Chapter 5
Sleep Laboratory Tests

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Abstract The spectrum of childhood sleep–wake disorders extends from sleep-disordered breathing to parasomnia, hypersomnias, and circadian rhythm disorders. Clinical history and examination help select the most appropriate diagnostic test. Nocturnal polysomnography is the gold standard for obstructive and central sleep apnea, while the multiple sleep latency test combined with polysomnography is utilized for the investigation of hypersomnias. Nocturnal seizures may mimic parasomnias; hence, extended electroencephalographic monitoring may be required for investigating some nocturnal episodic phenomena. Practice parameters and evidence-based reviews on indications for polysomnography in children have been recently published. Actigraphy and sleep logs are helpful in investigating suspected circadian rhythm sleep disorders.

Keywords Nocturnal polysomnography • Multiple sleep latency test (MSLT) • Actigraphy • Sleep apnea • Hypersomnia • Parasomnias • Actigraphy

Introduction

Sleep disorders of infants and children are challenging to diagnose because of their diverse etio-pathology and changes in predilection of some disorders to specific age and developmental stage of the patient. Further, the clinical history varies in accuracy depending upon the perceptions, communication ability, and biases of the patient, or parent. Also, normal values for parameters of sleep–wake function tend to change with maturation of central nervous system (CNS) and respiratory control mechanisms. Clinical history and examination are often unable to enable accurate

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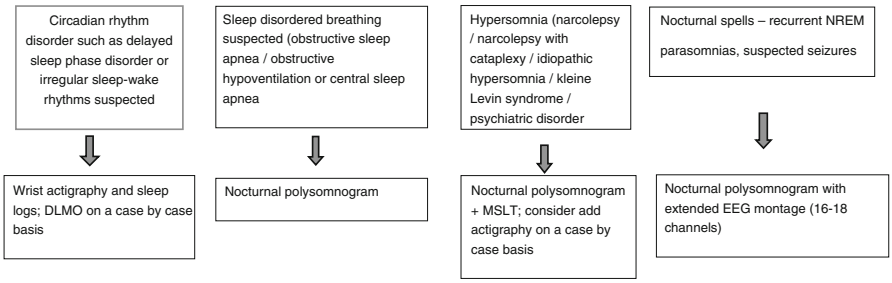

Fig. 5.1 Matching sleep–wake disturbance to sleep laboratory tests

diagnosis. Consequently, the sleep specialist has to periodically resort to laboratory tests to confirm the diagnosis. The nature of the sleep laboratory test and specific, step-by-step instructions pertaining to the actual performance are heavily dependent upon the accuracy of the sleep history. Technological advances in sleep–wake monitoring systems hardware and software, combined with publication of adult and pediatric polysomnogram scoring guidelines [1], practice parameters on indications for polysomnography [2, 3], and older reviews of this topic [4] underscore the need for its reassessment. This chapter aims to provide an overview of tests commonly employed in the practice of pediatric sleep medicine. Figure 5.1 helps to match sleep–wake symptoms with the appropriate type of investigation.

Nocturnal Polysomnography

Technical Aspects

The test consists of the recording of multiple physiological parameters during sleep. Most often this includes two to three channels of electroencephalogram (EEG), eye movements, chin and leg electromyogram (EMG), oronasal airflow, nasal pressure, thoracic and abdominal respiratory effort, oxygen saturation, and end-tidal carbon dioxide. The scalp EEG montage generally consists of C4-M1, F4-M1, plus O2-M1. The International 10–20 system is utilized for appropriate placement of EEG electrodes over the scalp [5]. Backup electrodes are placed at similar locations over the opposite scalp sites. Electrodes are fixed using collodion or paste while ensuring that the electrode impedance is kept low, i.e., below 5 kΩ. This helps to minimize picking up of extraneous artifact by the electrodes. The centrally placed EEG electrodes help to sample vertex sharp transients and sleep spindles, while occipital leads help to distinguish the waxing and waning amplitude alpha rhythm of wakefulness from the alpha to theta transition that is typical of stage N1 sleep as well as the predominant delta rhythm of stage N3, which is usually <4 Hz and >75 uv amplitude. In case of suspected nocturnal seizures, placement of a minimum

