Sleep Structure in Untreated Adults with Attention Deficit Hyperactivity Disorder: A Retrospective Study

Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder defined by behavioral characteristics such as hyperactivity, impulsivity, and inattention. However, in recent years, 49% to 66% of patients diagnosed with ADHD in childhood continue to have ADHD symptoms in adulthood, and the prevalence in adults is estimated to be 2.5% (Simon, V., et al., 2009). In addition, 52% of adult patients with ADHD have some comorbid psychiatric disorders, such as anxiety, mood, behavioral, and sleep disorders (Fayyad, J., et al., 2017). According to several cross-sectional, clinical, and epidemiological studies, the prevalence of comorbid sleep disorders in adult ADHD is 43–80%; among such disorders, insomnia, circadian rhythm disorder, restless legs syndrome (RLS), and/or obstructive sleep apnea are frequently observed (Brevik, E., J et al., 2017; Fisher, B., C et al., 2014; Fuller-Thomson, E., et al., 2016; Instanes, J., et al., 2018; Voinescu, B., et al., 2012)

In previous studies using polysomnography (PSG) or actigraphy, decreased sleep efficiency, increased sleep stage shifts, and shortened sleep duration have been reported in childhood ADHD (Cortese, S., et al., 2009). In contrast, in previous meta-analyses, sleep parameters in adult ADHD have not statistically differed from those of controls (Lugo, J., et al., 2020; Philipsen, A., et al., 2005; Sobanski, E., et al., 2008; Van Veen,

M. M., et al., 2010). However, the following limitations have been pointed out (Lugo, J., et al., 2020): 1) few studies have investigated a large number of patients; 2) as controls, only a few studies have used healthy subjects; others have used patients who did not meet the diagnostic criteria of ADHD; 3) the diagnostic criteria of ADHD in the Diagnostic and Statistical Manual of Mental Disorders (DSM), Fourth or Fifth Edition, the International Classification of Diseases (ICD)-10, and the Adult ADHD Self-Report Scale (ASRS) have not been used consistently; 4) the effects of comorbid psychiatric disorders that can affect sleep, such as mood and anxiety disorders, and the effects of medication, including treatment for ADHD, have seldom been excluded; and 5) Sleep disorders that are likely to comorbid with ADHD and affect sleep parameters (e.g., sleep apnea syndrome, RLS, central hypersomnia) have not been excluded.

In this retrospective study, we aimed to clarify the characteristics of PSG findings in adult ADHD more precisely by investigating untreated adult patients with sleep complaints and ADHD diagnosed based on the DSM-5, excluding those with ADHD-related sleep disorders, psychiatric diseases, and/or medication related to ADHD.

For convenience, we temporarily named those sleep disorders as “ADHD-related sleep disorders” in this paper: sleep apnea syndrome, narcolepsy, idiopathic hypersomnia, restless legs syndrome, and periodic limb movement disorder.

Materials and Methods

Participants

In this retrospective study, a total of 170 patients aged 18 years or older who visited the Sleep Outpatient Clinic at Kurume University Hospital with untreated sleep disorders during the 5-year period from April 2015 to March 2020 were investigated. All subjects of this study were drug-naïve patients and successively undergone both of PSG and MSLT after a 1-week sleep assessment using actigraphy.

Procedure

The patients' medical information (e.g., age, sex, height, weight, medical history, previous diagnosis of psychiatric and sleep medicine) was obtained from electronic medical records and interviews with the doctor in charge. First, patients who scored 4 points or higher on part A of the ASRS were extracted; among these patients, those who met the DSM-5 diagnostic criteria were defined as ADHD, and the others as non-ADHD. For subjective measurements, the Japanese version of the Epworth Sleepiness Scale (JESS), the Pittsburgh Sleep Quality Index (PSQI), the Morningness–Eveningness

Questionnaire Self-Assessment (MEQ-SA), the post-PSG sleep questionnaire[1], and the Japanese version of the Insomnia Severity Index (ISI-J) were used. For objective measurements, the parameters obtained from PSG, MSLTs, and actigraphy were analyzed. Fourteen patients with missing data for either subjective or objective items were excluded. Furthermore, patients with ADHD-related sleep disorders such as central hypersomnia (e.g., narcolepsy, idiopathic hypersomnia), sleep apnea syndrome with an apnea–hypopnea index (AHI) ≥ 5, RLS, and periodic limb movement disorder were excluded. Finally, the data of 28 patients with ADHD and 27 with non-ADHD were statistically analyzed **(Figure 1)**.

This study was conducted in compliance with the ethical principles laid down in the Declaration of Helsinki and in accordance with the Ethical Guidelines for Medical Research Involving Human Subjects. The Ethics Committee of Kurume University approved this study (No. 20104).

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[1]The post-polysomnography sleep questionnaire is an original assessment tool developed at Kurume University. This questionnaire evaluates the following sleep quality items just after polysomnography using a 5-point Likert scale: “time to fall asleep”, “quality of sleep”, and “poor quality of sleep”. It also includes a free-response format for “sleep duration”.

Measurement and Evaluation Methods for PSG, MSLTs, and Actigraphy

PSG

Signals from the following electrodes were recorded: four electroencephalograms (C3–A2, C4–A1, O1–A2, O2–A1); left and right electro-oculograms and electromyograms of the chin and anterior tibialis muscles; nasal and oral flow with a thermistor; thoracic and abdominal respiratory movements with a strain gauge; and arterial oxygen saturation with a finger oximeter (Pulsox IF-3 Interface; KONICA MINOLTA, Chiyoda-ku, Tokyo, Japan). Sleep stages were scored in 20-s epochs according to the criteria of Rechtschaffen and Kales (R&K, 1968), and respiratory events were scored using standard criteria by a technician blinded to the aim of the study and the identities of the participants. The extracted sleep measures included total sleep time, sleep efficiency (total sleep time / time in bed × 100), sleep latency, wake time after sleep onset (WASO), number of arousals, total amount of stages 1–4, REM sleep, percentage of stages 1–4, REM sleep, REM latency, and AHI score.

