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CASE REPORT

Actigraphy-based Sleep Parameters and Rest-activity Circadian Rhythm in a Young Scoliotic Patient Treated with Rigid Bracing: A Case Study

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The correct expression of circadian rhythmicity, together with a good sleep behavior, are key factors for the body homeostasis. Rest-activity circadian rhythms (RARs†) are involved in the control of the sleep-wake cycle and altered RARs could lead to a compromised health status. Therefore, we aimed to investigate the existence of RAR and to study actigraphy-based sleep behavior in a 14-year-old male patient affected by severe idiopathic scoliosis and treated with a rigid brace 23 hours per day. RAR and sleep parameters were studied through actigraphy for seven consecutive days in July 2018. The mean cosinor analysis revealed the presence of a significant RAR ($p < 0.001$), specifically: the percentage of rhythm was 23.4%, the mean MESOR was 84.6 Activity Count (AC), the amplitude registered a mean value of 74.4 AC's, and the acrophase occurred at 17:56 h. The subject reached a good sleep quantity: 507.9 ± 30.2 minutes of Time in Bed with a mean Total Sleep Time of 450.7 ± 20.1 minutes; Similarly, Sleep Efficiency was equal to 83.3 ± 7.2% and the Fragmentation Index was 27.3 ± 12.8%. We observed that both RAR and sleep behavior had normal trends in a 14-year-old patient treated with a rigid brace for a severe adolescent idiopathic scoliosis (AIS). Improved assessment of sleep in routine clinical practice can help to identify and manage health-related problems that could potentially affect some clinical outcomes, such as pain, mood state, and recovery process.

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†Abbreviations: AIS, Adolescent Idiopathic Scoliosis; RAR, Rest-Activity circadian Rhythm; MESOR, Midline Estimating Statistic Of Rhythm; A, Amplitude; Φ, acrophase; AC, Activity Count; PSG, PolySomnoGraphy; CI, Confidence Interval; SS, Sleep Start; SEnd, Sleep End; TB, Time in Bed; SL, Sleep Latency; SE, Sleep Efficiency; IT, Immobility Time; MT, Mobility Time; WASO, Wake After Sleep Onset; TST, Total Sleep Time; FI, Fragmentation Index.

Keywords: Brace, scoliosis, sleep, circadian rhythm, orthopedics

Author Contributions: JAV, FN, and GBa conceived the study rationale. JAV and FN conducted the data collection and JAV alone performed the statistical analysis. FN, GB, and SD recruited the patient and collected his clinical data. JAV, LG, and FN wrote the first draft of the text and all authors revised the final version of the manuscript.

INTRODUCTION

The important role of sleep in maintaining health and wellbeing is now widely recognized. Sleep can be considered a homeostatic process and it has many crucial functions related to growth, physical and cognitive development, recovery processes, and many others. [1]. The assessment of the risks and benefits associated with sleep behavior is a precondition to modify habits that are responsible for the development of pathological processes and also to prevent health-related problems [2,3]. Its relevance is also becoming increasingly recognized in adolescents and young adults; studies showed that almost 50 percent of male and female students aged 15 years old reported experiencing sleeping difficulties and not having enough sleep to be able to fully recover [4]. In addition, young subjects showed altered sleep/wake phases with a strong delay in sleep onset that often translates into sleep debt and a lower sleep efficiency [5]. It is also important to highlight that the correct expression of circadian rhythmicity is another key factor for the body homeostasis [6]. Rest-activity circadian rhythms (RARs) are involved in the control of the sleep-wake cycle [7] and they give important feedback on the activity-rest circadian patterns of many populations [8]. RARs could display some pathological features in young subjects too, *e.g.* decreased amplitude, loss of rhythm or delayed acrophase [9], and altered RARs could lead to a compromised health status [10].

