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Effects of general anesthesia on postoperative sleep cycles in dentally disabled patients

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Abstract

Aims: Although it has been reported that general anesthesia affect the perioperative sleep cycle, no studies have yet evaluated how general anesthesia affects dentally disabled patients. In this study, we investigated the alteration of perioperative sleep cycles in dentally disabled patients receiving dental treatment under general anesthesia.

Subjects and Methods: The study included 16 patients receiving dental procedures under general anesthesia. Using a sleep monitoring mat, the patients' sleep cycles were measured at home from 5 days before the scheduled surgery date until 5 days after discharge following general anesthesia. The change in all the variables of sleep cycles were analyzed in comparison to the value in preoperative period. Daily differences in these variables were assessed for statistical analysis.

Results: The percentage of deep sleep (Stages 3 and 4) decreased significantly on postoperative day 1, and the percentage of light sleep increased. Furthermore, sleep cycles were significantly extended on postoperative day 1.

Conclusion: The percentage of deep sleep decreased significantly on postoperative day 1 while the percentage of light sleep increased. Sleep cycles were also significantly extended on postoperative day 1. These results reveal that the sleep cycle is somehow affected on the first day following general anesthesia.

KEYWORDS
disabled patients, general anesthesia, sleep cycle

1 | INTRODUCTION

It has been well recognized that circadian sleep-wake cycle is an important function to maintain and regulate the fundamental physiological homeostasis such as cognitive function, glucose metabolism, memory consolidation, immune function, and growth hormone secretion.

Previous studies have suggested that sleep function and sleep cycles may be altered perioperatively with surgery and other interventions under general anesthesia in healthy

patients. Specifically, it has been reported that a rebound of increased rapid eye movement (REM) sleep occurs a few days after general anesthesia, because REM sleep is inhibited during general anesthesia.[1,2]

The principal perioperative complication is the upper airway obstruction but especially in patients with obstructive sleep apnea syndrome.[3] There is a risk of developing upper airway obstruction due to the muscle relaxation that accompanies REM sleep.[1,4–7]

Although general anesthesia is sometimes selected when interventions under normal procedure are deemed difficult in dentally disabled patients due to extreme noncooperation, several complications have been suggested to occur after general anesthesia that may be attributable to a sleep disorder (eg, increased hyperactivity, worsened self-harming behavior, and obvious insomnia). Recently, it has been clearly described by Matton S. and Romeo G.P. that the significant postoperative behavioral changes associated with use of general anesthetics occurred in 2 patients with autism spectrum disorder and attention-deficit/hyperactivity disorder.[8] The reported major behavioral changes were a complete loss of appetite, ongoing insomnia, daytime somnolence, and more aggressive behaviors with withdrawn from social interactions. They clearly raised an important awareness that the behaviors representative of these dentally disabled patients could worsen after a management with general anesthetic. Should iatrogenic complication of sleep disorders develop due to general anesthesia, this may predispose such patients to serious adverse events in the short-term postoperative period following general anesthesia.[9]

To date, no studies have investigated how general anesthesia affects the perioperative sleep cycle in individuals with disabilities. The objective of the present study is to determine the effects of general anesthesia on individuals with disabilities by comparing their preoperative and postoperative sleep cycles before and after procedures requiring general anesthesia.

2 | MATERIAL AND METHODS

2.1 | Subjects

The present study included 16 dentally disabled patients due to extreme noncooperation who underwent dental treatment of multiple teeth under general anesthesia. Among 29 patients recruited for this study with informed consent, the complete data acquisition has been performed in 16 patients because of the patients' noncooperation. There were 10 male and 6 female patients. All patients were at least 10 years old, with a mean age of 23.7 ± 7.6 years and body mass index (BMI) of 25.5 ± 7.7 (Table 1). Twelve patients had been diagnosed with autism spectrum disorder, 1 patient with "intellectual

disability" due to Lennox-Gastaut syndrome, and 1 patient with "intellectual disability" due to Smith-Magenis syndrome. Several patients were taking oral medication for concomitant epilepsy.