Sleep onset was determined at the first epoch of any sleep stage, and sleep latency was calculated as the time spent from the light-off to sleep onset . Apnea was defined as a total cessation of airflow lasting at least 10 s. Hypopnea was defined as a 50% or

greater reduction in airflow lasting at least 10 s and associated with arousal from sleep. AHI was defined as the number of apneas plus hypopneas per hour of sleep.

Multiple Sleep Latency Tests (MSLTs)

All patients underwent sleep latency tests four times a day of at the sleep laboratory the day after the PSG recording. Measurements included the following: four electroencephalograms (C3–A2, C4–A1, O1–A2, and O2–A1), left and right electrooculograms, chin electromyography, and arterial oxygen saturation using a finger oximeter. The measurements were performed at 10:00, 12:00, 14:00, and 16:00 according to the standard practices of the American Sleep Disorders Association (sleep onset was determined at the first epoch of any sleep stage) (Thorpy, M, J., et al., 1997). The MSLT score was calculated as the average of these four measurements.

Actigraphy

A wristwatch-type activity measuring item (Actiwatch; Philips Respironics, Murrysville, PA, USA) that calculated entry time, waking time, bedtime, sleep latency, sleep time, mid-waking time, number of awakenings, average awaking time, and sleep efficiency

was used. All the patients were asked to wear the Actiwatch on their nondominant arm all day for 1 week prior to the sleep study.

Evaluation of Data

The PSG and MSLT evaluations were conducted by a sleep technologist and an attending physician specializing in sleep. The findings were reviewed at a once-a-week regular conference with sleep medicine specialists certified by the Japanese Society of Sleep Medicine in Kurume University to ensure variation among the evaluators. The final diagnosis of all patients was determined from medical findings.

Statistical Analyses

Regarding the statistical analyses, the Mann–Whitney *U* test was used to compare nonparametric data between the two groups, with $p = 0.05$ set as the level of significance. As for the correlations in the nonparametric data, Spearman's rank correlation was used, with $p = 0.05$ set as the level of significance. All data analyses were performed using JMP Pro 15.1.0 statistical software (SAS Institute Inc., Cary, NC, USA).

Results

Participants' Characteristics

The characteristics of the participants are shown in Table 1. The total number of participants was 55, of whom, 28 (40%) were in the adult ADHD group and 27 (60%) were in the non-ADHD group. The mean age was 24.1 ± 5.6 years in the ADHD group and 28.0 ± 8.6 years in the non-ADHD group, with no significant difference between the two groups. The sex ratio was not different between the two groups. No comorbidities of psychiatric disorders or history of ADHD treatment were found.

Comorbidity of Sleep Disorders (Table 2)

The comorbidity of sleep disorders is shown in Table 2-1. Patients with comorbidities such as central hypersomnia (narcolepsy and idiopathic hypersomnia), sleep apnea syndrome (AHI ≥ 5), RLS, and periodic limb movement disorder were excluded from the analysis (Table 2-2). In the case of a patient with multiple diagnoses, all of the diagnoses were counted.

Subjective Measurement Items

The results of the subjective scales are shown in Table 3. The average score of the ISI-J showed no significant difference between ADHD group and non-ADHD group. However, the average score of the JESS was significantly higher in ADHD group than in non-ADHD group. In addition, all the average scores of ISI-J and JESS were beyond the cutoff values (ISI-J:8 points, JESS: 11points)) in ADHD and non-ADHD groups. As for the sub-items of the PSQI, the average score for C7 (difficulty in maintaining wakefulness during the day) was significantly higher in the ADHD compared with the non-ADHD group ($p = 0.0367$). Regarding the MEQ-SA, the average scores were significantly lower in the ADHD than in the non-ADHD group ($p = 0.0457$), representing a nocturnal chronotype tendency in the ADHD group. No significant differences were found in the other measures.

Objective Measurement Items

The results of the objective measurement items are shown in Table 4.

PSG

The average TST score did not differ between the two groups. The average WASO time was shorter in the ADHD than in the non-ADHD group ($p = 0.0127$). The average slow

wave sleep (SWS) time was significantly longer in the ADHD than in the non-ADHD group (Stage 3, $p = 0.0005$; Stages 3+4(SWS), $p = 0.0065$).

MSLT

The MSLT scores are shown in Table 4. No significant differences were found between the two groups.

Actigraphy

No significant differences in average sleep duration for the 1 week before PSG were found, as shown in Table 4.

Correlations between Objective and Subjective Measurement Values

The total SWS time correlated to the "sleep quality" scores in the post-PSG waking sleep questionnaire, JESS, and the sub-item C1 "sleep quality" in the PSQI, as shown in Figures 2–4. These findings indicate that more SWS was associated with stronger daytime sleepiness in the ADHD group.

Discussion

Chronotype Features in Adult Patients with ADHD

The average total MEQ-SA scores at the first visit to the clinic in the adult ADHD group (39.6 ± 6.4) were significantly lower than those of the non-ADHD group, which showed a nocturnal chronotype tendency in adult ADHD. Previous studies have also reported that patients with ADHD tend to be nocturnal, suggesting the possible involvement of abnormalities in the body clock mechanism (Spera, V., et al., 2020). In patients with ADHD, the onset of melatonin secretion is delayed, and delayed sleep-wake phase disorder is a frequent complication (Kooij, J, J, S., et al., 2013; Snitselaar, M., et al., 2013; Van der Heijden, K. B., et al., 2005); the lack of clock genes (PER2, BMAL1) has recently been reported in adults with ADHD (Baird, A. L., et al., 2012).