Adolescent idiopathic scoliosis (AIS) is a tridimensional deformity of the spine. It is a common pathology as it affects, with a wide range of severity, as much as 1 to 3 percent of the population [11,12]. However, only around 10 percent of the diagnosed cases require treatment, and only 0.1 to 0.3 percent require surgical correction [13]. The most important parameter considered in the choice of treatment is the angle of scoliosis measured on the standing frontal radiograph, the Cobb Angle. It is a crucial parameter as it is directly correlated with the choice of the treatment [13]. The most common scoliosis treatment, depending on severity, are observation, scoliosis specific exercises, bracing, and in the most severe cases, surgery [14]. Rigid bracing is an effective therapy [15,16] mostly used for scoliosis curvature between 25° and 45° Cobb degrees [17]. Use of bracing has been proposed even for more severe curvature in patients who refuse surgical treatment [18]. Dosage is essential in brace treatment, as the number of hours of brace wear are correlated to the results of the treatment [16,19]. However, compliance is not at all guaranteed as bracing it is a demanding treatment as the patient, usually a young adolescent, is asked to wear a brace for 18 to 23 hours, and can impact the quality of life of the patient [20]. Patients, especially in early stage of the treatment, often report both physical discomfort (pain, excoriations, difficulties in breathing) and psychological issues (depressed mood, social isolation) that can both affect sleep [21].

To the best of our knowledge, no previous study objectively examined sleep and rest-activity circadian rhythm in scoliotic patients treated with non-invasive techniques. Therefore, this case study aimed to investigate the existence of RAR, describing also its characteristics (*i.e.*, MESOR, acrophase, and amplitude) and to study actigraphy-based sleep behavior in a 14-year-old patient affected by severe idiopathic scoliosis and treated with a rigid brace 23 hours per day.

CASE PRESENTATION

Clinical Presentation

The patient analyzed is a 14-year-old boy affected by severe AIS. He was recruited for the study in a tertiary outpatient clinical center specializing in conservative treatment of spinal disorders. The patient presented two primary curves, a right thoracic curve (60° Cobb angle) and left lumbar curve (63° Cobb angle) (Figure 1). He was 170 cm and 70 kg (Body Mass Index (BMI): 24.22; Tri-Ponderal Mass Index (TMI) [22]: 14.25). Aesthetic impairment was observed as he obtained a score of 51.1 at the TRACE test in the recently developed Rasch version [23] (Figure 2). Radiological parameters of the curves, both in brace and out brace, are described in Table 1. In-brace spine x-ray is shown in Figure 3.

The patient had come to our attention with a prescription of a rigid brace (Lyonese) 23 hours per day; nevertheless, self-reported compliance was just 8 to 10 hours per day. Because of the severity of the curves that well exceeded threshold for surgery consideration (63°), surgical treatment was advised; however, the patient refused surgery. For this reason, a very rigid brace (Sforzesco) was prescribed 23 hours per day. A thermic sensor was applied (Thermobrace) in order to objectively verify compliance [23].

Observations

Study design: The present case report adheres to the CARE (CAse REporting) structure and reporting Guidelines [25]. The present study is a case study with a prospective observational design. Additional and non-invasive procedures have been used, *i.e.* actigraphy. The subject's rest-activity data were recorded for one consecutive week, at home, through an accelerometer, in the last week of July 2018; that period of the season was the holiday period for the subject, with no school commitments. The period coincided with the first days of Sforzesco brace wear 23 hours per day. The study protocol was conducted in accordance with the current national and inter-

Table 1. Radiological parameters of the frontal x-ray both in-brace and out-brace.

	In-brace	Out-brace
	Right thoracic curve	
Upper limit	T5	T5
Lower limit	T11	T11
Apex	T8	T8
Proximal slope	21°	24°
Distal slope	28°	36°
Cobb Degrees	49°	60°
	Left lumbar curve	
Upper limit	T11	T11
Lower Limit	L3	L3
Apex	L2-L3	L2
Proximal slope	28°	36°
Distal slope	21°	27°
Cobb Degrees	49°	63°
Risser	2	2

A scoliotic curve is defined from an upper vertebral limit (the most tilted upper vertebra), an apex (the most rotated but least tilted vertebra) and a lower vertebral limit (the most tilted lower vertebra). The sum of the slope of the upper endplate of the upper vertebral limit with the slope of the lower endplate of the lower vertebral limit is the Cobb degree. The Risser sign is an indirect measure of skeletal maturity, that evaluates the ossification of iliac apophysis; it goes from 0 (lowest skeletal maturity) to 5 (highest skeletal maturity).

