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A potentially new evaluation method to visualize rest-activity rhythm based on inpatient activity amount

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入院患者の活動量を指標とした休息活動リズムを視覚化する可能性のある新しい手法

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Abstract

BACKGROUND：A 24-hour periodic regression analysis is often conducted for the humans' rest-activity rhythm indexed by activity amount. However, this analysis cannot be said to accurately capture the rest-activity rhythm of inpatients. **OBJECTIVE：**We preliminarily developed a new evaluation method to accurately visualize the complex 24-h rest-activity rhythms of inpatient life. **METHODS：**Physical activity of one male inpatient was measured. The periodic regression analysis in a 24- or 12-h cycle as well as a synthetic 24- and 12-h cycle were applied to the activity amount data. **RESULTS：**A periodic regression analysis with only a 24-h period resulted in y = 1.19352 + 0.115537 × cos (15･t-183.662). The multiple contribution ratio (R^2) was 0.76. A periodic regression analysis with only a 12-h period resulted in y = 1.19352 + 0.0444696 × cos (30･t-273.522). The R^2 was 0.11. The results of the synthetic periodic regression curve combining the 24- and 12-h periodic components were y = 1.19352 + 0.115537 × cos (15･t-183.662) + 0.0444696 × cos (30･t-273.522). The R^2 was 0.87. The synthetic periodic regression curves were able to capture the subject's rest-activity rhythms more accurately. **CONCLUSION：**The synthetic periodic regression analysis on the activity amount was able to capture more accurately the rest-activity rhythm of the subject. In the future, it is necessary to examine the reliability and validity of the rest-activity rhythm based on synthetic periodic regression analysis by increasing the number of subjects.

Keywords：Circadian rhythm, Physical activity, Periodic regression analysis, Rehabilitation, Patients

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Introduction

Humans have a 24-h daily rhythm. We generally awaken in the morning, perform activities during the day, and sleep at night. Various human physiological systems also have 24-h rhythms, such as blood pressure, heart rate, and body temperature.[1)]

Various health problems occur when rest-activity rhythms are disrupted. Lifestyle disruptions lead to increased mortality[2)] and increased susceptibility to ischemic heart disease[3)] and metabolic syndrome.[4)] Rest-activity rhythms reportedly change with age. Since the elderly go to bed earlier and awaken earlier, their rest-activity rhythms advance in phase and decrease in amplitude.[5)] Such age-related changes in rest-activity rhythms may be among the causes of the increased prevalence of cardiovascular diseases due to aging. Therefore, it is important to accurately understand the rhythm of human life and restore an appropriate rhythm to maintain health and prevent various diseases. In addition, people with dementia have decreased daily activities, including an increase in nighttime arousal and a gradual decrease in daytime arousal.[6)] As dementia progresses, irregular rest-activity rhythms worsen further,[6)] and if nighttime wakefulness leads to nighttime wandering, caregiver burden increases. To reduce caregiver burden and correct disordered rest-activity rhythms, it is important to accurately understand the daily rhythms of people with dementia, such as the time of day when they are most active and the time of day when they are most likely to sleep.

There are currently several methods for assessing rest-activity rhythm, including self-administered subjective assessments using questionnaires,[7)] electroencephalography (EEG),[8)] and activity-based assessments.[9)] However, self-administered methods are unreliable for collecting data from patients who are elderly and have dementia and do not accurately assess their 24-h rest-activity rhythms. EEG cannot evaluate a subject’s actual rhythm of life because it is difficult for the subject to lead a normal life while wearing the device. The evaluation method based on activity amount is quantitative and can evaluate the actual living conditions. However, simply looking at the average amount of daily activity or the maximum or minimum values does not evaluate the rest-activity rhythm.[10)] In recent years, the evaluation of rest-activity rhythms using periodic regression analysis of activity amounts in a 24- or 12-h cycle has become the main method.[11-13)] However, the evaluation of rest-activity rhythms by periodic regression analysis of the 24- or 12-h cycle caused a gap between the subject’s actual rest-activity rhythm and the analytical results. The results in the periodic regression analysis of the 24-h or 12-h cycle do not fit the original data well. Notably, there is a wide gap in the time of peak activity (acrophase) between the original data and the analysis result. The reason may be that humans do not simply have only one cycle of daily activity.[14,15)] In addition to the 24-hour cycle, human daily activity also has a 12-hour circasemidian rhythm.[14,15)] Therefore, it is essential to develop a system that can accurately evaluate both rest-activity rhythms of the 24-h and 12-h cycle, simultaneously. This study aimed to identify a new evaluation method for complex human rest-activity rhythms and accurately visualize human rest-activity rhythms.