Characteristics of Subjective Sleep Measures

The average ISI scores at the first visit to the clinic in the ADHD group were higher than the cutoff scores for insomnia in this study.

Regarding daytime sleepiness, the average JESS and C7 scores (difficulty in maintaining daytime wakefulness) on the PSQI in the ADHD group were significantly higher than the cutoff score for hypersomnia and that in the non-ADHD group.

According to a cross-sectional study that used an Internet survey of adult patients with ADHD, the risk of feeling sleepy was 1.91 times higher in the ADHD than in the control group and was associated with inattentive symptoms (Ito, W., et al., 2017). In a cohort study of adult patients with ADHD, the complication rate of hypersomnia was very high, i.e., almost the half of the patients with ADHD had daytime sleepiness; 22% of those met the diagnostic criteria for central hypersomnia (Lopez, R., et al., 2020). However, excessive sleepiness and difficulty in maintaining wakefulness during the daytime were observed even after excluding the data from patients diagnosed with central hypersomnia in the present study (JESS, ADHD: 16.5 ± 5.0, non-ADHD: 12.9 ± 4.9, $p = 0.0169$; C7 scores on the PSQI, ADHD: 2.5 ± 0.7, non-ADHD: 2 ± 1, $p = 0.0465$). The pathophysiology of ADHD includes the dysfunction of dopaminergic and noradrenergic nerves, which are believed to play an important role in the control of arousal levels (Sasai-Sakuma, T., et al., 2015; Volkow, N. D., et al., 2007). Therefore, excessive daytime sleepiness may be related to the neurological pathology underlying ADHD.

Findings of PSG, MSLT, and Actigraphy after Excluding ADHD-related Sleep Disorders, Psychiatric Disorders Except ADHD

In the present study, no significant difference was found in TST, sleep efficiency, or parameters related to REM sleep latency between the ADHD and non-ADHD groups, consistent with previous studies.

However, the average SWS time was significantly longer (by 24.9 min) in the ADHD than in the non-ADHD group ($p < 0.0065$). Notably, the average time of sleep stage 3 was significantly longer (by 17.4 min) in the ADHD than in the non-ADHD group ($p < 0.0005$). The average sleep time for 1 week before the sleep examinations as measured by actigraphy was more than 8 h in both groups, but no significant difference was detected. Therefore, it is difficult to consider that the increased amount of SWS was caused by insufficient sleep as a behavioral feature in ADHD.

According to a previous study examining SWS activity (SWA) in childhood ADHD, SWA, such as delta and theta waves, was significantly higher and beta waves were significantly lower in children with ADHD compared with children with normal development (Clarke, A. R., et al., 2001). In addition, a systematic review of the sleep architecture of patients with ADHD reported an association between SWA and theta oscillations during non-REM and REM sleep (Biancardi, C., et al., 2021). In a systematic review comparing changes in SWA during sleep over time with maturation from childhood to adolescence, SWA during sleep appeared more in patients with

ADHD at younger ages than in controls with healthy development, but decreased with age. It was also reported that significantly higher SWA levels persisted into adolescence in untreated patients with ADHD; however, SWA levels tended to decrease in those who were being treated or had been treated (Biancardi, C., et al., 2021). SWA is involved in brain maturation (especially cortical maturation), such as in neurogenesis and cognitive function (Campbell, G, I., et al., 2016). Structural imaging studies have confirmed that patients with ADHD have delayed maturation of the cerebral cortex (Shaw, P., et al.2007) (Proal, E., et al., 2011). Therefore, these findings suggest that the SWS increase observed in ADHD patients could reflect the delayed brain maturation and delayed synaptic pruning (Biancardi, C., et al., 2021), and that SWA remains at high levels even in adult patients before receiving treatment for ADHD. Moreover, brain cortical thickness correlates with synaptic density and amount of SWS appearance (Furrer, M., et al. 2019). Compared with normal development, ADHD patients have thinner cortical thickness and smaller gray matter volume. It is reported that gray matter is especially involved in the occurrence of SWS. Similar to our results, the previous studies also show an increase of SWS in ADHD compared to normal development (Ringli, M., et al. 2013). Thus, it is considered that the increased SWS appearance might be caused by the delayed cortical maturation and synaptic pruning in ADHD. On

the other hand, the administration of methylphenidate (MPH) decreases the appearance of SWS; the administration of methamphetamine normalizes gray matter volume in children with ADHD (Shaw, P., et al.2009). Therefore, it is suggested that those central nerve stimulants may improve not only the symptoms of ADHD but also the dysfunction in oscillating system of SWS in ADHD.

Relationships between Subjective Sleep Measurements and Sleep Parameters

In this study, positive correlations were found between total time of SWS and subjective sleep scales regarding daytime sleepiness, such as the JESS score ($r = 0.40324$), PSQI sub-item C1 score (sleep quality) ($r = 0.5073$), and sleep quality as assessed using the PSG post-awakening sleep questionnaire ($r = 0.7885$) in the ADHD group. These results indicate an exact opposite relationship in ADHD compared with that in healthy controls. In a meta-analysis that examined the relationship between subjective and objective sleep assessment in adults with ADHD, no correlation was found in patients with ADHD (Lugo, J., et al., 2020).