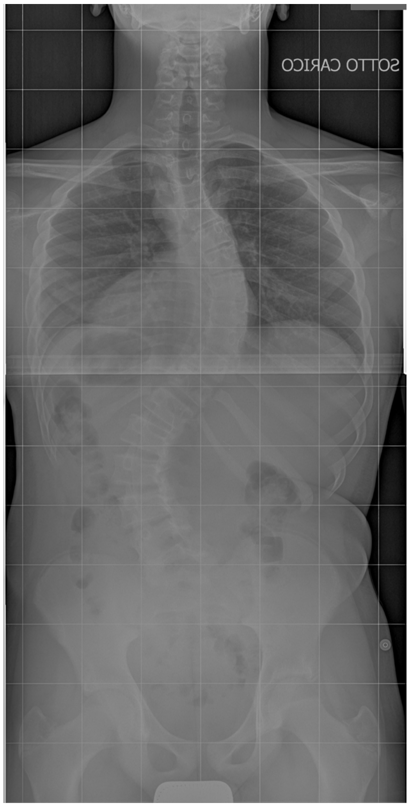
national laws and regulations governing the use of human subjects (Declaration of Helsinki II). The subject, before the beginning of the study, signed an informed consent that explained the study protocol highlighting its benefits and possible risks.

Assessment of RARs: Actigraphy is widely used to study insomnia, sleep and rest-activity circadian rhythms disorders [8,26]; it represents a valid and practical tool that is extremely less invasive than the traditional polysomnography (PSG). An actigraph recording can be performed at home without hospitalization, lasting for many consecutive weeks [8]. It was also shown that the circadian period of the actigraph-defined sleep/wake rhythm accurately predicted the period of the PSG-defined activity-rest cycle [27].

RAR was recorded using an the Actiwatch 2 actigraph (Philips Respironics, OR, USA). The device is composed by a piezoelectric triaxial accelerometer able to convert axial movements over time in electrical signals. The subject's activity counts (AC) were recorded 24 hours/day for one week, *i.e.* seven consecutive days, from Monday to Sunday. The ACs data were transferred from actigraph to a PC with the use of the Philips Actiware 6 Software (Philips Respironics, OR, USA) and then exported and analyzed, epoch per epoch (1 epoch = 60 seconds), in an Excel working sheet (Microsoft Corporation, WA, USA) before performing the rhythmometric analysis (see statistical analysis for details).

Rhythmometric analysis of RARs: To determine the existence of RAR for each single day and for the week of monitoring, the ACs were analyzed using the single and the population mean cosinor method respectively [28,29]. Both methods studies the cosine mathematical function that best fits the data as a function of time and they describe three specific rhythmometric parameters: MESOR, the Midline Estimating Statistic of Rhythm; A, the amplitude; and Φ, the acrophase. The MESOR is a rhythm-adjusted mean for a 24-h period, A is the measure of one half the extent of the rhythmic variation in a cycle, and Φ indicates the time interval within which the highest values are observed. The three parameters are reported with the relevant 95% confidence intervals (CI) (Table 2). The statistical rhythmometric analyses were carried out using the Time Series Analysis Serial Cosinor 6.3 (Expert Soft Technology, Richelieu, France). Significance was set at $p < 0.05$.

Assessment of sleep parameters: In parallel with RAR monitoring, sleep parameters were also objectively monitored for seven consecutive nights with the same actigraph (Philips Respironics, OR, USA). The Actiwatch 2 is a widely used actigraph worn on the non-dominant wrist that has the capability to determine both RARs but also sleep parameters [30] and it has been validated against PSG in healthy children and adults [31]. It is