Materials and Methods

Subject

As a preliminary study, only one subject was included in this study. We used the data of one patient with a cerebellar tumor who had been admitted to Hospital A in Japan for more than one month. The first criterion for the selection of the subject was normal cognitive function with a cut-off score of 24 points or higher on the Mini-Mental State Examination.[16)] The second criterion was absence of delirium, meaning that the patient was able to live in accordance with the hospital’s daily schedule. Moreover, the subject did not perform independent training irregularly because the necessary exercise was secured by physical therapy (PT) and occupational therapy (OT). The patient was transferred to our hospital for PT and OT after passing the acute stage of the cerebellar tumor. He was an 81-year-old man who was able to walk with a cane. The content of the study was explained to him, and he agreed with the ethical considerations before evaluation. The study was approved by the hospital’s ethics committee (approval number : 2018-06).

Study protocol

The subject wore a wristband-type life recorder, a Life Microscope (manufacturer : A&D, Inc.), to collect data on his physical activity and sleep status for 7 days.[17,18] The device was a 3-axis acceleration wristwatch lifestyle monitoring device that calculates exercise intensity as metabolic equivalents (METs).[19] Sleep status was automatically determined using an automatic sleep-wake discrimination algorithm proposed by Cole et al.[20] Because this device was not water-resistant, it was removed during bathing. The subject was asked to write down his bed and waking times on a behavioral record sheet.

The subject was asked to live according to his usual daily schedule. His morning schedule consisted of waking up at 6:00 a.m., getting ready for the morning such as changing and dressing after the lights came on at 7:00 a.m., and having breakfast in the dining room at 7:30 a.m. After breakfast, he returned to his room and spent time lying in bed or watching TV until his morning physical and occupational therapy sessions began. PT and OT were conducted 40 min to 1 h between 9 and 12 o'clock, during which muscle strength training and gait training were performed with the therapists. Afterwards, he returned to his room to lie down in bed and rest before having lunch in the dining room at 12:00. After lunch, he lay down to rest. The afternoon schedule consisted of a second PT and OT session after 1:00 p.m., followed by a third PT and OT session after a break of approximately 1 h. The patient left his room at 6:00 p.m. to eat dinner in the dining room. After dinner, he returned to his room, changed his clothes, and brushed his teeth. The patient went to bed after the lights were turned off at 10:00 p.m. The subject followed a similar schedule for the 7-day data collection period. Bathing was provided twice during the week and lasted 20 minutes each time.

Statistical analysis

For the subject's 7-day activity METs value data, the average value of the data at the same time was calculated for each minute. Periodic regression analysis was applied to the moving METs average. Periodic regression analysis was first performed for a single 24-h period and the best-fit periodic regression curve was obtained.[11,12] The percentage of agreement of the periodic regression curve with the data of the original METs values was calculated using the multiple contribution rate (R^2).[12] The significance of the periodic regression equation was confirmed by the results of multiple contributions. The periodic regression curve for 24 h was expressed by the equation $y = M + A \cos(\omega t - \theta)$. From the equation, we could obtain three parameters of the rest-activity rhythm : mesor (M) was the mean value, amplitude (A) was the value from the mesor to the maximum or minimum value, and acrophase (θ) was the phase angle of the maximum value in the cosine curve. The acrophase was converted to time, which was defined as the maximum phase time. The phase time at which the minimum value was taken was called the minimum phase time.

