to 3.²⁸ There is a positive correlation between the severity of symptoms and the assigned ratings. In the analysis of questionnaire results, changes of 1% or less were deemed insignificant, while changes of 10% or greater were deemed significant. All research investigations encompassed individuals below the age of 18 diagnosed with ASD, and were conducted exclusively within the geographical boundaries of the Europe or United States.

Bedtime resistance

Bedtime resistance refers to a behavioral phenomenon characterized by a child's unwillingness to adhere to the designated bedtime, resulting in various behaviors such as delaying the act of going to bed or requiring the presence of a parent in order to initiate the sleep process. According to Nishioka et al. [5], a notable proportion of children aged one to five, specifically around twenty-five to thirty percent, demonstrate active resistance towards bedtime. This resistance is characterized by behaviors such as shouting out or leaving their room after the designated bedtime. Bedtime resistance can be classified as dyssomnia, specifically under the category of "not otherwise specified" in the mental disorders manual for diagnosis and statistics. Additionally, it can serve as a fundamental element of behavior clusters that can be categorized alongside other diagnoses, such as attention deficit hyperactivity disorder and oppositional defiant disorder. If left unattended, difficulties in initiating sleep can persist for an extended period of time. In addition, there exists a correlation between pediatric sleep disorders and a range of adverse outcomes, such as reduced cognitive abilities and heightened behavioral challenges. Therefore, it is imperative to intervene in a manner that promotes productivity.

The most commonly used behavioral intervention for children who exhibit bedtime refusal is extinction, which involves the deliberate parental practice of ignoring the child's behavior. Parental acceptance of extinction is challenging, despite its effectiveness. This phenomenon can be attributed, at least in part, to the temporary increase in resistance observed during the initial stages of intervention, commonly referred to as the extinction burst. Alternatively, another approach known as the nighttime pass involves the implementation of two components: (a) the provision of a small notecard that can be exchanged for a single excursion outside the bedroom after the child has been put to bed, and (b) the utilization of extinction techniques. In the absence of observable extinction bursts in the initial phases of intervention, the implementation of the bedtime pass technique yielded positive outcomes for two siblings, aged 3 and 10 years. Furthermore, a total of 20 parents expressed a preference for the intervention over the conventional method of extinction.

Only a single Class II research has evaluated the impacts of melatonin in conjunction with family cognitive-behavioral therapy (CBT). No additional relevant research was identified. **Fig. 1** illustrates the frequency of resistance to sleep observed on a nightly basis across all stages of the experiment. The baseline phases exhibited elevated and diverse frequencies of vocalizations or departures from the room, while the intervention phases demonstrated reduced frequencies. In the majority of instances, these outcomes were observed to occur expeditiously. Bedtime resistance was successfully reduced without the occurrence of the typical extinction bursts commonly observed in treatments based on extinction. Initially, Greg's resistance exhibited a resemblance to the baseline levels upon the implementation of the pass plus extinction technique. Furthermore, the reduction of the target behavior required a greater amount of time to

accomplish when the combined intervention was employed, in contrast to the utilization of either intervention in isolation. However, there was no significant increase in the frequency of either crying out or leaving the room during the intervention period compared to the baseline period. Furthermore, during Night 19 for Jim and Night 64 for Walter, the level of resistance exhibited by both participants was found to be comparable to the baseline rates. It is worth noting that the reported unusual events by their respective parents, such as Jim's complaints of illness and Walter's sister making a phone call, likely had an impact on the observed outcomes.