Recently, the triple pathway model has been noted as a cause of ADHD. They are believed to be three pathways: executive dysfunction, reward delay/inhibitory control disorder, and temporal processing dysfunction (Sonuga-Barke, E., et al., 2010). It has

been reported that both the volume of the cerebellum, which is implicated as a central site of temporal processing function, and the caudate nucleus are significantly smaller in those with childhood ADHD than in normally developing individuals. However, the difference in cerebellar volume between normally and abnormally developing individuals increases with age, whereas the difference in the volume of the caudate nucleus decreases (Hvolby, A. 2015). Furthermore, the symptoms associated with impairments in inhibitory control and reward latency improve by 40–50% with treatment. In contrast, the symptoms associated with impairments in temporal processing improve much less (by 20%) after pharmacotherapy and are more likely to persist into adulthood compared with executive and reward latency impairments (Castellanos, F, X., et al., 2002).

On the other hand, a systematic review of the sleep structure in patients with ADHD revealed an association between SWA and theta oscillations during non-REM and REM sleep, suggesting that SWA, mainly theta activity, may have a negative impact on cognitive functions such as memory performance and inhibitory control in patients with ADHD (Scarpelli, S., et al., 2019). Furthermore, it has been reported that the appearance rate of cyclic alternating pattern (CAP) subtype A1 is lower in children with neurodevelopment disorders, including ADHD, than in normal controls. CAP is

well known as an index of sleep instability; the CAP rate, calculated as the amount of CAP time/total non-REM sleep time × 100, correlates more strongly with subjective sleep assessments than parameters detected using the method of Rechtschaffen and Kales (Bruni, O., et al., 2010; Terzano, M, G., et al., 2000). Basically, CAP subtype A1 (including delta bursts) activity is relevant to the construction and maintenance of SWS; CAP subtype A1 correlates with cognitive functions, such as verbal and nonverbal fluency memory, verbal and visual–spatial attention and working memory, and learning and memory (Arico, D., et al., 2010). These findings suggested that decreased CAP activity may be related to cognitive functioning and paradoxical sleep assessment in ADHD.

In the future, PSG data needs to be analyzed incisively in drug-naïve patients from the viewpoint of subtype A1 using the CAP method to reveal the details regarding the underlying mechanism of increased SWS observed in adult patients with ADHD.

Limitations

This study had some limitations. First, it was a retrospective study. Second, there may have been a selection bias in terms of the participants because this study was conducted at a single institution. Third, patients complaining of sleep problems who did not meet

the DSM-5 criteria for ADHD were used as controls; no comparison was made with healthy controls.

Conclusion

In recent years, the relationship between neurodevelopmental and sleep disorders has been attracting increasing attention. Sleep structure problems may provide powerful insights for understanding the pathogenesis of ADHD. The increased amount of SWS in untreated adult patients with ADHD identified in this study may suggest the immaturity of the central nervous system in ADHD. In the future, we believe that a longitudinal study of SWS in untreated patients, especially focusing on stage 3, could contribute to a better understanding of the pathogenesis of ADHD.

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Declaration of Conflicting Interests

The authors have no conflicting interests to declare.

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Ethics Declaration

This study was conducted in compliance with the ethical principles laid down in the Declaration of Helsinki and in accordance with the “Ethical Guidelines for Medical Research Involving Human Subjects.”

Data Availability

The data obtained in this study may be used for other research. In such cases, information will be anonymized in the same manner as in this study to protect personal information. In the case of conducting incidental research, the research plan will be reviewed and approved by the Ethics Committee before use.