Second, considering that humans do not operate in a single cycle of 24 h per day, but in two 12-h cycles,[14,15] we performed a cyclic regression analysis in a single cycle of 12 h to find the best-fitting cyclic regression curve.[13] The 12-h cyclic regression curve was shown by the equation $y = M + A \cos(\omega t - \theta)$ equation. From the equation, we could obtain three parameters of the rest-activity rhythm : mesor (M), amplitude (A), and acrophase (θ). The acrophase was converted to time, which was defined as the maximum phase time. The phase time at which the minimum value was taken was called the minimum phase time.

Third, considering that humans have both a 24- and 12-h cycle,[14,15] we performed a periodic regression analysis with a synthetic periodic regression that combined a 24-h cycle with a 12-h cycle to obtain the best-fit periodic regression curve.[21,22] The synthetic periodic regression curve was shown by the equation $y = M + A1 \cos(\omega 1t - \theta 1) + A2 \cos(\omega 2t - \theta 2)$, where the parameters of the 24-hour cycle were the amplitude A1 and the acrophase θ1, while the parameters of the 12-h cycle were the amplitude A2 and the acrophase θ2. The mean mesor value of the synthetic periodic regression curve was M. The point occupying the highest value in the synthetic periodic regression curve was the maximum value, and the time at which the maximum value was taken was the maximum phase time. The point that occupies the lowest value was the minimum value, while the minimum value was taken as the minimum phase time. The range was defined as the maximum value minus the minimum value.

Results

The first was a periodic regression analysis with only a 24-h period, and the periodic regression equation resulted in y = 1.19352 + 0.115537 × cos(15･t-183.662). The mesor was 1.19 with an amplitude of 0.12, the acrophase was 183.7, the maximum phase time was 12.24 (12:14 p.m.), and the minimum phase time was 0.24 (0:14 a.m.). The multiple contribution ratio (R^2) was 0.76 (Table 1, Figure 1). The test results of the periodic regression equation were significant ($p < 0.001$).

Table 1. Measured physical activity (METs) and 24- and 12-h periodic regression analyses

	24-h	12-h	24- and 12-h
Mesor [METs]	1.19	1.19	1.19
Amplitude [METs][*1]	0.12[*1]	0.04[*1]	0.28[*2]
Range [METs][*2]			
Maximum phase time	12:14 p.m.	9:07 a.m. 9:07 p.m.	10:22 a.m.
R^2	0.76	0.11	0.87

[*1] 24-h or 12-h periodic regression analysis shows Amplitude.
[*2] 24-h and 12-h synthetic periodic regression shows Range.

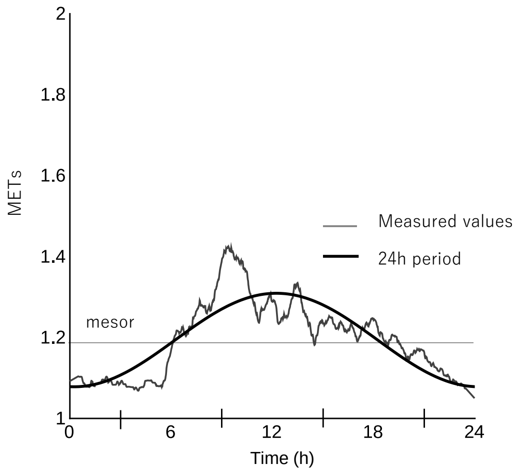

Fig. 1. Measured physical activity (METs) and 24-h periodic regression curve.

Second, the result of the periodic regression equation of the periodic regression analysis with only a 12-h period was y = 1.19352 + 0.0444696 × cos(30･t-273.522). The mesor was 1.19, the amplitude was 0.04, the acrophase was 273.5, the maximum phase times were 9.12 (9:07 a.m.) and 21.12 (9:07 p.m.), and the minimum phase times were 15.12 (3:07 p.m.) and 3.12 (3:07 a.m.). The multiple contribution ratio (R^2) was 0.11 (Table 1, Figure 2). The test results of the periodic regression equation were significant ($p < 0.001$).