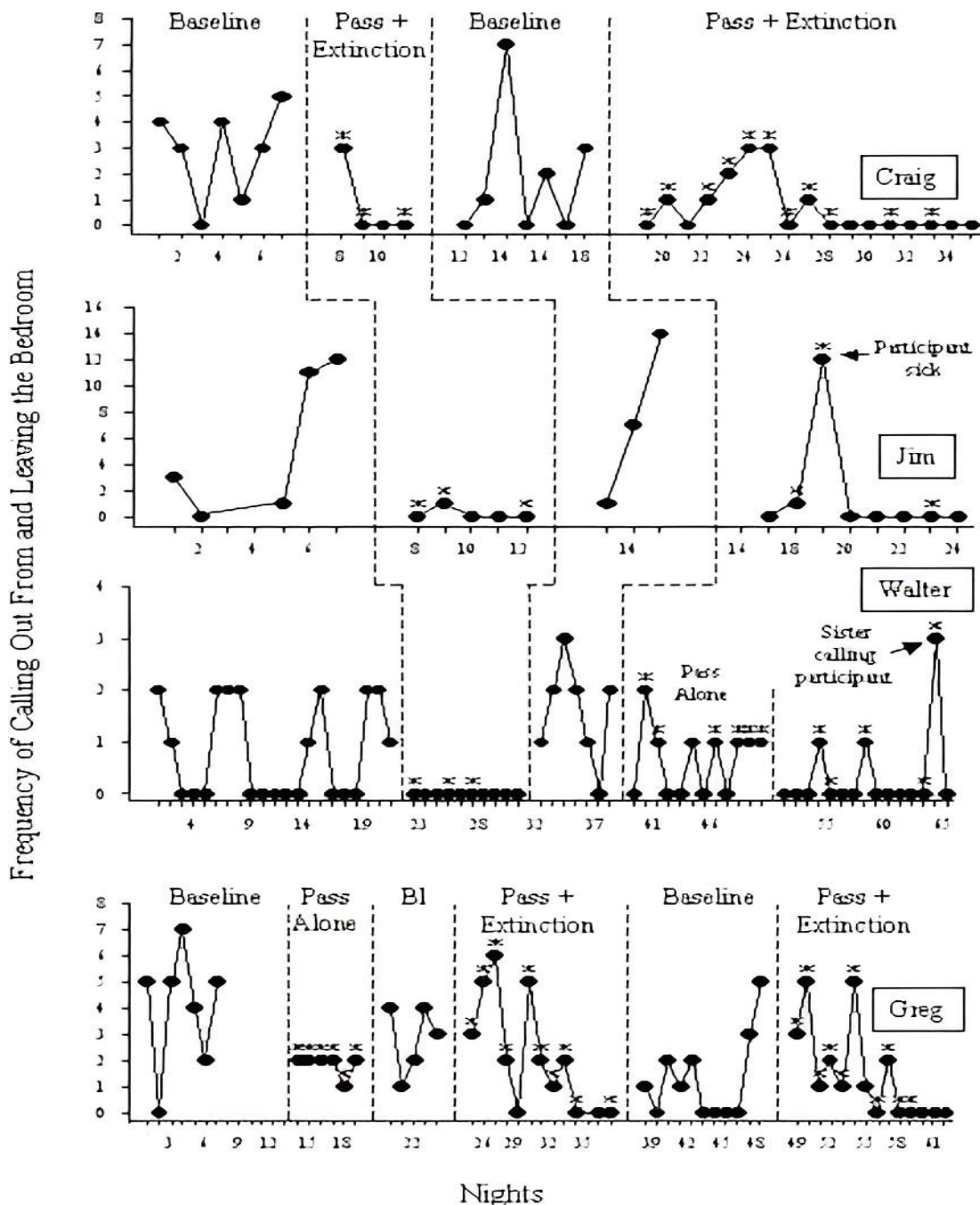


Fig 1. The mean frequency at which individuals exit their room or vocalize during the nocturnal period

The absence of data points during certain nights serves as evidence of data collection deficiencies by healthcare providers, and is utilized to visually represent the progression of time. The participants' names are marked with asterisks on the evenings when they made use of the bedtime pass. The acronym BL is an abbreviation for the term "baseline."

Melatonin and CBT I

The pineal gland and its associated hormone, melatonin, have been found to be associated with circadian rhythm regulation in animals. The involvement of melatonin in the regulation of seasonal cycles of hibernation and daily torpor,

tolerance to heat stress, and the core body temperature set points determination is subject to variation depending on the specific species being studied. The melatonin circadian rhythms and CBT exhibit a strong association in human beings, wherein the decline of CBT during nighttime is inversely correlated with the increase of melatonin. There is substantial empirical evidence indicating that melatonin has a significant impact on CBT reduction. Conversely, the available evidence regarding the relationship between a decrease in CBT and the subsequent production of melatonin is inconclusive. The administration of melatonin during the day, when its natural release is absent, leads to a reduction in CBT by approximately 0.3 to 0.4 degrees Celsius. Conversely, the suppression of melatonin at night results in an increase in CBT of a similar magnitude. Hence, the elevation of melatonin levels during the nocturnal period is a contributing element to the circadian amplitude of CBT.

The precise mechanism by which melatonin inhibits CBT remains unclear. Although the thermoregulatory effects of melatonin in increasing heat loss have been extensively documented, it is imperative to acknowledge the potential impact of melatonin on reducing heat production. The primary mechanism by which melatonin suppresses CBT is believed to occur mainly within the hypothalamus, where thermoregulatory centers are located. Additionally, melatonin may also affect peripheral vasculature to promote heat dissipation. Zuluaga and Danner [6] indicate that the impact of melatonin and intense light on the circadian phase is limited, as their effects primarily involve acute thermoregulation. There are two physiological circumstances, namely aging and the luteal phase of the menstrual cycle, that diminish the activity of melatonin, leading to eventual energy conservation. In both scenarios, the typical effects of melatonin in reducing cognitive behavioral therapy (CBT) will be negated. This observed phenomenon could potentially suggest a correlation between age and physiological changes in adult females. However, during the luteal phase, it could serve as a mechanism to regulate nocturnal core body temperature (CBT) levels, thereby enhancing the likelihood of successful embryo implantation and subsequent survival.

The Class II trial encompassed four primary outcomes, with the administration of placebos to the participants. A randomized assignment was conducted on children between the ages of 4 and 10 who have been identified with ASD and experiences maintenance insomnia, sleep onset insomnia, or both. These children were divided into four groups: one group received a dosage of 3 milligram of protracted release melatonin ($n = 34$ at 9 PM), another group participated in four 50-minute sessions per week of family-oriented CBT trailed by $n = 33$ maintenance sessions twice a month, a third group received a combination of melatonin and CBT ($n = 35$), and a fourth group received a placebo ($n = 32$). The melatonin provided was of high purity, with a concentration of 99.9%. It was administered in two doses: an immediate delivery of 1 mg and a subsequent release of 2 mg over a period of 6 hours.