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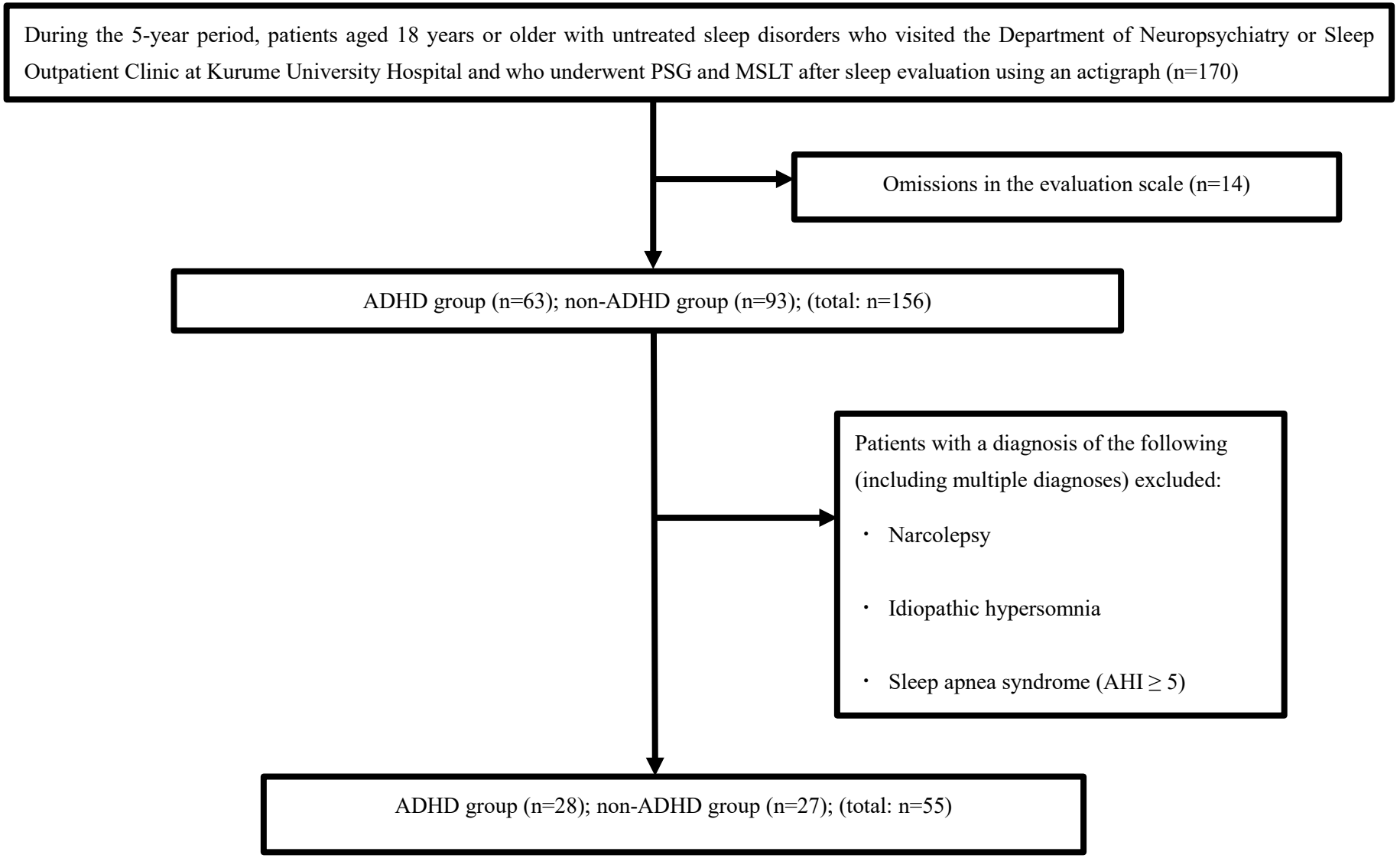
During the 5-year period, patients aged 18 years or older with untreated sleep disorders who visited the Department of Neuropsychiatry or Sleep Outpatient Clinic at Kurume University Hospital and who underwent PSG and MSLT after sleep evaluation using an actigraph (n=170)
Omissions in the evaluation scale (n=14)
ADHD group (n=63); non-ADHD group (n=93); (total: n=156)
Patients with a diagnosis of the following (including multiple diagnoses) excluded:
・ Narcolepsy
・ Idiopathic hypersomnia
・ Sleep apnea syndrome (AHI ≥ 5)
ADHD group (n=28); non-ADHD group (n=27); (total: n=55)