2.2 | Sleep assessment

A sleep monitoring mat (Sleepscan®, Tanita Corporation, Tokyo, Japan) was to measure the quality of sleep. This device is primarily composed of a sensor mat and a console. Purified water is sealed in the sensor mat, which is connected to a pressure sensor that is enclosed together with a circuit board in the console at the end of the mat. Its design confers no patient discomfort associated with its use and its safety. It is therefore suitable for assessing sleep in individuals with disability who may be uncooperative. The device operates on the principle that the body emits vibrations during sleep together with respiration, pulse, and body movement. When placed under the bedding, the mat detects these vibrations through an internal pressure sensor. The signal detected by the pressure sensor is divided into respiration and pulse components by the frequency filter in the mat's circuit board; significantly larger signals are interpreted as body movements. Data are converted from analog to digital with sampling frequency of 16 Hz, and are then recorded on a secure digital card during the period of use (typically overnight). Finally, the sleep monitoring mat extracts the changes in respiratory rate, pulse rate, and body movements from the recorded data, and is programmed to determine sleep stages by analyzing the combined data. There are several devices currently on the market able to evaluate sleep besides electroencephalogram measurements such as polysomnography. However, previous devices have been limited to simply discerning between sleep and wakefulness. In contrast to this, the sleep monitoring mat is able to determine the depth of sleep. Previous studies have shown that this device can determine sleep onset latency and detect sleep with high precision, even when compared to polysomnography that quantitatively evaluates sleep states. In sleep studies involving individuals with a disability who have difficulty communicating and may be uncooperative with examinations, measurement devices such as polysomnography are not usually accepted by the patient. Even measurements with a wrist actigraph[10] are often not usable. For these reasons, the use of a noncontact type sleep monitoring device may be necessary despite the device's limitations. It has been reported that the noncontact type sleep monitoring device used in the present study still leaves room for improvements in terms of its consistency with polysomnography examinations,[11–15] however, there are also reports that have indicated that it can sufficiently evaluate sleep stages when compared to actigraph measurements.

To summarize the algorithm: first, wakefulness and sleep are distinguished at every epoch based on the

TABLE 1 Characteristics of patients

No.	Sex	Age	Weight	Height	BMI	Disease	Anesthesia time	Procedure time	Drug	Procedure	Analgesia
1	Female	11	30.4	1.24	19.7	MR, Epilepsy	350	280	None	8DT, 5Ext	Acetaminophen
2	Male	27	101.9	1.80	31.5	ASD, MR	210	140	Antiepileptic drug	2Br	
3	Female	15	68.0	1.51	29.8	ASD	350	270	Antipsychotic drug	4DT, 2RT	Acetaminophen
4	Male	19	39.4	1.53	16.8	CP, MR, SMsynd.	514	460	Antiepileptic drug	3RT	Acetaminophen
5	Female	18	87.7	1.47	40.6	MR, Epilepsy	270	200	Antiepileptic drug	7DT	
6	Female	26	65.8	1.50	29.2	CP,MR, Epilepsy	285	225	Antiepileptic drug	13DT,3Ext	Acetaminophen
7	Male	16	63.0	1.58	25.2	ASD, MR	212	180	Antipsychotic drug	6DT, 1Ext	Acetaminophen
8	Male	26	99.4	1.69	34.8	ASD, MR	303	260	None	4DT, 1RT	
9	Male	33	43.7	1.47	20.2	MR, Donw	308	245	None	1RT, 2Ext	
10	Male	18	47.0	1.68	16.7	ASD	235	183	Antipsychotic drug	9DT	
11	Male	30	95.1	1.61	36.9	ASD, MR, Epilepsy	226	163	Antiepileptic drug	11DT, 1Ext	
12	Male	17	42.0	1.50	18.7	ASD, MR	226	148	Antiepileptic drug	6DT, 1Ext	
13	Female	36	59.8	1.60	23.4	ASD, Epilepsy	251	180	Antiepileptic drug	1DT, 4RT, 6Ext	
14	Female	31	41.0	1.46	19.2	MR, Epilepsy	318	265	Antiepileptic drug	2DT, 1Ext	Acetaminophen
15	Male	33	76.5	1.66	27.8	ASD, Epilepsy	360	300	Antiepileptic drug	2DT, 1Br	
16	Male	23	51.0	1.68	18.1	ASD, Epilepsy	229	180	Antiepileptic drug	2RT, 1Ext	