The researchers employed the CSHQ-Bedtime Resistance subscale, which measures bedtime reluctance on a scale ranging from 6 to 18 points. A total of 12 week scores and 26 baseline scores were recounted; nonetheless, the present data was not enough to effectively ascertain the average change variations between different groups with CIs (confidence intervals). At the end of a period of two weeks, it was observed that all active treatment groups experienced a decrease in scores related to bedtime resistance when compared to the placebo group. The combination therapy group showed a reduction of 5.64 (95.0% CI, 6.45 to 4.83), the melatonin group showed a reduction of 3.60 (95.0% CI, 4.60 to 2.60), and the cognitive-behavioral therapy (CBT) group showed a reduction of 2.48 (95.0% CI, 3.49 to 1.47). The administration of melatonin was found to be highly tolerable. No adverse effects were described.

Sleep onset latency

The period of time required for an individual to transition from a state of complete wakefulness to the initial stage of sleep, commonly referred to as the lightest phase of non-rapid eye movement (REM) sleep, is commonly referred to as the sleep onset latency (SOL) within the domain of sleep research. Ehsan [7] provides a comprehensive account of the inception and initial formulation of the concept of sleep, as well as the subsequent establishment of the inaugural assessment tool known as the Multiple Sleep Latency Test (MSLT), in [8]. Kima [9] aimed to obtain an unbiased quantification of daytime drowsiness in order to enhance the assessment of sleep disorders' effects. During the process of data analysis, a significant correlation was observed between the duration of time individuals required to fall asleep in bed and their self-reported levels of fatigue. While acknowledging that the concept and execution of an objective measure of fatigue may not appear to be a groundbreaking development, Chinese Sleep Research Society [10] contend that it constitutes a noteworthy advancement in the realm of sleep research.

The MSLT was initially developed by Usui et al. [11] through the implementation of a protocol in which participants were instructed to recline in a dimly lit room on a bed, with their eyes closed, and to engage in relaxation. The duration of time required for an individual to fall asleep was measured, ranging from 0 to 20 minutes. The experiment was concluded, and participants who remained awake after 20 minutes were assigned a rating indicating maximum alertness and minimum drowsiness. The findings of the study indicate that individuals who experience sleep deprivation may exhibit a rapid onset of sleep, potentially within a minute. Furthermore, it is suggested that sleep latency could decrease to less than one minute. A positive correlation was observed between the extent of sleep deprivation and the magnitude of changes in sleep latency scores.

The research conducted by Jawinski et al. [12] ultimately led to the conclusion that the brain maintains an accurate record of the amount of sleep it requires. The concept of "sleep debt" refers to the impact on an individual's sleep latency score and their ability to fall asleep promptly when they have experienced insufficient sleep over an extended duration.

Melatonin and CBT II

We identified two studies categorized as Class II and a single research categorized as Class I. In a Class I research study, a total of 125 young children that range in terms of age from 2 to 17 years, who were diagnosed with Autism Spectrum Disorder (ASD) and experienced sleep issues persisting for a period exceeding three months, were arbitrarily allotted to a 1 of the 2 categories. These children had previously undergone four weeks of behavioral treatment without any positive response. The two categories were administered either prolonged-release melatonin at a dosage of 2-5 mg per day (with the possibility of titration up to 10 mg per day) or a placebo. Prior to the administration of the treatment, all participants underwent a two-week period during which they were given a single-blind placebo. The study found that the average sleep onset latency (SOL) in the melatonin group decreased by 25.3 minutes (95.0% CI: -44.7 to -5.7) more compared to the placebo group over a period of 13 weeks.

The evaluation of Class II study SOL involved the utilization of actigraphy and the CSHQ- SOD (Sleep Onset Delay) subscale, as previously documented. The study found that children who were administered prolonged-release melatonin in conjunction with family-oriented cognitive-behavioral therapy (CBT) had a significantly lower 12-week sleep onset latency (SOL) compared to those who received a placebo. The results showed a decrease in SOL as measured by actigraphy of 45.91 minutes (95.0% CI, 57.93 to 33.89) and a decrease in SOL as determined by CSHQ-SOD (Children's Sleep Habits Questionnaire Sleep Onset Delay) of 1.24 (95.0% CI, 1.50 to 0.98). In comparison to a placebo, both prolonged-release melatonin and cognitive behavioral therapy demonstrated a reduction in sleep onset latency (SOL) at the 12-week mark. Prolonged-release melatonin showed a decrease in SOL as measured by actigraphy of 34.38 minutes (95.0% CI, 47.90 to 20.87) and by the CSHQ-SOD of 0.83 (95.0% CI, 1.07 to 0.59). Cognitive behavioral therapy resulted in a decrease in SOL as measured by actigraphy of 20.47 minutes (95.0% CI, 34.98 to 5).

The evaluation of sleep onset latency (SOL) was conducted through the utilization of sleep diaries in a Class II crossover research design. The study involved the administration of standard-release melatonin, with dosages ranging up to 10 mg per day and a modal dosage of 7 mg, to a taster of children aged 3 to 16 years old diagnosed with Autism Spectrum Disorder (ASD) and experiencing insomnia. The sample size for this study was 17 participants. The behavioral therapy intervention administered to a group of 32 individuals did not yield significant improvements in their excessive sleep latencies, which were defined as exceeding 30 minutes. The study observed a significant SOL reduction of 46 minutes (95.0% CI: -78.50 to about -14.90) between the weeks where participants were treated with melatonin and those where they received a placebo. The safety profile of melatonin was found to be favorable. There were no reported adverse events.