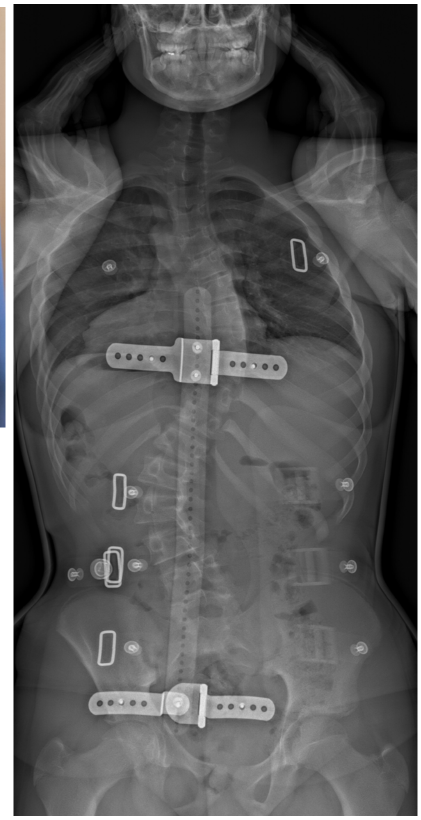


Figure 1 (left). Out-brace standing frontal x-ray of the spine of the patient. We can notice the two primary curves, a right thoracic curve (60° Cobb) and left lumbar curve (63° Cobb), and a Risser sign of 2. **Figure 2** (middle). Picture of the trunk of the patient, with an important asymmetry of all the principal components considered in the TRACE test: shoulder, scapulae, hemi-thorax and waist [23]. **Figure 3** (right). In-brace x-ray of the spine of the patient. The brace used was a Sforzesco brace, a very rigid thoracolumbar brace able to reduce both the right thoracic curve from 60° to 49° and the left lumbar curve from 63° to 49°. Sforzesco brace is built using the SPoRT concept, that means Symmetric, Patient oriented, Rigid, Three-dimensional and Active [24].

however important to underline that sleep parameters can be derived from Actiwatch 2 recordings using three different threshold settings (low, medium, or high) for detection of movements. The threshold settings use different magnitudes of activity for discriminating sleep and wake states, and thus affect the sleep parameters derived from the actigraph. Therefore, in the present case study, a low actigraphic sensitivity threshold (80 counts per epoch) was selected since this cut-off value seems to provide the best combination of sensitivity and specificity in young subjects [31,32].

Ten sleep parameters were measured:

I) Sleep Start (SS): the start of sleep was derived automatically using the Actiwatch 2 algorithm; it is expressed in hours and minutes (hh:mm);

II) Sleep End (SEnd): the end of sleep was derived automatically using the Sleepwatch algorithm; it is expressed in hours and minutes (hh:mm);

III) Time in Bed (TB): the difference between SS and Send, expressed in minutes;

IV) Sleep Latency (SL): the period of time, in minutes, between bedtime and sleep onset time;

V) Sleep Efficiency (SE): the percentage of time in bed actually spent sleeping;

VI) Wake After Sleep Onset (WASO), the amount of time spent awake after sleep has been initiated; WASO is typically expressed in minutes;

VII) Total Sleep Time (TST), the amount of sleep, expressed both in minutes and percentage, obtained during a sleep period;

VIII) Immobility Time (IT), the total time, expressed both in percentage and minutes, spent without recording any movement during time in bed;

IX) Mobility Time (MT), the total time, expressed both in percentage and minutes, spent recording significant movement during time in bed;

X) Fragmentation Index (FI), the sum of the percentages of mobility and immobility accesses in one minute, divided by the number of immobility accesses. FI is expressed in percentage.

Table 2. Rhythmometric analysis (Mean Cosinor method) of RAR for the study subject.

	PR (%)	*p*-value	MESOR [mean and 95% CI]	Amplitude [mean and 95% CI]	Acrophase	
					Degrees [mean and 95% CI]	***Hour*** [hh:mm]
RAR characteristics	23.4	<0.001	84.6 [74.3 – 94.9]	74.4 [59.9 – 88.9]	269 [257 – 280]	17:56

PR: percentage of rhythm. MESOR: Midline Estimating Statistic of Rhythm. Amplitude: half the difference between the highest and the lowest points of the cosine function best fitting the data. Acrophase (degrees and hours) indicates the time in which the highest values occur.

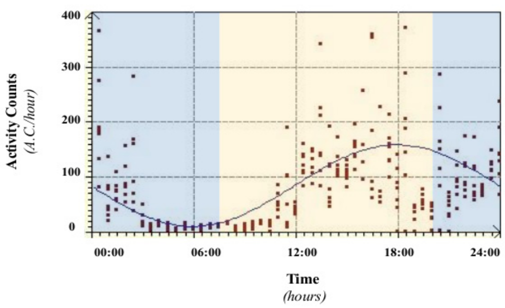


Figure 4. Rest-activity circadian rhythm (RAR) of the patient affected by AIS. *Legend*: On the x-axis are reported the hours of the day and on the y-axis the averaged Activity Counts (A.C.). Blue boxes: night hours; Yellow box: day hours.

The data are reported as mean±SD. Together with the actigraph, the study subject received a sleep diary to record bed time, wake up time, the number of nocturnal awakenings, or the time spent without wearing the device.

Test Results

Thermobrace results: The sensor applied showed a very good compliance to treatment in the period analyzed with an objectively reported compliance of 22.8 hours per day.