MR, mental retardation; ASD, autism spectrum disorder; CP, cerebral palsy; DT, dental treatment; exp, dental treatment of 3 teeth = 3DT; Ext(Extraction of teeth); RT, root canal treatment.

presence/absence and type of body movement as well as the duration of these body movements. The sleep stages are then categorized based on changes in respiratory rate and pulse rate. Sleep onset time is determined by roughly distinguishing wakefulness from sleep through analysis of changes in body movement, and then obtaining information on these changes during initial measurement and alterations in respiratory signals. These data are then combined. Total sleep time (minutes), sleep cycle (minutes), sleep onset latency (minutes), wake after sleep onset time (minutes), percentage of light sleep (stages 1 and 2) (%), percentage of deep sleep (stages 3 and 4) (%), percentage of REM sleep (%), percentage of wakefulness (%), and other variables were calculated using these methods.

2.3 | General anesthesia procedure

After conducting a preoperative medical interview and performing examinations that are acceptable to the patient, patients arrived at the hospital in the morning on the day of general anesthesia together with their careers or guardians. After verifying vital signs and preoperative fasting status, the patient was taken to the operating room. An intravenous catheter was inserted in patients who allowed this procedure. Either Mask induction (n = 4) with oxygen (6 L/min) /sevoflurane (5-8%) or rapid intravenous induction (n = 6) (propofol 2 mg/kg) was performed depending on the patient's

understanding and cooperation. In all patients, nasal intubation was performed after administering a muscle relaxant (Rocuronium Bromide 0.6 mg/kg), and anesthesia was maintained with air (2 L/min) /oxygen (1 L/min) /sevoflurane (1.5-2.0%) and remifentanil (0.2-0.3μ/kg/min).

The mean anesthesia time for all patients was 308 ± 92 minutes. There were no significant issues with emergence from anesthesia in any patient, and awakening and extubation proceeded uneventfully. After anesthesia, the patient was returned to the general ward. Patients whose anesthesia was of long duration were hospitalized for 1 day. All other patients were examined 3 hours later to see if they could tolerate fluids. After confirming absence of complications, patients were discharged if they met outpatient general anesthesia criteria for returning home, and the patient returned to his/her home or institution.

2.4 | Statistical analysis

Daily differences were assessed for statistical analysis. One-way analysis of variance was used to determine significant differences and Bartlett's test was used as a post hoc test. A P value of less than 0.05 was considered to be statistically significant.

This study was approved by an ethics committee (Nagasaki University Hospital ethical approval No.14010981) and/or follows the tenants of the Declaration of Helsinki.
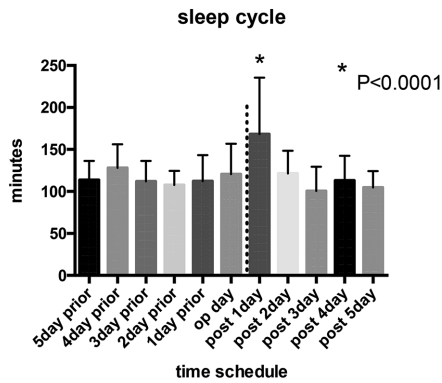
FIGURE 1 The change of sleep cycle due to perioperative time schedule of general anesthesia. There is significant increase in sleep cycle (minutes) on post 1 day after anesthesia
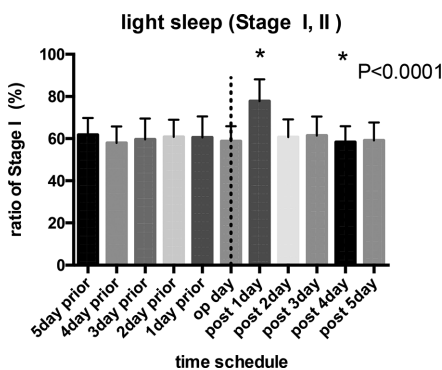