A random-effect meta-analysis was steered to combine the findings of three studies, based on the following hypotheses: (1) there is no significant difference between the prolonged-release and standard forms of melatonin, (2) actigraphy and diaries provide similar measurements of sleep onset latency (SOL), and (3) the reduction in SOL scores over a 12-week period is comparable to the mean transformation in SOL, presuming constant baseline SOL, in both the placebo and melatonin groups. According to the findings of this meta-analysis, the administration of melatonin to children spotted with ASD and experiencing sleep disruption resulted in a statistically significant mean reduction in sleep onset latency (SOL) of 33.1 minutes. The confidence interval (95.0% CI) for this mean decrease ranged from 43.5 to 22.6 minutes. It is worth noting that the heterogeneity among the included studies, as indicated by the I^2 statistic, was negligible ($I^2 = 0\%$).

Parent-based sleep education I

It is imperative that children diagnosed with epilepsy adhere to a consistent sleep schedule as an integral component of their therapeutic regimen, given that insufficient sleep constitutes a significant contributing element to the occurrence of seizures in this population. Insufficient adherence to appropriate sleep hygiene practices has the potential to exacerbate the impact of seizures and induce excessive daytime somnolence, both of which can exert detrimental influences on the neurocognitive development of children. The implementation of consistent sleep schedules and the provision of behavioral counseling have been suggested as potential strategies to mitigate the problem. The Commission for terminology and classification of the ILAE (International League Against Epilepsy) has established a valuable framework for classifying various forms of seizures and epilepsy.

The recent classification of seizures by the International League Against Epilepsy (ILEA) [13] does not represent a substantial deviation, but rather offers enhanced alternatives and improved elucidation in terms of the nomenclature for various types of seizures. Based on the classification system established by the ILEA, a significant proportion of the participants in our study, specifically 56%, were classified as young individuals. A significant proportion of the participants (n=59, representing 92.2% of individuals utilizing anti-epileptic medications) were exclusively prescribed either carbamazepine or sodium valproate. In the study, a total of 64 children were included. Among them, 39 children (60.9%) received carbamazepine, while 22 children (34.4%) received valproic acid either as a standalone treatment or in combination with levitiracetam or clobazam. A single child was subjected to monotherapy with either topiramate or levetiracetam. In the past, polytherapy has been primarily employed in the treatment of intractable seizures in a singular pediatric patient.

According to Marmura and Kumpinsky [14], a significant proportion of patients (77%) were prescribed anti-epileptic drugs (AEDs) as monotherapy. In contrast, Testa, Polenta, Monteburini, Boni, Sio, and Mazzanti [15] reported that

68.6% of patients were receiving monotherapy, while 23.2% were receiving bi-therapy. In this study, the majority of children, specifically 61% (93.7%), were found to be undergoing treatment with a single antiepileptic drug (AED). Conversely, a small proportion of children, only three individuals (4.7%), were receiving bi-therapy. Sleep behaviors, including a child's bedtime routine, sleeping environment, and parent-child interactions, can be measured quantitatively using the FISH questionnaire. A positive correlation is observed between a higher score and improved sleep hygiene. The results of the study indicate that parents whose children took part in the intervention demonstrated a statistically significant enhancement in their FISH scores.

The efficacy of the FISH questionnaire in improving parents' behavioral interactions with their children has been empirically established, as it effectively increases parents' self-awareness regarding their own parenting styles. Through the examination of parents' FISH inventory ratings prior to and subsequent to the intervention, it becomes evident that parents who possess knowledge and motivation are capable of effecting favorable modifications in their child's daily and nocturnal routines, thereby fostering improved sleep patterns. Parents also observed a decrease in diurnal somnolence when their children commenced experiencing uninterrupted sleep during the night. Krossbakken et al. [16] demonstrated that the implementation of a parental behavioral intervention resulted in a significant increase in the FISH score.

Sleep architecture disturbances, such as the elongation of Stage 1 sleep and a delayed initiation of REM sleep, could potentially be a contributing factor to the excessive daytime somnolence observed in pediatric patients diagnosed with epilepsy. Tabara et al. [17] discovered significant disparities in various sleep-related factors, such as bedtime challenges, sleep initiation time, parasomnias, nocturnal parent-child interaction, excessive daytime sleepiness, non-restorative sleep, and sleep disruption, when comparing children diagnosed with seizure disorder to their typically developing siblings. The Sleep Disturbances Scale for Children (SDSC) can be employed to gain further insights into the sleep-wake cycle of children and identify the underlying causes of their sleep difficulties. Previous research has demonstrated the reliability of utilizing this method to assess sleep disturbances in pediatric populations with diverse health conditions, such as epilepsy. The results obtained from the analysis of scores on the FISH inventory and the SDSC questionnaire suggest that the implementation of the educational package had a significant impact on improving the sleep patterns and profiles of children diagnosed with seizure disorder. With the exclusion of arousal disorders, all subscales of the SDSC sleep scale exhibited improvement following the intervention.

Both the Class II and Class III studies incorporated parental education on the importance of establishing consistent bedtimes and personal hygiene routines. In this study, participants were assigned to Class II for actigraphy results. The trial involved randomizing parents of children aged 2 to 9 years with ASD and an average Sleep Onset Latency (SOL) of 30 minutes. The participants were divided into two groups: one group received a 4-page instructional leaflet ($n = 19$), while the other group received no intervention ($n = 17$). The brochure provided comprehensive instructions on establishing an optimal sleep environment, implementing a consistent bedtime routine for children, eliminating daytime napping, and ensuring timely awakening in the morning. There was no significant difference in the sleep onset latency (SOL) between children whose parents obtained the booklets and those with parents did not receive any training. The relative mean difference in SOL at two weeks was 11 minutes (95.0% CI, 37.15 to 13.55), and the variation in average transformation between baseline and two weeks was 16 minutes (95.0% CI, 39.2 to 6.4).