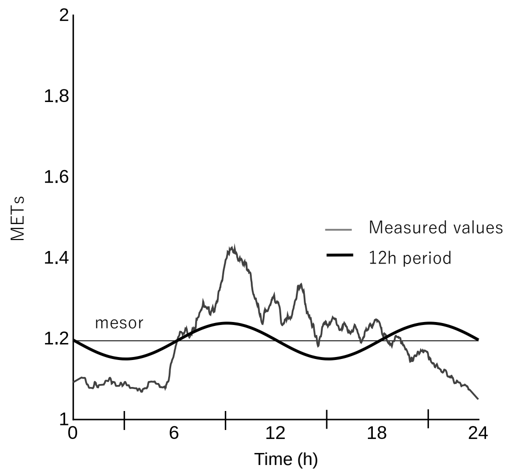

Fig. 2. Measured physical activity (METs) and 12-h periodic regression curve.

Third, the result of the synthetic periodic regression curve combining the 24- and 12-h periodic components was y = 1.19352 + 0.115537 × cos (15･t-183.662) + 0.0444696 × cos (30･t-273.522). The mesor was 1.19, the maximum value was 1.33, and the maximum phase time was 10.37 (10:22 a.m.), the minimum value was 1.05, and the minimum phase time was 1.97 (1:58 a.m.). The range was 0.28. The multiple contribution ratio (R^2) was 0.87 (Table 1, Figure 3).

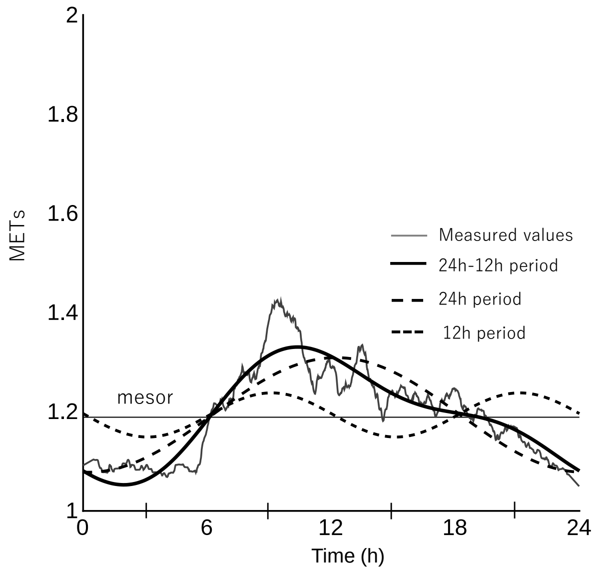

Fig. 3. Measured physical activity (METS) and 24h and 12h periodic regression curve.

Discussion

The results of the 24-h periodic regression curve showed that the mesor was 1.19, the amplitude was

0.12, the maximum phase time was 12:14 p.m., and the minimum phase time was 0:14 a.m. The R^2 indicates the degree of agreement between the original data and the periodic regression curve. Because the R^2 was 0.76, only 76% of the original data could be used to show the rhythm of the subject's activity in the 24-h periodic regression curve. The peak of the activity of the original data comes at 10:00 p.m. The maximum phase time of the 24-h period regression curve, that is, the peak of the activity, is approximately 12:15 p.m. The peak of the activity of the original data and that of the 24-h cyclic regression curve deviate from each other by approximately 2 h, and the result of the 24-h cyclic regression curve is not consistent with the data of the original subjects. In other words, the 24-h cycle regression curve does not accurately capture the daily rhythms of human activity. Humans did not have a simple 24-hour cycle.[14] This could be the rationale that the 24-hour cyclic regression curve cannot accurately explain the rest-activity rhythm of human activity.

Humans have 12-h circasemidian rhythm.[14,15] We calculated a 12-h cycle regression curve. The results of the 12-hour cycle regression curve showed that the mesor was 1.19, the amplitude was 0.04, and the maximum phase times were 9:07 a.m. and 9:07 p.m., respectively. Because the R^2 is 0.11, only 11% of the original data could show the rhythm of the subject's activity in the 12-h cyclic regression curve. On the resulting graph, the peak of activity in the original data came at 10:00 a.m. The maximum phase time of the 12-h periodic regression curve, that is, the peak of activity, was approximately 9:00 a.m. and 9:00 p.m. The peak of activity in the original data and the first peak of activity around 9:00 a.m. in the 12-h cyclic regression curve deviated by approximately 1 h. The second peak of activity in the 12-h cyclic regression curve was approximately 9:00 p.m. However, around 9:00 p.m. is the time when people lie down to sleep, and the original graph shows a gradual decrease in the amount of activity and no peak in the amount of activity. Therefore, the results of the 12-h periodic regression curve did not match the subject's original data. In other words, the 12-h cyclic regression curve cannot accurately capture the rest-activity rhythm of human activity. This may be because humans do not have the same activity pattern twice per day, nor do they have a simple cycle of two 12-h periods.