16-channel EEG montage is recommend. The usual sensitivity for EEG recording is 7 uv/mm, though it may need to be decreased to 10–15 uv/mm if the amplitude of the activity is too high, as happens in preschool-age children. Eye movements are generally recorded using a left outer canthus–right outer canthus montage, with the electrodes being placed in a slightly oblique plane in order to capture both horizontal and vertical eye movements. The transition from wakefulness into N1 sleep is associated with the onset of slow rolling eye movements, while transition to REM sleep is associated with rapid eye movements. Monitoring of end-tidal CO2 is essential in all patients to capture hypoventilation. If the EtCO2 sensor (it yields breath by breath values) is not tolerated by infants and toddlers due to anxiety or increased perioral sensitivity, a transcutaneous CO2 sensor can be utilized (this yields a trended value). For sampling the chin EMG, 2–3 electrodes need to be affixed under the chin. The absolute amplitude of the EMG is not relevant, but the relative changes in amplitude help distinguish wakefulness, NREM sleep, and REM sleep from each other.

Data are recorded and stored in a computerized polysomnogram system which is composed of preamplifiers for both alternative current (AC) and direct current (DC) input. The AC channels are useful for recording EEG, EMG, and eye movements, whereas the DC channels help record slow biopotentials like respiratory effort. Sleep is scored in 30 s epochs by the attending technologist, with subsequent verification of the scored record by a certified polysomnographer. Nap sleep studies are not recommended as the quantity and type of sleep sampled are variable. Only technician-attended, all night sleep studies are recommended. The technical guidelines for scoring sleep and sleep-related events have been published by the American Academy of Sleep Medicine.

For infants of age 2 months or less, sleep can be scored simply as active or quiet sleep, i.e., REM and NREM sleep. A low-voltage, irregular pattern is associated with active sleep while a high-voltage, slow pattern is characteristic of quiet sleep. After age 2 months, the standard criteria that are utilized in children and adults can be applied, with breakdown of NREM sleep into N1, N2, and N3 categories. For details about sleep scoring, the reader is again referred to the scoring manual of the American Academy of Sleep Medicine [1]. Parameters scored in polysomnography include start time, stop time, total time in bed, total sleep time, sleep efficiency, percentage of time spent in the various sleep stages, arousals per hour of sleep, percentage of arousals related to respiratory events, total number of apneas and hypopneas with attention to occurrence in REM or NREM sleep and relationship to body position, oxygen saturation nadir and mean, EtCO2 nadir, high and mean, percent of time with EtCO2 greater than 50 mm, frequency of periodic limb movements, and comments about any unusual events observed in the simultaneous video recording. A flattened contour on the nasal pressure tracing may be indicative of the upper airway resistance type of obstructive sleep apnea. The polysomnogram report should provide data in a tabular form, coupled with narrative about the overall impression and recommendations of the polysomnographer.

Indications

The definitions of levels of evidence utilized by the AASM and how emphatic the recommendation are for PSG in specific sleep disorders are shown in Table 5.1 [refs 2–4]. The investigation of sleep-disordered breathing is a major indication for PSG (Standard). This includes habitual snoring, suspected obstructive sleep apnea, obstructive hypoventilation, central sleep apnea, and congenital central hypoventilation syndrome. Monitoring of end-tidal carbon dioxide (EtCO2) or, if this is not available, transcutaneous carbon dioxide is mandatory for assessing hypoventilation – this is a major component of sleep-disordered breathing in Down syndrome, Prader–Willi syndrome, obesity, neuromuscular disorders, and kyphoscoliosis. Reference values for respiratory parameters differ from those of adults. For instance, the duration of obstructive apneas in children is generally in the 5–10 s range (two-breath duration), whereas in adults, scored obstructive apnea events are invariably 10 s or longer in duration. The investigation of excessive daytime sleepiness, including suspected narcolepsy, requires a PSG followed the next day by the multiple sleep latency test (MSLT). This recommendation is also at Standard level (Table 5.1). A key tenet in narcolepsy is that there is excessive daytime sleepiness despite adequate sleep duration at night. PSG is also indicated in nonverbal children with suspected restless legs syndrome/periodic limb movement disorder in order to document