A cohort of children between the ages of 2 and 10, diagnosed with Autism Spectrum Disorder (ASD) and exhibiting a SOL of at approximately thirty minutes on about 3 nights/week, were the subjects of a Class II research investigating the effects of parental sleep instruction. The research design employed a Class IV methodology, which did not include a control group, for the entire research population. However, a Class II design was utilized to compare the actigraphy results obtained from individual instruction with those obtained from group instruction. At the 4-week mark following the intervention, there was no discernible disparity in SOL between children with parents that obtained individual instruction and those with parents that obtained group education. The relative mean difference was 0.2 minutes, with a 95.0% confidence interval ranging from 9.79 to 9.39.

In this study, a cluster of parents whose children had been diagnosed with ASD and experiencing sleep disturbances, with an average age of 3.5 years, were selected randomly. The parents were divided into two groups: one group received sleep-specific behavioral training ($n = 20$), while the other group received non-sleep-related education ($n = 20$). The study followed a Class III placebo-controlled design, although more than 20% of participants were lost for actigraphy outcomes. The study had four primary outcomes and did not employ allocation concealment. During the duration of 8 weeks, both groups participated in a total of 5 sessions. The study utilized activity monitors placed in beds to track sleep patterns during nighttime shifts. The sample size for this study was 27 participants. The available data included 8-week, 4-week and baseline scores; however, there was insufficient information to compute the mean change variations between different groups alongside their interval of confidence. The control group's baseline sleep onset latency (SOL) exhibited a standard deviation (SD) of 27 minutes, while the behavioral training group's SOL displayed an SD of 35 minutes. There was no statistically significant difference in sleep onset latency (SOL) at 8 weeks between children with parents that obtained sleep-focused instruction and those that parents did not (mean difference: 4 minutes; 95.0% confidence interval, 14 to 22).

Weighted blankets

The study involved children between the ages of 5 and 16 who have Autism Spectrum Disorder (ASD). The study followed a crossover design and lasted for a duration of two weeks. Actigraphy was used to measure sleep patterns, and the results were classified as Class II. The analysis included 74% of the individuals who were randomly assigned to the study. Sleep diaries were also used to assess sleep, and the results were classified as Class III. A total of 36 children (with a sample size ranging from 54 to 67, depending on the arm) were included in the study. These children reported experiencing sleep complaints for a duration of 5 months or less. Importantly, they did not exhibit any signs of night terrors, OSA (obstructive sleep apnea), or other disorders of sleep. The utilization of a weighted blanket did not yield a decrease in sleep onset latency (SOL) when compared to the use of a conventional blanket. The mean change difference for actigraphy was 2 minutes (95.5% CI, 5.3 to 9.5), whereas for the sleep diary was 1 minute (95.5% CI, 6.60 to 3.40).

Sound-to-Sleep (STS) mattress initiative

A single random crossover experiment was conducted to investigate the utilization of STS mattress technology. The study involved a 45 children sample, aged 2 to 12 years, who were diagnosed with Autism Spectrum Disorder (ASD) and exhibited severe sleep problems, as indicated by a CSHQ score of 41. The STS mattress has been specifically engineered to incorporate synchronized vibrations that correspond to a music source chosen by the user. The actigraphy findings were classified as Class II, while the diaries were classified as Class III. Actigraphy readings were not initially collected. The results of the 2-week study on the sustained attention span of the 38 children who took part did not reveal any statistically significant variation between the off condition (mean duration: 18 minutes) and the on condition (mean duration: 14.11 minutes) (mean difference: 4 minutes; a 95.0% confidence interval, 11 to 3).

Sleep continuity: sleep efficiency (SE)

The metric used to quantify the degree of sleep consolidation attained during a specific night is referred to as "sleep continuity." The measures of continuity encompass OSA, overnight awakenings frequency, wake after sleep onset (WASO), and sleep efficiency (SE). The SE is a term used to describe the proportion of time an individual spends in bed, encompassing the duration it takes to fall asleep and wake up.

Melatonin and CBT

The group of children who were administered both prolonged-release melatonin and family-based cognitive behavioral therapy (CBT) exhibited significantly higher mean actigraphy sleep efficiency (SE) scores after 12 weeks compared to the groups that received either melatonin alone, CBT alone, or placebo. The effect sizes, as measured by the relative mean differences were 12.53% (95.0% CI, 10.40-14.66) for the combination therapy, 10.78% (95.0% CI, 8.69-12.87) for melatonin alone, and 7.65% (95.0% CI, 5.78-9.52) for CBT alone, when compared to the placebo group.