FIGURE 2 The change of ratio of Stage I and II period due to perioperative time schedule of general anesthesia. There is significant increase in ratio of Stage I and II (%) on post 1 day after anesthesia

FIGURE 3 The change of ratio of Stage III and IV due to perioperative time schedule of general anesthesia. There is significant decrease in ratio of Stage III and IV (%) on both 0 day and post 1 day after anesthesia

FIGURE 4 The change of ratio of REM period (%) due to perioperative time schedule of general anesthesia. There is significant increase in ratio of REM period (%) on post 0 day after anesthesia

3 | RESULTS

The mean duration of general anesthesia was 290.4 ± 78.7 minutes. Postoperative respiratory and cardiovascular abnormalities were not observed. Postoperative vomiting was also absent. All patients underwent dental interventions, with 6 patients receiving concomitant tooth extractions.

Time-dependent changes in the sleep cycle are shown in a table and graphs.

Sleep cycles were significantly prolonged on the day following general anesthesia (168.9 ± 69.4 minutes) compared to those recorded in at home in the 5-day period before patients received general anesthesia (107.6 to 128.9 minutes) ($P < 0.0001$) (Figure 1). The percentage of light sleep (Stages 1 and 2) was significantly increased on the day after general anesthesia (78.2 ± 10.5%) compared to that of the 5-day period at home before general anesthesia (57.7% to 61.8%) (Figure 2). The percentage of deep sleep (Stages 3 and 4) was significantly decreased on the day of (8.0 ± 4.2%) and the 1 day after (6.3 ± 3.7%) general anesthesia, compared to that of the 5-day period at home before general anesthesia (14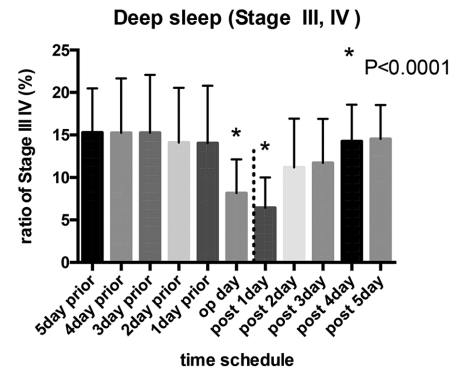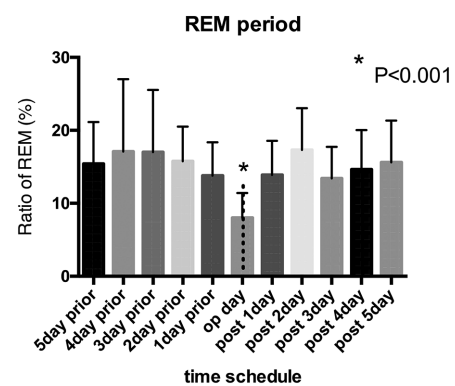.0% to 15.3%) (Figure 3). The percentage of REM sleep was significantly decreased on the day of general anesthesia (8.2 ± 3.5%) compared to that of the 5-day period at home before general anesthesia (13.7% to 17.2%) ($P < 0.005$) (Figure 4). The percentage of wakefulness was significantly increased on the day of general anesthesia (103.6 ± 68.6%) compared to that of the 5-day period at home before general anesthesia (44.8% to 48.2%). There were no significant changes in total sleep time (Figure 5), sleep onset latency, body movement frequency, sleep efficiency, and wake after sleep onset time.

4 | DISCUSSION

The results from the present study suggest that sleep disorders may occur in individuals with disability following general anesthesia. In particular, the percentage of deep sleep (Stages 3 and 4) decreased significantly in the postoperative period, while the percentage of light sleep (Stages 1 and 2) increased. Furthermore, the significant, albeit transient extension of the sleep cycle, indicated the risk of sleep disorders following general anesthesia.
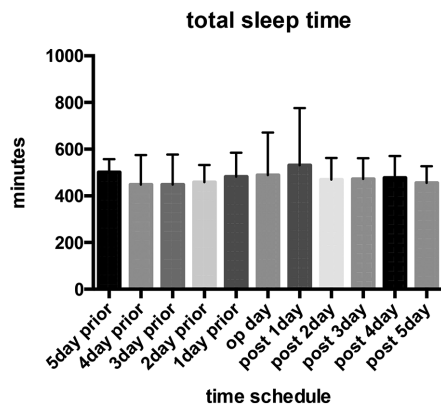
total sleep time