Table 5.1 AASM level of recommendation for polysomnography and sleep disorder

Level	Definition	Disorder
Standard	This is a generally accepted patient care strategy that reflects a high degree of clinical certainty and generally implies the use of level 1 evidence or overwhelming level 2 evidence	Periodic limb movement disorder Narcolepsy Diagnosis of obstructive sleep apnea, to evaluate for residual obstructive sleep apnea after adeno-tonsillectomy; follow-up of children on chronic PAP support, for PAP titration
Guideline	This is a patient care strategy that reflects a moderate degree of clinical certainty and implies the use of level 2 evidence or a consensus of level 3 evidence	NREM parasomnias, epilepsy, nocturnal enuresis, assessment of sleep-related hypoventilation, apparent life-threatening event
Option	This is a patient care strategy that reflects uncertain clinical use and implies either inconclusive or conflicting evidence or conflicting expert opinion	Restless legs syndrome, when supportive information is needed for diagnosis; hypersomnia from causes other than narcolepsy; follow-up of children needing oral appliance or rapid maxillary expansion; patients on mechanical ventilation for adjustment of their machine settings; tracheostomy patients being considered for decannulation, if there is suspicion of a sleep disorder in cystic fibrosis/asthma/kyphoscoliosis/pulmonary hypertension

presence of periodic limb movements in sleep. In this regard, preschool-age children are often candidates for PSG. Reference values for the periodic limb movement index in children have been extrapolated from adults at 5 or less. With regard to parasomnias, PSG is not indicated routinely as clinical history may be sufficient to make a diagnosis. If there are recurrent parasomnia-like events or if one is unable to exclude the diagnosis of nocturnal seizures, however, PSG is indicated. The investigation of nocturnal seizures requires the utilization of a 16–18 channel EEG montage. REM sleep behavior disorder may accompany daytime sleepiness in children with narcolepsy–cataplexy; hence, when PSG is being conducted for diagnosing narcolepsy, it is important to carefully examine segments of REM sleep for the presence of the electrophysiological marker of RBD, i.e., persistence of muscle tone during REM sleep, which is also called REM sleep without atonia.

Limitations

PSG is the gold standard procedure for the investigation of many childhood sleep disorders. It is however an expensive and labor-intensive tool. Patient and parent anxiety about the procedure may affect variables such as sleep latency, REM latency, and sleep efficiency. There might also be some degree of night to night variability in parameters like periodic limb movement index. Alternative strategies for diagnosing obstructive sleep apnea include home overnight oximetry. This procedure has limited sensitivity, however, and may be positive only in severe cases. Consequently, if oximetry is noninformative in a child with suspected OSA, one might still need to resort to PSG. The Pediatric Sleep Questionnaire (PSQ) and the Sleep Disturbance Scale for Children (SDSC) may be applied for screening for sleep-disordered breathing [6, 7], but PSG is unfortunately still necessary to confirm the diagnosis.

Multiple Sleep Latency Test (MSLT)

In combination with the nocturnal polysomnogram, the MSLT forms the gold standard in the assessment of daytime sleepiness in both children and adults. This applies especially to the diagnosis of narcolepsy and idiopathic hypersomnia. The strengths of the test lie in its intuitive design (sleepy individuals are likely to fall asleep more quickly in the daytime than those who are not sleepy), its reliability, and the availability of normative data across various ages [8].

The lower age limit at which one can apply the MSLT seems to be 5–6 years [9]. Application of the MSLT in children younger than this age is difficult because physiological daytime napping is common in preschool-age children. To the extent possible, the total sleep time on the preceding night's PSG must be similar to the sleep duration at home. As sleep loss in the days prior to the MSLT may influence the test findings, the parents should be advised to keep a log of the patient's sleep–wake

schedule for 1–2 weeks prior to the MSLT. Alternatively, wrist actigraphy for 1–2 weeks prior to the PSG and MSLT can be utilized to gauge sleep time and sleep schedules at home. Medications that can influence sleep, such as stimulants/antidepressants/benzodiazepines/antihistamines, should be discontinued at least 2 weeks prior to the test. Long-acting selective serotonin reuptake inhibitors like fluoxetine that suppress REM sleep may need to be stopped for 4–6 weeks prior to the PSG and MSLT. The decision to stop antidepressants for the purpose of obtaining valid PSG and MSLT should be carefully thought out after weighing the risks and benefits. A discussion with the prescribing physician is also indicated in this regard. The patient's general physical examination should include a Tanner staging of sexual development as normal values for the mean sleep latency in children vary according to individual stages (Table 5.2; [10]). The test consists of the provision of four or five daytime nap opportunities at two hourly intervals, e.g., 0900, 1100, 1300, 1500, and 1700 h, during which the EEG, chin EMG, and horizontal as well as vertical eye movements (using at least two channels) are monitored. The time constant for the electrooculogram should be long enough to allow for the recording of slow, rolling eye movements seen at the onset of N1 sleep (250 ms). Electrode impedances should be below 5 kΩ.