Parent-based sleep education II

The study observed that study participants whose parents received the Class II educational leaflet demonstrated superior improvement in sleep efficiency (SE) after 12 weeks, as measured by actigraphy. The mean change in SE was found to be +2.3% for participants whose parents received the leaflet, compared to 1.7% for participants whose parents did not receive the leaflet. This resulted in a difference in mean change of 4.0%, with a 95.0% confidence interval ranging from 0.18% to 7.82%. At the 12-week mark, no statistically relevant disparity was pragmatic between the children and the control group regarding their SE ($75.1\% \pm 6.7\%$ vs $77.8\% \pm 7.0\%$; relative mean difference: 2.75%; 95.5% CI, 1.77 to 7.17). A Class II research was conducted to compare the effectiveness of individual and group parent sleep education sessions. The findings indicated that there was insignificant variation in child sleep efficiency (SE) at 4 weeks between the two types of sessions.

The SE percentages were 78.7% for individual sessions and 79.8% for group sessions. The relative mean difference was 1.10%, with a 95.0% confidence interval (CI) ranging from 3.61% to 1.41%. These findings were evaluated using actigraphy. The Class III trial, which aimed to compare the efficacy of 8 weeks of sleep-specific behavioral training to control parental education, found that the baseline sleep efficiency (SE) was greater than 80% in both groups. After a duration of 8 weeks from the commencement of the study, no statistically significant distinction in sleep efficiency (SE) was observed between the two groups, as assessed by actigraphy. The SE percentages were found to be $86\% \pm 6\%$ in children with that parents obtained sleep-specific education, and $85\% \pm 9\%$ in children with that parents were provided with non-sleep-based education. The relative mean difference in SE was 1.0%, with a 95.0% confidence interval (CI) ranging from 7.17 to 5.17.

Weighted blankets

There was no significant difference in the standard error (SE) observed between the periods of using a weighted blanket and a conventional blanket in the previously conducted Class II experiment (95.0% CI 1.41 to 0.81; relative mean difference: 0.3%).

STS mattress technology

In a study utilizing Sleep Tracking System (STS) mattress technology, specifically Class II for actigraphy, it was observed that participants experienced an increase in sleep efficiency (SE) from Week 2 to Week 4. During Week 4, when the STS technology was active, the SE was measured at 78.27%. Conversely, during Week 4 when the technology was inactive, the SE decreased to 75.45%. The difference in SE between the two conditions was found to be 2.82% relative mean difference, with a 95.0% confidence interval ranging from 1.14% to 4.50%.

Sleep continuity: night awakenings

The period of wakefulness occurring between the initiation of sleep and the typical bedtime of individuals is commonly denoted as Wake After Sleep Onset (WASO). The phrase "night awakenings" is employed to denote the cumulative frequency of instances in which an individual rouse from sleep subsequent to initial slumber.

Melatonin and CBT

The research identified that there was insignificant variation in the overall wake time (0.079 minutes; 95.5% CI, 7 to 6 minutes) or awakenings frequency (0.1%; 95.5% CI, 0.4 to 0.2) between children who were administered prolonged-release melatonin for a duration of 13 weeks and those who were given a placebo. In the Class II trial, the assessment of wake after sleep onset (WASO) was conducted using actigraphy, while the measurement of night awakenings was performed using the Children's Sleep Habits Questionnaire Night Wakings (CSHQ-NW) subscale. This trial also involved the melatonin administration and family-oriented cognitive-behavioral therapy (CBT). Among the children, there was a statistically significant difference in wake after sleep onset (WASO) between the combined treatment and placebo groups at 12 weeks (mean difference: 40.46; 95.0% confidence interval, 25.03 to 55.89). Comparable decreases in wake after sleep onset (WASO) were observed in both the melatonin and placebo cohorts of children (relative mean difference: 27.9 minutes; 95.5% CI, 44 to 11).

The administration of cognitive-behavioral therapy (CBT) as a standalone intervention did not yield significant improvements in wake after sleep onset (WASO) when compared to the administration of a placebo. The mean difference in WASO between the two groups was -8.98 minutes, with a 95.0% confidence interval ranging from -26.78 to -8.82. The 12-week CSHQ-NW ratings of all three therapy groups were found to be superior to those of the placebo group. The combination therapy group had a relative mean difference of 3 (95.0% CI, 3.8 to 3.0), the melatonin single group had a mean difference of 2.8 (95.0% CI, 3.3 to 2.4), and CBT single group had a mean difference of 0.8 (95.0% CI, 1.3 to 0.4). The findings of Class II crossover trial indicated that there was no statistically significant distinction in the frequency of night awakenings (NW), as described by contributors, during weeks during which they were administered melatonin (2-10 mg/d) and the weeks during which they obtained placebo (relative mean difference: 0.11; 95.0% CI, 0.27 to 0.07).

The aforementioned assumptions were utilized in random-effects meta-analyses. In the comparison between melatonin and placebo, no statistically significant differences were observed in wake after sleep onset (WASO) (12 minutes; 95.0% confidence interval (CI), 40.2 to 143; $I^2 = 88\%$) or awakenings number (0.1; 95.0% CI, 2.3 to 0.04; $I^2 = 0.001\%$).

Parent-based sleep education III

There was no statistically relevant distinction observed between categories that had parental involvement and those that did not in the Class II instructional pamphlet research. This conclusion was based on actigraphy data, which showed a minimal difference in 2-weeks scores (1 minutes; 95.0% CI, 17.97 to 18.97) and an average change variation of 8 minutes (95.0% confidence interval 21 to 4). A Class II research was conducted to compare the effectiveness of group and individual sleep education. The study found no significant variation in the wake after sleep onset (WASO) measured by actigraphy between parents who received individual sessions and those who participated in a group setting. The relative mean difference in WASO at 4 weeks was 1 minute (95.0% CI, 10.25 to 12.25), and the variation in the average change was 2 minutes (95.0% confidence interval, 7.66 to 2.86).