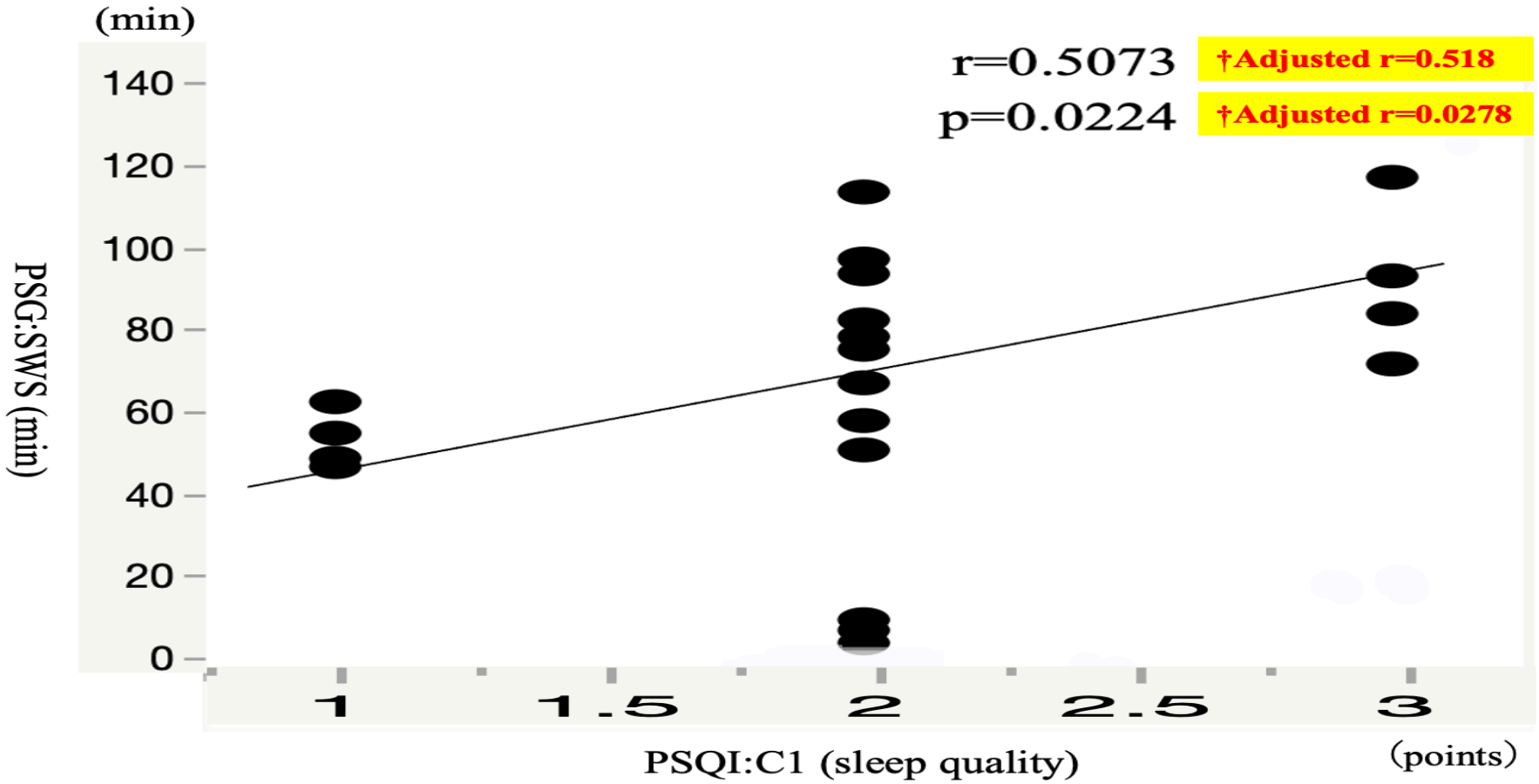

Figure2; Correlation between total SWS time and PSQI:C1 (sleep quality) in ADHD patients (n = 28). PSQI, Pittsburgh Sleep Quality Index ; SWS, Slow wave Sleep; ADHD, attention deficit hyperactivity disorder. Analysis: Spearman's rank correlation.

†:ajusted of age and sex

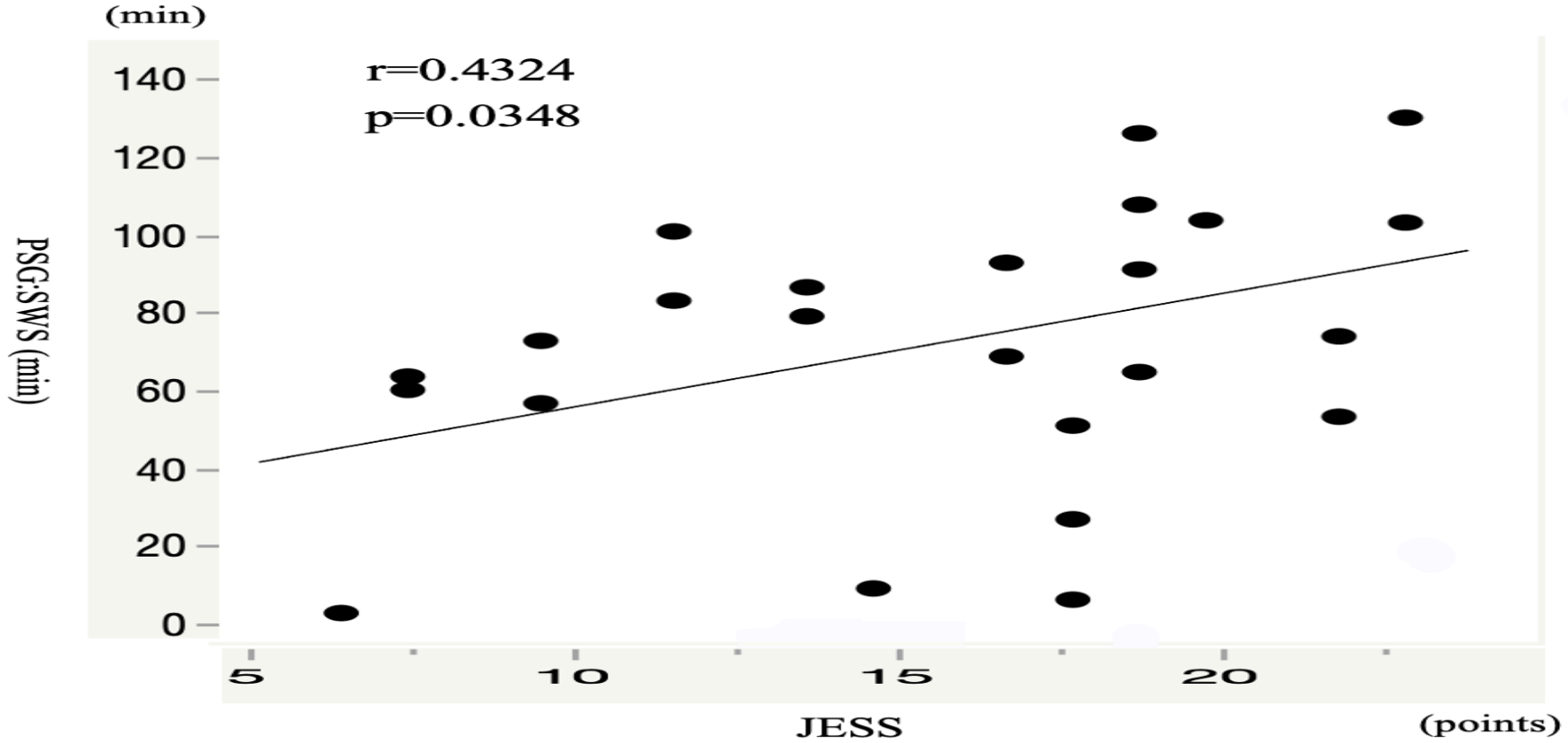

Figure3; Correlation between total SWS time and JESS score in ADHD patients (n = 28). JESS, the Japanese version of the Epworth Sleepiness Scale; SWS, Slow wave Sleep; ADHD, attention deficit hyperactivity disorder. Analysis: Spearman's rank correlation.