RAR characteristics: The single cosinor method revealed the presence of a statistically significant RAR for each single day (p < 0.001). Similarly, the population mean cosinor applied to total data of the seven days of monitoring, revealed the presence of a significant RAR (p < 0.001); specifically: the percentage of rhythm was 23.4%, the mean MESOR was 84.6 ACs, the amplitude registered a mean value of 74.4 ACs and the acrophase occurred at 17:56 h. Table 2 reports the rhythmometric parameters of RAR and Figure 4 shows graphically the rhythm.

Actygraphy-based sleep behavior: Table 3 and Table 4 report both the raw data and the mean±SD of all sleep parameters. The subject showed a large variability in all ten parameters with a large gap between minimum and maximum values. For instance: SL ranged from 0 to 89 minutes with a mean value of 25.9 ± 35.9 minutes and, similarly, FI ranged from 11.3% to 43.2% with a mean value of 27.3 ± 12.8%. In general, the subject reached a good sleep quantity: 507.9 ± 30.2 minutes of TB with a mean TST of 450.7 ± 20.1 minutes, corresponding to the 88.9 ± 4.3% of time spent sleeping; on the contrary, as expected, sleep quality, although not bad, was not excellent: SE was equal to 83.3 ± 7.2%, mean WASO value was 57.1 ± 24.6 minute, and IT registered a mean value of 86.3 ± 4.4%. It is also important to note that sleep timing, *i.e.* SS and SEnd, showed an expected marked delay: on average, the subject started to sleep at 01:36 ± 01:02 h and woke up at 09:55 ± 00:40 h.

DISCUSSION

In the present case report, we described sleep behavior and RAR's characteristics in a young subject affected by severe AIS and treated with a rigid brace. To the best of our knowledge, this was the first study that examined sleep and the activity-rest circadian rhythm in a young patient conservatively treated for scoliosis. Main results are: 1) patient's sleep quantity and quality were, on average, good enough with delayed sleep/wake timing and a large variability was observed in all sleep parameters; 2) the existence of significant rest-activity circadian rhythm was verified. In general, the conservative treatment of scoliosis did not negatively affect the RAR and sleep and behavior of the patient.

It is commonly known that the biology of sleep differs within different age ranges [33] and specific sleep characteristics can be observed in young subjects. Adolescents, especially males [34-36], stay awake and wake up later, and this leads to a biological delay in the timing of sleep onset. To confirm this, we observed delayed SS (01:36 ± 01:02 h) and SEnd values (09:55 ± 00:40) in the study subject and this predisposition toward eveningness was even more pronounced since the monitoring period occurred during summertime; it has indeed been already

Table 3. Actigraphy-based sleep parameters (raw data and mean±SD), for the seven nights of monitoring, of the study subject.

	Sleep Start	Sleep End	Time in bed	Sleep Latency	Sleep Efficiency	Wake After Sleep Onset	Total Sleep Time	
	(hh:mm)	*(hh:mm)*	*(minutes)*	*(minutes)*	*(%)*	*(minutes)*	*(minutes)*	*(%)*
Night 1	00:54	09:26	512	12	76.5	81	431	84.1
Night 2	23:47	09:17	570	0	81.6	95	475	83.3
Night 3	01:02	09:24	502	65	79.5	50	452	90.0
Night 4	01:25	09:27	482	89	73.7	60	422	87.5
Night 5	02:45	10:44	479	4	92.2	25	454	94.7
Night 6	02:17	10:38	501	1	87.9	55	446	89.0
Night 7	02:06	10:35	509	10	91.1	34	475	93.3
Mean ± SD	***01:36 ± 01:02***	***09:55 ± 00:40***	***507.9 ± 30.2***	***25.9 ± 35.9***	***83.3 ± 7.2***	***57.1 ± 24.6***	***450.7 ± 20.1***	***88.9 ± 4.3***

Table 4. Actigraphy-based sleep parameters (raw data and mean±SD), for the seven nights of monitoring, of the study subject.