Weighted blankets

The evaluation of sleep disruption in the weighted blanket crossover research involved the utilization of four distinct methodologies (Actigraphy Class II and diary outcomes Class III). The actigraph device was utilized to capture the frequency of awakenings experienced by the children, while also quantifying their wake after sleep onset (WASO). Additionally, the sleep diary was employed to document the proportion of nights per week during which awakenings occurred, as well as to record the average duration of WASO. When conducting a comparison between days of utilizing the weighted blankets and days of utilizing the control blankets, no significant differences were observed in Wake After Sleep Onset (relative mean difference: 2 minutes; 95.0% CI, 9.50 to 4.50 or the awakenings number (relative mean difference: 0.21; 95.0% confidence interval, 1.1 to 0.7) as measured by actigraphy. There were insignificant variations observed over diagnoses on the basis of nights' percentages with about a single awakening (0.01; 95.0% confidence interval, 0.1 to 0.04) or mean period of considering being awake (relative mean difference: 0 minutes; 95.0% confidence interval, 1.40 to 1.42), as assessed through the use of sleep diaries.

STS mattress initiative

During the STS mattress initiative crossover trial, actigraphy data collected over a period of two weeks indicated that the mean wake after sleep onset (WASO) was 18.79 minutes when technology was turned off and 17.85 minutes when technology was turned on. The difference in mean WASO between the two conditions was 0.94 minutes, with a 95.0% confidence interval ranging from 1.912 to 0.032 minutes. Similarly, the sleep diary data revealed that the mean WASO was 0.13 minutes when technology was off and 0.12 minutes when technology was on. The difference in mean WASO between the two conditions was 0.01 minutes, with a 95.0% confidence interval ranging from 0.043 to 0.023 minutes. Importantly, neither the actigraphy nor the sleep diary data showed any statistically significant differences in WASO between the two conditions.

Total sleep time

The term “total sleep time” alludes to the time of sleep in a particular timeframe of the night. A lower total sleep time (TST) has been found to be correlated with prolonged sleep onset latency (SOL), nocturnal awakenings, and early morning awakenings. Instead of referencing sleep duration recommendations specific to different age groups, the studies included in this analysis compare the effects of therapy on total sleep time (TST) changes.

Melatonin and CBT

The children enrolled in the Class I research who obtained prolonged release melatonin demonstrated a significant increase in total sleep time (TST) over a period of 13 weeks. The rise in TST was measured to be 32.43 minutes (95.0% CI, 2.48-62.38) based on the data recorded in their diaries. The duration of total sleep time (TST) at the 12-week mark exhibited a statistically significant increase in both the melatonin and family-based cognitive-behavioral therapy (CBT) treatment groups when compared to the placebo group. The relative minimum difference was found to be 88.78 minutes (95.0% confidence interval: 70.3 to 107.3). Particularly, the melatonin group experienced an increase of 64 minutes (95.0% confidence interval: 46.1 to 83.6), whereas the CBT group observed an increase of 28.90 minutes (95.0% CI: 6.53-51.27). At the 12-week mark, the groups receiving melatonin exhibited similar results compared to the placebo group on the CSHQ-SD (CSHQ-Sleep Duration) subscale results that have a score range of 3-9.

The combination treatment group had a relative mean difference of 2.01 (95.0% confidence interval, 2.6 to 1.5) whereas the melatonin group had relative mean difference of 1.58 (95.0% CI, 2.13 to 1.03). When conducting a comparison between the group that received only cognitive-behavioral therapy (CBT) and the group that received a placebo, no statistically relevant variation was witnessed in scores of CSHQ-SD (Children's Sleep Habits Questionnaire-Sleep Disturbance) (relative mean difference: 0.3; 95.0% confidence interval, 0.3 to 0.9). The Class II crossover trial results indicated that melatonin had a greater effect on total sleep time (TST) in children and adolescents compared to placebo (mean difference: 52 minutes; 95.0% confidence interval: 19.2 to 5.5). According to a random-effect meta-analysis, children treated with ASD and experiencing sleep disruption exhibited a significantly increased total sleep time (TST) of 52 minutes (95.0% confidence interval, 33.1 to 72.2; $I^2 = 39.0\%$) when administered melatonin, as compared to those who received a placebo.

Daytime behavior

Melatonin

In a Class II crossover trial, it was observed that the administration of melatonin for several weeks resulted in lower overall DBC scores compared to the use of a placebo (relative mean difference: 6.0; 95.0% CI, 12.0 to 0). The sole notable disparity among the subscale scores was observed in the domain of communications (relative mean difference: 1.59; 95.0% CI, 3.2 to 0.1).

Weighted blankets

There was statistically insignificant disparity observed in the overall ABC score (2.3; 95.0% CI, 5.75 to 1.15) between the instances when participants utilized the weighted blanket and the instances when they utilized a standard blanket during the Class II weighted blanket experiment. The results of the subscales exhibited no variations.