†:ajusted of age and sex

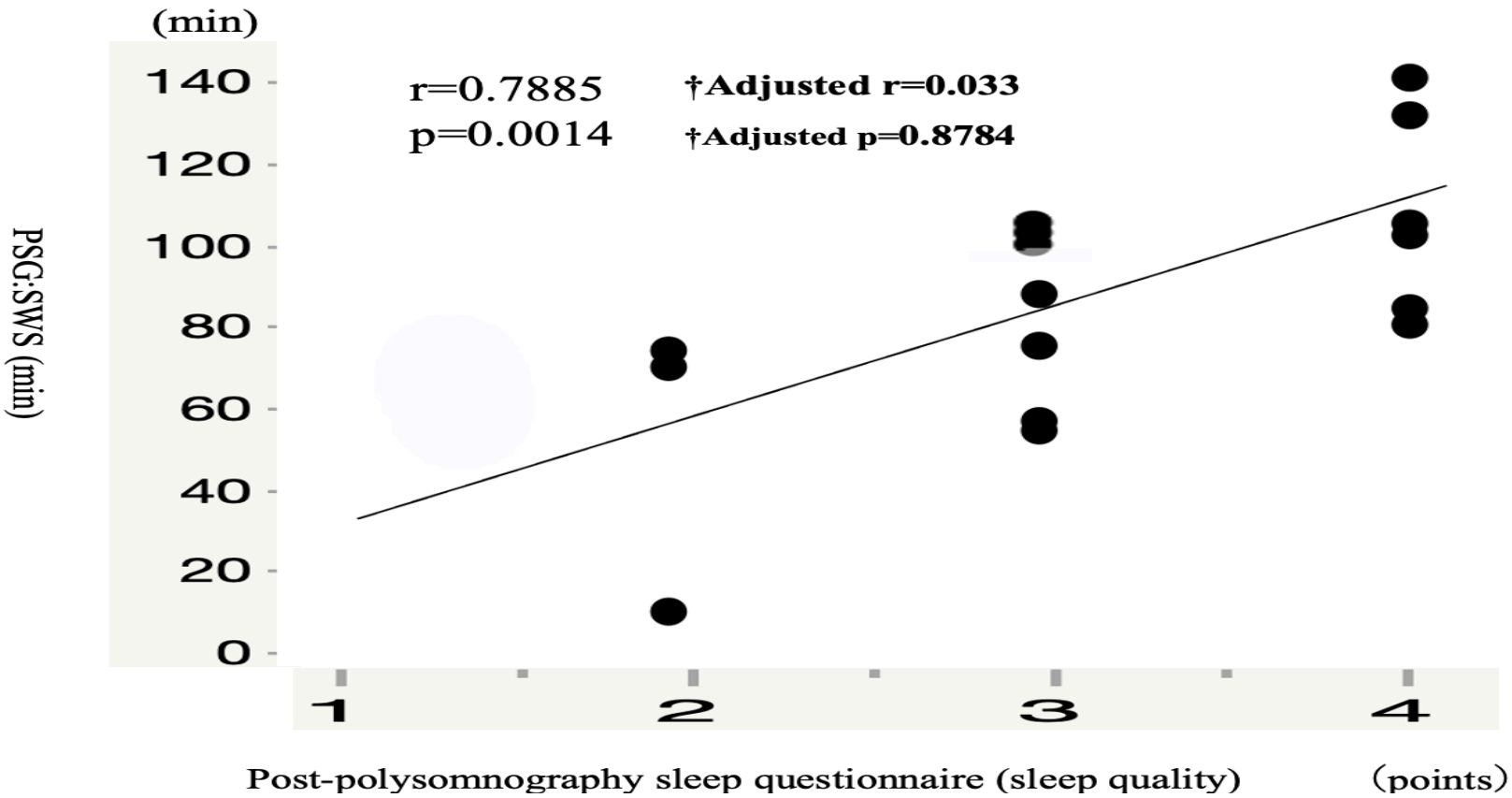

Figure 4. Correlations between total SWS time and the post-polysomnography sleep questionnaire (sleep quality) in patients with ADHD (n=28). SWS, slow wave sleep; ADHD, attention deficit hyperactivity disorder. Spearman's rank correlation was used for the analysis.

The post-polysomnography sleep questionnaire is an original assessment tool developed at Kurume University. This questionnaire evaluates the following sleep quality items just after polysomnography using a 5-point Likert scale: "time to fall asleep", "quality of sleep", and "poor quality of sleep". It also includes a free-response format for "sleep duration"

Table 1. Characteristics of the Participants Excluding ADHD-related Sleep Disorders as Determined by Polysomnography and Multiple Sleep Latency Testing.

	ADHD group (n=28)	Non-ADHD group (n=27)	p value (Wilcoxon test)
Age (years)	24.1±5.6	28.0±8.6	0.1661
Sex (F/M)	15 / 13	12 / 15	0.4985
Past history of mental illness	None	None	
ADHD medication	None	None	

ADHD group: Patients meeting the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (n=28).

Non-ADHD group: Patients not meeting the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (n=27).

Table 2. Comorbidity of Sleep Disorders among Participants Based on the ICSD-3.

Table 2-1. Comorbidity of Sleep Disorders among Participants Based on the ICSD-3.

	ADHD group (n=63)		Non-ADHD group (n=93)	
	Number of patients	%	Number of patients	%
Insomnia (including those associated with mood disorders)	34 (18)	38%	95 (26)	50%
Sleep apnea syndrome	24	27%	33	17%
Insufficient sleep syndrome	13	15%	17	9%
Narcolepsy	7	7%	21	11%
Idiopathic hypersomnia	0	0%	6	3%
Circadian rhythm sleep–wake disorder	6	7%	13	7%
Periodic limb movement disorder	1	1%	2	1%
Other	4	4%	3	2%

ADHD group: Patients meeting the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (n=63).

Non-ADHD group: Patients not meeting the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (n=93).

Insomnia, sleep apnea syndrome, sleep deprivation syndrome, narcolepsy, idiopathic hypersomnia, circadian rhythm sleep–wake disorder, and periodic limb movement disorder were diagnosed according to the International Classification of Sleep Disorders, Third Edition (ICSD-3).

ADHD, attention deficit hyperactivity disorder.