At the designated hour, usually starting 2 h after the final morning awakening from the PSG, the lights are turned off, and the patient is encouraged to relax, close eyes, and to try to fall asleep while the electrophysiologic parameters are being monitored. For each nap, the time from "lights out" to sleep onset is termed the sleep latency. The nap is continued for 15 min after sleep onset. Thus, theoretically, if the patient does not fall asleep in the nap till min 19, the test is continued for a total of 34 min (15 + 19) from the time of commencement of the nap recording. If the patient does not fall asleep by min 20, the nap opportunity is terminated, the lights are turned on, and the sleep latency is designated as 20 min. An identical protocol is followed during all four to five nap opportunities. The patient is kept awake in between the nap opportunities. The assistance of the parents is helpful in this regard. The mean sleep latency is the average of the sleep latency derived from all five naps. Normal values for the pediatric MSLT that have been adapted from a single night's polysomnogram are listed in Table 5.2. Mean sleep latencies for prepubertal children are higher than those of adults, approximating 16–18 min. The

Table 5.2 Reference values for the MSLT

Tanner stage	General corresponding age (years)	Mean sleep latency	Standard deviation
Stage 1	<10	18.8	1.8
Stage 2	10–12	18.3	2.1
Stage 3	11.5–13	16.5	2.8
Stage 4	13–14	15.5	3.3
Stage 5	>14	16.2	1.5
Older teenagers	>14	15.8	3.5

Data from Carskadon [10]

MSLT is however well suited for diagnosing narcolepsy, in which the mean sleep latency is invariably below 8 min [3]. Daytime sleep latencies for MSLT naps parallel the circadian drive for wakefulness, with increased sleep propensity in the afternoon (low sleep latency).

The MSLT also helps evaluate whether the transition from wakefulness into sleep is into REM or NREM sleep. A sleep-onset REM period (SOREMP) is defined by the occurrence of REM sleep within 15 min of sleep onset. About 80 % of patients with narcolepsy show two or more SOREMPs during the MSLT [11]. If the patient manifests a SOREMP on the polysomnogram obtained on the night prior to MSLT, one needs to document only one SOREMP on the latter study for making a diagnosis of narcolepsy [12]. False-negative results may occur in the early stages of childhood narcolepsy, when the patient may manifest daytime somnolence documented by reduced mean sleep latencies, but only 0–1 SOREMPs. Further, one must also recognize that otherwise healthy teens may at times show a SOREMP during the first nap of the MSLT.

There is level 1 evidence regarding the clinical utility of MSLT in the diagnosis of narcolepsy. With regard to hypersomnia disorders other than narcolepsy, such as idiopathic hypersomnia or Kleine–Levin syndrome, however, there is less available evidence. Nevertheless, the MSLT is still utilized in diagnosis of these disorders based on empiric, clinical rationale. In adults, the sensitivity of the MSLT in the diagnosis of narcolepsy in adults has been reported to be around ~61 % [13]. There was no major difference in the diagnostic sensitivity of the test between patients who manifested narcolepsy with cataplexy versus those having narcolepsy without cataplexy. The diagnostic specificity for narcolepsy in adults has been reported to be ~94 % [13] when two or more SOREMPs are present. In children, the diagnostic sensitivity of the MSLT for the diagnosis of narcolepsy is 79–100 % [3, 4].

Merits and Limitations of the MSLT

One advantage of the MSLT is that it has been reliably validated as a tool for assessing sleep propensity in several conditions such as sleep loss [8, 10] and sleep disruption [14] and the effects of hypnotics and alcohol [15, 16]. It measures the propensity for daytime sleepiness at multiple times of the day and provides numerical values which correlate with the level of sleepiness. A disadvantage is that it cannot accurately assess the effects of treatment, e.g., if there is a reliable increase in sleep latency after starting stimulant medication for narcolepsy treatment. Also, while one can control external variables like noise and light that impact sleep latency, the MSLT can in no way control for intrinsic variables that impact sleep latency such as anxiety or emotional disturbance. The issue of whether the MSLT in children should consist of four naps or five naps has not been adequately studied. Based on clinical experience, however, it is this author's opinion that a four-nap test is generally sufficient to diagnose narcolepsy.