STS mattress initiative

There were no significant changes observed in the ABC scores during the 2-week periods of both technology usage and non-usage in the STS mattress initiative crossover research. The study was classified as Class III for questionnaire data. The mean difference was 6.8, with a 95.0% confidence interval ranging from 14.8 to 1.3. The STS mattress system integrates resonators within the bed's foundation, enabling the playback of an audio file and subsequent translation into a tactile experience. The independent manipulation of the volume and vibrational intensity of the resonators can be achieved by utilizing a distinct control apparatus that is interconnected with the resonators. In this study, participants were issued with a chance to exert control over the auditory and tactile aspects of the background music, with a particular focus on parents and, when possible, their children.

This control encompassed the ability to adjust both the volume and intensity of the vibrations experienced. The utilization of headphones was discretionary for children. The audio file can be played back by utilizing either headphones or a pair of external speakers. In the event that the young individual did not make a selection, the resonators would

continue to emit a faint auditory disturbance in the surrounding environment. The audio file included the copyrighted electronic composition STS ohm due to its recognized ability to induce a calming and pleasant effect. Upon completion of the study, participants who were parents were requested to provide feedback regarding their usage of audio in combination with vibration, vibration alone, or both modalities.

Frazier, Krishna, Klingemier, Beukemann, Nawabit, and Ibrahim [18] incorporated an introductory phase on mattress technology and the integration of actigraphy-watch accommodation within a randomized crossover design. A two-week period was designated for the collection of sleep data for each group. Concealing the usage of the technology from parents, children, or the study coordinator was not feasible in a predictable manner. The actigraphy data was evaluated by a sleep technician and a pediatric sleep medicine doctor, both of whom were blinded to the status of the STS mattress. The assessment of inclusion/exclusion criteria and study eligibility took place during the screening appointment. Individuals who satisfied the specified criteria were invited to participate in a preliminary assessment. During the visit, participants were instructed on the utilization of the STS mattress technology and the watch for monitoring their children. Furthermore, they were provided with practical opportunities to engage with all three components.

The study coordinator dedicated time to engage in a discussion and provide a practical demonstration of desensitization techniques that could potentially be employed to enhance the ability to tolerate watching, if deemed necessary. The participants were given a lead-in period of 5-7 days following the baseline visit. In some cases, this period was extended to a maximum of 2 weeks for children who experienced initial difficulties in adapting to the STS mattress technology or wearing the actigraphy watch. If a child exhibited an adverse reaction to either the watch or the STS mattress technology, they were excluded from the trial. If the child demonstrated proficiency in utilizing the watch or mattress technology, the family was assigned an STS mattress order (on/off vs. off/on) through a random selection process, and provided with detailed instructions on its implementation. The commencement of the initial therapy group took place during the evening of the following day.

Following random assignment, participants diligently maintained a daily actigraphy and sleep journal. In instances where data gaps were present, we employed a method of calculating the mean value of the available data points over the entire duration of the two-week period. The Self-Perception Profile (SSP), the Family Involvement in School and Homework Questionnaire (FISH), and the Children's Sleep Habits Questionnaire (CSHQ) were administered at the commencement, midpoint, and culmination of the research endeavor. The initial assessment of the patient's condition was established based on the screening values obtained from these instruments. Measurements were obtained at three different time points: baseline, midpoint (also known as crossover), and final. The surveys at each interval were completed by a single parent consistently.

IV. CONCLUSION

The lack of definitive clinical test (like blood tests) for Autism Spectrum Disorder (ASD) poses challenges in the process of diagnosis. When conducting a diagnosis on a child, medical professionals take into account both the child's behavior and their level of development. In specific instances, ASD can potentially be detected as early as 18 months of age. It is widely believed that a professional diagnosis conducted at the age of two is highly accurate. However, a conclusive diagnosis is frequently delayed until the child reaches a more advanced age. The diagnosis of certain conditions may not occur until an individual reaches adolescence or adulthood. Due to the presence of this delay, people with ASD may encounter challenges in receiving prompt and necessary interventions. Melatonin supplementation, when administered in conjunction with or without cognitive behavioral therapy, has been found to improve various sleep-related outcomes. The current body of research lacks substantial evidence supporting the efficacy of alternative therapies. There appears to be a lack of evidence supporting a correlation between sleep quality and the utilization of various interventions, such as a parent education booklet, parental sleep education (either in a one-on-one or group setting), weighted blankets, or STS mattress technology. The limited availability of evidence from a singular Class III trial precludes us from making definitive assertions regarding the effectiveness of sleep-specific behavioral training for parents.

The Sound-to-Sleep (STS) mattress system integrates resonators within the bed's foundation, enabling the playback of an audio file and subsequent translation into a tactile experience. The independent manipulation of resonator volume and vibrational intensity can be achieved by utilizing a distinct control device that is interconnected with the resonators. In this study, participants were allocated the opportunity to exercise control over the auditory and tactile stimuli, specifically the music playback, volume, and intensity of vibrations, with a particular focus on parents and, when possible, their children. The utilization of headphones was discretionary for children. The audio file can be played back by utilizing either headphones or a pair of external speakers. In the event that the young individual does not make a selection, the resonators would continue to emit a low level of auditory disturbance in the surrounding environment. The audio file included the copyrighted electronic composition STS ohm due to its recognized ability to induce a soothing and enjoyable experience. At the conclusion of the study, the parents were surveyed regarding their utilization of audio with vibration, vibration in isolation, and any possible combination of the two.

Data Availability

No data was used to support this study.

Conflicts of Interests

The author(s) declare(s) that they have no conflicts of interest.

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Ethics Approval and Consent to Participate

Not applicable.

Competing Interests

There are no competing interests.

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