Table 2-2. Comorbidity of Sleep Disorders among Participants Based on the ICSD-3, Excluding ADHD-related Sleep Disorders.

	ADHD group (n=28)		non-ADHD group (n=27)	
	Number of patients	%	Number of patients	%
Insomnia (including those associated with mood disorders)	23 (13)	54%	19 (10)	59%
Insufficient Sleep Syndrome	10	24%	7	22%
Circadian rhythm sleep–wake disorder	5	11%	5	15%
Other	4	9%	1	1%

ADHD group: Patients meeting the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (n=63).
Non-ADHD group: Patients not meeting the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (n=93).
Insomnia, sleep apnea syndrome, sleep deprivation syndrome, narcolepsy, idiopathic hypersomnia, circadian rhythm sleep–wake disorder, and periodic limb movement disorder were diagnosed according to the International Classification of Sleep Disorders, Third Edition (ICSD-3).
ADHD, attention deficit hyperactivity disorder.

Table 3. Comparison of Subjective Measures between the Two Groups.

	ADHD group (n=28)	Non-ADHD group (n=27)	p value (Wilcoxon test)
Questionnaire for initial examination			
PSQI† (points)	8.4±2.4	8±3.9	0.5967
PSQI:C1 (Sleep quality)	2±0.6	1.8±0.7	0.3104
PSQI:C2 (Time to fall asleep)	1.3±1.3	1.6±1.2	0.4916
PSQI:C3 (Sleep time)	1.1±0.9	0.8±0.9	0.4547
PSQI:C4 (Sleep efficiency)	0.4±0.7	0.3±0.7	0.9216
PSQI:C5 (Difficulty in sleeping)	0.8±0.6	0.7±0.5	1
PSQI:C6 (Use of sleeping pills)	0.5±1.1	0.8±1.4	0.3517
PSQI:C7 (Difficulty in maintaining wakefulness during the day)	* 2.6±0.7	1.9±1.1	0.0367

ISI-J‡	(points)	12±4.3	12.6±5.2	0.7336
ESS§ *	(points)	16±4.9	13.1±4.3	0.0307
MEQ-SA¶*	(points)	39.6±6.4	44.9±8.3	0.0457
Post-polysomnography sleep questionnaire				
Time to fall asleep	(points)	2.3±1.2	2.3±1.1	0.8941
Sleep quality	(points)	2±0.6	2.2±0.6	0.251
Sleep time	(h)	7.7±1.6	6.9±1.5	0.0542
Poor sleep quality	(points)	3 .1±0.9	3.4±0.8	0.3059

ADHD group: Patients meeting the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (n=28).

Non-ADHD group: Patients not meeting the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (n=27).

***groups differed significantly at $p<0.05$.**

†Pittsburgh Sleep Quality Index (PSQI), ‡Japanese version of the Insomnia Severity Index (ISI-J),

§Epworth Sleepiness Scale (ESS), ¶Morningness–Eveningness Questionnaire Self-Assessment (MEQ-SA).

The post-polysomnography sleep questionnaire is an original assessment tool developed at Kurume University. This questionnaire evaluates the following sleep quality items just after polysomnography using a 5-point Likert scale: “time to fall asleep”, “quality of sleep”, and “poor quality of sleep”. It also includes a free-response format for “sleep duration”

Table 4. Comparison of Objective Measures between the Two Groups.

	ADHD group (n=28)	Non-ADHD group (n=27)	p value. (Wilcoxon test)
Polysomnography parameters			
Time in bed (min)	531±88.2	518±72.1	0.4639
Total sleep time (min)	431.6±112.5	414.3±101.2	0.2927
Sleep efficiency (%)	82±18.9	79.8±15	0.1234
Sleep latency (min)	42.6±51.2	21.5±19.3	0.0843
WASO†* (min)	38.4±25.5	64.4±49.2	0.0127
REM latency (min)	110.6±74.7	105.3±62.8	0.8491
Arousal index	12.8±5.6	15.1±8.1	0.3326
Sleep stage parameters			
Stage 1 (min)	44.4±27	57.8±26.6	0.0582
Stage 2 (min)	238.8±63	226.5±66	0.4639
Stage 3*‡ (min)	42.2±17.7	24.8±17.6	0.0005
Stage 4 (min)	26.1±25.9	18.6±24.3	0.1308
SWS‡ *‡ (min)	68.3±31	43.4±36.6	0.0065
REM (min)	98.6±44.5	86.6±50.4	0.3415
Stage 1 (%)	10.7±7.3	14±7.1	0.056

Stage 2 (%)	59.7±42.2	52.3±11	0.9062
Stage 3*⁑ (%)	10.8±6.7	6.2±5.6	0.0017
Stage 4 (%)	8.1±16	4.1±5	0.1717
SWS‡*⁑ (%)	18.9±20.1	10.3±8.3	0.0206
REM (%)	23.8±18.5	18.2±8.7	0.285
MSLT parameters			
Average sleep latency (min)	9.6±5	10.4±4.4	0.419
Actigraph parameters			
Average sleep time (hr)	8.6±1.7	9.1±2.5	0.9022

ADHD group: Patients meeting the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (n=28).

Non-ADHD group: Patients not meeting the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (n=27).

***groups differed significantly at p<0.05. ⁑Significant difference by FDR(Benjamini-Hochberg)method**

† wake time after sleep onset (WASO), ‡ slow wave sleep (SWS).

The post-polysomnography sleep questionnaire is an original assessment tool developed at Kurume University. This questionnaire evaluates the following sleep quality items just after polysomnography using a 5-point Likert scale: “time to fall asleep”, “quality of sleep”, and “poor quality of sleep”. It also includes a free-response format for “sleep duration”