Maintenance of Wakefulness Test (MWT)

The MWT is the mirror-image opposite of the MSLT. It measures the ability of the patient to stay awake in a darkened, quiet environment during the daytime [17]. Electrodes are applied for monitoring the EEG, eye movements, and chin EMG in a manner identical to the MSLT. The patient is provided five nap opportunities at two hourly intervals. The patient is advised to take the usual sleep-related medications in the morning, including stimulants. The MWT has been found useful in adult subjects in the assessment of effects of medications on sleepiness; for example, in the follow-up of patients with narcolepsy for quantifying the level of improvement following therapy with stimulant medications, or to determine the presence of a "carryover" effect of daytime sleepiness after nighttime hypnotic administration. In the management of children and adolescents with narcolepsy, the test may provide an estimate of the degree of residual sleepiness despite taking medications such as stimulants. Information derived from the MWT may help in adjustment of the total daily dose or of the time of administration of narcolepsy-related medications [18]. On other occasions, teens with chronic daytime sleepiness may wish to drive, for which this test may provide guidance. While the driving issue is best dealt with on a case by case basis, the clinician may utilize MWT data to help decide whether or not it will be safe for the patient to drive (author's opinion).

Actigraphy

This miniature device is about the size of a large wristwatch and can be conveniently strapped around the wrist. It consists of an acceleration sensor that translates physical motion into a numeric representation [19]. This numeric representation is sampled at regular intervals, e.g., every 0.1 s, and aggregated at a constant interval or epoch. Ambient illumination can also be recorded. The epoch length is usually 1 min. The stored movement data may be transferred to a computer for display, scoring, interpretation, and printing of results. By convention, the device is usually strapped to the non-dominant wrist. For deriving meaningful inferences about sleep–wake schedules, the duration of actigraph recordings has to be 1–2 weeks. Actigraphy is able to provide reliable data about average values of total time in bed, total sleep time, sleep efficiency, and sleep onset and offset times and if there has been excessive muscle activity during sleep.

Major indications for actigraphy include the investigation of insomnia and suspected circadian rhythm sleep disorders, e.g., delayed sleep phase syndrome. In patients with suspected narcolepsy, the actigraph recording can help ascertain whether there was adequate sleep at night prior to conducting PSG and MSLT. Actigraphy is also indicated for the investigation of sleep–wake problems of children with neurodevelopmental disorders such as autism and attention deficit hyperactivity disorders and to document treatment responses [20]. Conventional

polysomnography may be difficult to obtain in this patient population due to lack of cooperation. Sadeh et al. [19] have found that the minute-by-minute agreement between actigraphic scoring and polysomnographic scoring was 90.2 % for normal adults and 89.9 % for children [21].

Utility and Limitations

Actigraphy is an excellent tool for the investigation of circadian rhythm disorders and insomnia. Advantages include its noninvasive nature and the ability to gather longitudinal information about sleep–wake function in the home environment over a 2–3-week period. It is relatively inexpensive when compared to nocturnal polysomnography. Actigraphy is however unable to reliably differentiate REM from NREM sleep or assess sleep-disordered breathing. In-depth information about sleep architecture, e.g., percentage of time spent in various sleep stages or sleep electroencephalographic events, also cannot be determined.

Dim Light Melatonin Onset (DLMO)

Melatonin is a major sleep-inducing and sleep-maintaining hormone that is produced in the pineal gland following sympathetic neural activation by the suprachiasmatic nucleus (SCN) of the hypothalamus. The SCN, in turn, is responsive to activation by light input from the retinohypothalamic pathway. There is generally good correlation between serum and salivary levels of melatonin. A rise in serum/salivary levels of melatonin usually occurs 2–3 h prior to sleep onset (dim light melatonin onset or DMLO) and signals sleep onset. DLMO is the most reliable measure of the timing of the circadian clock [22, 23]. The melatonin secretion rhythm is not affected by the rest–activity cycle, prior sleep, activity, or stress [24]. Melatonin has low levels during the daytime. Onset of darkness brings on a gradual rise in melatonin secretion. Typically, salivary or serum samples are collected every 30 min for 6 h prior to sleep onset. As melatonin secretion is very sensitive to perturbation by ambient light exposure, the sample gathering is done in dim light (less than 30 lx). The samples are analyzed using radioimmunoassay techniques. The time of the clock at which there is a rise in melatonin levels by two standard deviations above the mean of three daytime values is termed DLMO [25]. The significance of DLMO is that it is the most reliable measure of activity of the SCN. A disadvantage of the DLMO testing process is that it requires considerable patient cooperation as well as involvement of sleep laboratory technical staff if the patient has a neurodevelopmental disability. DLMO is indicated in the investigation of circadian rhythm disorders such as delayed sleep phase syndrome, advanced sleep phase syndrome, irregular sleep phase syndrome, and irregular sleep–wake rhythms. Disorders in which there is inversion of melatonin secretion, with low levels at night