	Immobility Time		Mobility Time		Fragmentation Index
	(minutes)	*(%)*	*(minutes)*	*(%)*	(%)
Night 1	419	81.8	93	18.1	37.2
Night 2	461	80.8	109	19.1	46.2
Night 3	443	88.2	59	11.7	24.9
Night 4	398	82.5	84	17.4	34.4
Night 5	439	91.6	40	8.3	11.3
Night 6	449	89.6	52	10.3	13.1
Night 7	454	89.1	55	10.8	23.6
Mean ± SD	***437.6 ± 21.9***	***86.3 ± 4.4***	***70.3 ± 5.2***	***13.7 ± 4.3***	***27.3 ± 12.8***

shown that adolescents have later bedtimes in the summer compared to during the school year [37]. The natural attitude toward a delayed sleep phase is mostly due to changes in the two processes that are involved in sleep regulation; the intrinsic circadian timing system and the homeostatic sleep-wake system [36]; in line with this statement, we also observed that the acrophase of the subject's RAR occurred late in the day, specifically at 17:56 h (see Figure 4 and Table 2 for details). The delayed sleep phase is considered a physiological behavior of young male adolescents; however, it could result in significant sleep quantity deprivation if the individual's daily routines do not allow for a late awakening [38]. Fortunately, we did not observe a strong sleep quantity reduction in the study subject since he spent about 8:30 hours in the bed of which 7:30 hours sleeping. This positive outcome is related to the monitoring period that allowed the subject to sleep longer in the morning; indeed, previous studies showed that the sleep volume significantly differed between holiday- and school-night in adolescents and that this discrepancy was between 1 and 2 hours per night, with a greater sleep quantity recorded during holidays [39]. For what concerns sleep quality, the results were fairly positive: SE reached a mean value of 83.3 ± 7.2%, FI was 27.3 ± 12.8% and also IT and MT showed on average good values during the seven nights of monitoring (86.3 ± 4.4% and 13.7 ± 4.3% respectively). The present data on sleep quality are in line with a recent review by Galland and colleagues [40] that reported normal values for pediatric nighttime sleep measured by actigraphy. Therefore, it seems that treating severe scoliosis with a rigid brace in a young subject did not negatively influence the patient's sleep quality; on the contrary, it is known that invasive treatment, such as surgery, could lead to sleep problems in patients. Recent studies reported that sleep disturbances commonly occur in young children in the initial days after surgery and that post-surgery sleep disturbance is associated with persistent pain [41]. Bracing is the most efficient non-surgical method of treatment for idiopathic scoliosis patients and it has been reported that increasing the number of brace-wearing hours per day did not affect the children's sleep quality and did not interfere with their social relations [21]. Nonetheless, it is crucial to say that further studies, with large cohorts of patients, with specific clinical primary outcomes [42], and with pre-to-post longitudinal design, are needed to support these preliminary observational findings.

Last but not least, the existence of a significant RAR was verified. This was an important clinical result since the correct expression of circadian rhythmicity is crucial for the body homeostasis and humans perform optimally when all biological rhythms are in synch without altered peaks or flattened cosine curves [6]. The rest-activity cycle showed similar characteristics to the sleep/wake behavior of the patient: a delayed acrophase was observed with peaking values registered about at 18:00 and this result is in line with the observed delayed sleep phase remarking the typical attitude toward eveningness of young male subjects [43]. Conversely, amplitude and MESOR registered low values highlighting the scarce level of physical activity reached by the subject, 74.4 ACs (95% CI: 59.9 – 88.9) and 84.6 ACs (95% CI: 74.3 – 94.9 ACs) respectively. To confirm this, we compared the activity data registered by the Actiwatch 2 with the validated thresholds for various intensities of physical activity in adolescents using actigraph accelerometers and we observed that the patient conducted a marked sedentary lifestyle, *i.e.*, 0 to 400 counts/min [44].

CONCLUSIONS

We observed that both RAR and sleep behavior had normal trends in a 14-year-old patient treated with a rigid brace for a severe AIS. RAR's characteristics, sleep quantity, and quality were all comparable to the normative age-matched data reported in the scientific literature. A conservative treatment for scoliosis could be a suitable clinical choice to avoid sleep complaints and sleep-related issues. Sleep plays a key role in the health of adolescents and young adults (and for the world population, too) and many adverse outcomes have been shown to be associated with poor sleep within this population. The present case study has obvious limitations in terms of generalizability due to the design of the study, however, it opens new perspectives as it shows that full time brace wear slightly affected sleep behavior in the present case. Improved assessment of sleep in routine clinical practice can help to identify and manage health-related problems that could potentially affect some clinical outcomes, such as pain, mood state, and recovery process. The use of simple screening tools, such as actigraphy, can give a practical and valid support in the study of sleep and circadian rhythms in many contexts and populations. Investigations of circadian timing mechanisms and homeostatic sleep processes may provide insights into biological underpinnings of behavioral changes.

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