FIGURE 5 The change of total sleep time due to perioperative time schedule of general anesthesia. There are no significant changes in total sleep time (minutes)

4.1 | Sleep disorder following general anesthesia

The risk of REM sleep disorder after general anesthesia, characterized by increased REM sleep rebound, has previously been reported.[1,4,6,16] Knill et al reported that the proportion of REM sleep increases in the postoperative period of abdominal surgery performed under general anesthesia. It considered that, while the effects of pain from abdominal surgery cannot be completely eliminated, δ-waves are the primary brain wave changes observed during general anesthesia. By contrast, α-waves are predominantly seen in the REM stage of natural sleep and are rarely observed during general anesthesia, except during the wakefulness stage before general anesthesia. As such, suppressed REM sleep appears all at once following general anesthesia. Chung et al reported significant changes to sleep architecture on the first night after general anesthesia in patients with sleep apnea syndrome as well as in healthy subjects. Although the general mechanism that occurs after general anesthesia is still unclear, metabolic abnormalities and cardio respiratory complication such as ischemia due to perioperative sleep disorder have serious consequences when considering postoperative holistic management of patients.

Strategies for prevention of sleep disorder after general anesthesia include reducing postoperative stress such as pain management and promoting an early return to activities of daily living through early mobilization. It has been reported that local anesthesia can also induce postoperative sleep disorder, indicating that pain management is an essential factor. Our results showed that the percentage of REM sleep after general anesthesia significantly decreased on the day of general anesthesia, but did not significantly change thereafter. This may be due to limitations of the measurement device employed, and a future, in-depth examination is therefore warranted.

Even healthy individuals have reduced sleep efficiency, REM sleep cycling, and slow-wave sleep on the first night after surgery.[1,2,6,9,17] It has also been shown in pediatric patients undergoing tonsillectomy that sleep efficiency, slow-wave sleep, and REM sleep phase are suppressed on the first night after surgery.[18] Additionally, sleep efficiency is known to decline with ageing.[19] Furthermore, increased REM sleep phase rebound and slow-wave sleep have been observed on the third night after surgery due to significant suppression of REM sleep phase during general anesthesia.[1,2]

The choice of anesthetic agent may affect changes in sleep architecture. Patients in the present study were subjected to either a slow anesthesia induction with sevoflurane or a rapid intravenous induction with propofol. Total intravenous anesthesia (TIVA) with both propofol and remifentanil was employed for maintenance. Although it has been reported that propofol abolishes REM sleep,[20] it has also been reported that this agent is not associated with increased REM sleep phase rebound.[21] It is also known that opioids suppress slow-wave sleep and REM sleep via the μ receptor.[6,22,23] We consider that anesthetic agents used in the present study do not affect sleep architecture because half-life in blood of Propofol and Remifentanil is short, and blood/gas partition coefficient of Sevoflurane is very low from the point of view in wakefulness from general anesthesia.

Some causes of sleep disorders following surgery under general anesthesia include surgical wound factors (site and duration of surgery), inflammatory factors (wound pain, opioid requirements), psychological factors, and environmental factors (ambient noise, nursing interventions, and light),[23] because one of major risk factor causing sleep problem might be existence of pain perception due to regional wound after treatment especially after extraction of teeth.[24] We suppose that the influence of pain on sleep disturbance could be negligible, because acetaminophen injection drug has been administered during anesthesia if needed in case of teeth extraction.

Furthermore, the increased amount daytime sleep is considered to reduce sleep efficiency, REM sleep, and slow-wave sleep.[9] We suppose that existence of daytime insomnia symptoms due to reduced total daytime sleep are commonly experienced with autism spectrum disorder[24,25] might be major factor to potentiate sleep cycle disturbance after general anesthesia.