and higher secretion during the daytime, such as Smith–Magenis syndrome, may require round-the-clock sampling. Based upon longitudinal studies of DLMO, Carskadon et al. have lately raised an intriguing possibility of a decline in the pineal secretion of melatonin around puberty [26]. This might be one of the mechanisms underlying the sleep-onset phase delay that occurs in adolescents.

Sleep Survey Instruments

There are several excellent, clinically validated survey instruments that can be utilized in clinical practice and clinical sleep research. Only a few sleep survey instruments are reviewed here. Detailed reviews of the approximately 70 published survey instruments are available [27, 28]. Based upon the nature of patients in the practice, the sleep clinician should become familiar and comfortable with use of at least two to three survey instruments. In this era of rising healthcare costs where expensive and labor-intensive tools like PSG have limited in access, it is critical for the clinician to utilize survey instruments when possible. Assessment of treatment outcomes is also facilitated by the longitudinal use of sleep questionnaires.

The *Children's Sleep Habits Questionnaire* (CSHQ) is a 45-item validated questionnaire that asks parents to respond to questions about sleep–wake function of their child in the preceding 2 weeks. It is applicable to children between 4 and 10 years of age [29]. The eight domains of sleep disturbance that are addressed by CSHQ include bedtime resistance, sleep-onset delay, sleep duration, sleep anxiety, night awakenings, parasomnias, breathing disturbance, and daytime sleepiness. Responses are categorized as rarely, sometimes, or usually. Scores of 41 or greater correlate with a sleep disorder. The internal consistency of this questionnaire in a community sample of 4–10 year olds was 0.36–0.70, while the test–retest reliability over a 2-week period was 0.62–0.79 [29].

The *Sleep Disturbance Scale for Children* [7] is applicable to children 5–15 years of age. It is completed by the parent. Time consumed for survey completion is about 10 min. There are 27 items, with responses arranged on a 1–5 Likert scale. It is useful for evaluating insomnia, hypersomnia, parasomnias, and sleep-related respiratory disturbances. The questionnaire was developed after study of a large, predominantly urban, working, and middle-class Caucasian population from four public schools in Rome. It has excellent internal reliability (Cronbach's α 0.79 in a community sample and 0.71 in sleep disorder subjects). Test–retest reliability is also very good ($r = 0.71$).

The *Pediatric Sleep Questionnaire* [6] was developed for use in children ages 2–18 years. It's most commonly used 22-item sleep-disordered breathing subscale has sensitivity of 0.85 and specificity of 0.87 for sleep-disordered breathing. The scale is completed by the parent. The sleep-disordered breathing subscale takes 5–10 min for completion. Reference values for this scale are <0.33, and scores higher than this are generally associated with childhood obstructive sleep apnea.

The *Pediatric Daytime Sleepiness Scale* [30] is a self-report questionnaire, applicable to children 11–15 years of age. It was validated in a sample of 450, sixth to eighth grade students at a middle school, with 90 % of the sample being white, reminder being a mix of other ethnicities. It has eight items that are scored on a 0–4 Likert scale, with scores higher than 16–18 indicative of sleepiness. It has good internal consistency (Cronbach's α 0.81)

Conclusions

Sleep laboratory tests yield accurate information and help guide management when they are integrated into the overall clinical assessment along with history and physical examination. Survey instruments are valuable in baseline and longitudinal assessment and in assessing impairments in the quality of life. Though there has been a shift toward unattended in-home polysomnography in adults, the indications, utility, and limitations of home sleep studies in children need study. The MSLT remains the gold standard test for study of daytime sleepiness. It is likely that with advances in the biomedical field, there will be further qualitative improvements in the assessment of sleep–wake function of children.

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