It is emerging that general anesthesia strongly affects postoperative sleep architecture and/or circadian rhythm.[26] However, much remains unclear through what mechanism general anesthesia affects sleep architecture or the circadian rhythm at both the cellular level of the central nervous system and from a behavioral perspective. To elucidate the clinical significance of postoperative sleep disorder, it is necessary to conduct both molecular biology investigations as well as behavioral studies. It may also be necessary to develop a standardized protocol which considers the potential for postoperative sleep disorder following general anesthesia.

4.2 | Sleep disorder specific to individuals with disability

In terms of general anesthesia, unlike healthy adults in particular, individuals with disability often encounter communication difficulties preoperatively. Patients may experience stress not only as a result of being sedated under general anesthesia, but also by taking what may seem like a daunting visit to the hospital. Patients with autism spectrum disorder commonly present with sleep disorders even under normal living conditions, and there are studies that have indicated the association between sleep disorder and self-harming behavior.[27]

In the present study, the assessment of sleep began at home, 5 days before general anesthesia. These everyday sleep patterns, specific to the individuals with disability, served as preoperative control values. Thus, even if the patients' sleep architecture were already modulated compared to other patients who do not present with underlying mental disorders, the patient-specific preoperative values can be used to compare the changes in sleep architecture after general anesthesia. If some type of sleep disorder were to occur after general anesthesia, even of short duration, the patient would be at risk of developing extremely serious complications when combined with a pre-existing sleep disorder.

It has been recently pointed out that local anesthesia can exacerbate pre-existing sleep disorders.[28] To reduce sleep disorders after general anesthesia in patients with disability, previous reports have indicated the importance of minimizing excitement during emergence as much as possible by using additional sedation or small doses of anesthetic agents, as well as the necessity for adequate pain management and stress reduction. This is particularly important, since individuals with disability are markedly more sensitive to pain and even minimal discomfort than unaffected individuals. The importance of communication with the parent and/or career has been suggested. Special considerations are therefore necessary when separating the patient from their parent(s) in the ward and operating room. The timing of arrival at the hospital for surgery or anesthesia and the timing for discharge after surgery are crucial. Arrangements should also be made to reduce the number of vital sign measurements performed by nursing staff in the ward or recovery room and to minimize environmental changes to the hospital room. Anxiolysis may also be necessary, necessitating effective premedication such as preoperative sedatives.

It would be important to consider that sleep disorder has a strong relationship between sleep quality and oral medication, such as antiepileptic drug and/or antipsychotic drug. Patients with autism spectrum disorder associated with intellectual disability often have a pre-existing sleep disorder.[29–31] It has been suggested that insomnia symptoms of sleep problems, such as increased sleep onset latency, increased wake after sleep onset episodes and reduced total sleep time are common nature experienced with autism spectrum disorder.[24,25] In this study, 11 subjects had medication of antiepileptic drug and 3 subjects had antipsychotic drug, except 3 patients without any medication. Therefore, we consider that daily medication of this drug for maintenance of mental condition might affect major influence on sleep quality. It is reasonable to estimate that there is a significant risk factor for sleep disorder in patients with autism spectrum disorder or mental retardation.

For minor surgical or dental procedures under general anesthesia in individuals with disabilities, ascertaining the quality of everyday sleep is necessary, in addition to evaluating systemic complications and the patient's general condition. To achieve this, it may sometimes be necessary to investigate the characteristics of the patient's sleep architecture through screening, using an actigraph or sleep monitoring mat that is acceptable to the patient. If a patient presents with a significant preoperative sleep disorder, treatment with sleep aids such as hypnotics and melatonin should be considered upon consultation with the attending physician.

5 | CONCLUSION

The present study investigated how general anesthesia affects sleep cycles in the perioperative period in 17 individuals with a disability who received dental treatment under general anesthesia. Results showed that the percentage of deep sleep decreased significantly on postoperative day 1 while the percentage of light sleep increased. Sleep cycles were also significantly extended on postoperative day 1. These results reveal that the sleep cycle is somehow affected on the first day following general anesthesia.

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