Considering that human activity has a 24-hour cycle and a 12-hour cycle,[14,15] we constructed a synthetic periodic regression curve that combines the 24-h and 12-h periodic regression curves. The results of the synthetic periodic regression curve showed that the mesor was 1.19, the range was 0.28, the maximum value was 1.33, and the maximum phase time at the maximum value was 10:22 a.m., the minimum value was 1.05, and the minimum phase time at the minimum value was 1:58 a.m. The R^2 of 0.87 indicated that the synthetic cyclic regression curve showed 87% of the original data in the subject's activity rhythm.

When the resulting graph was compared with the subject's routine, the synthetic periodic regression curve also had a steep upward curve at that time in accordance with the 6:00 a.m. waking, 7:00 a.m. morning preparation after turning on the lights, and 7:30 a.m. breakfast. Then, in accordance with the rehabilitation at 9:00 a.m. to 10:00 a.m. and lunch at 12:00 p.m., rehabilitation at 1:00 p.m. to 2:00 p.m. and 3:00 p.m. to 4:00 p.m., a mountain peak was created in the synthetic periodic regression curve that descended gently in the evening. This was followed by a gradual downward curve that coincided with dinner at 6:00 p.m. and a steep downward curve with bedtime after the removal of lights at 9:00 p.m. The valley phase time of around 02:00 a.m. occurred during the nighttime

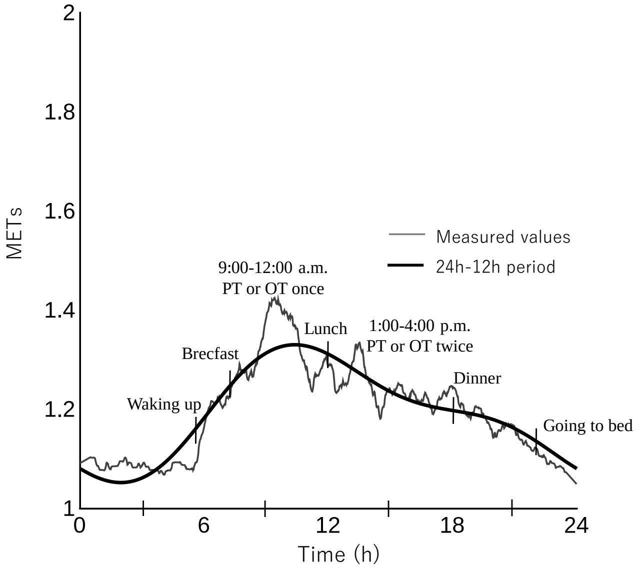

Fig. 4. 24- and 12-h periodic regression curves and the subject's daily life schedule.

period before waking up, and the curve rose sharply in time with waking at 6:00 a.m. (Fig. 4) . The maximum phase time at which the maximum value was obtained was approximately 10:30 a.m. and coincided with the peak activity of the original data. The synthetic cyclic regression analysis fits the original data of the subjects better than the 24-h or 12-h cycle regression analyses. Therefore, the synthetic periodic regression curve was considered able to accurately capture the daily activity rhythms of the subject.

The method of synthetic cyclic regression analysis by adding a 12-h cyclic component to the 24-h cyclic component has been used to examine the rhythm of human blood pressure.[21,22] This method has been used to understand the normal blood pressure rhythm, understand the standard of normal subjects, and examine the effect of blood pressure medication.[21] Since the synthetic periodic regression analysis was conducted for blood pressure, this method is appropriate. The fact that the rest-activity rhythms of the subjects can be captured more accurately with objective indices suggests that this method can be used in a wide range of fields, such as the rest-activity rhythms of the elderly, rest-activity rhythms of people suffering from lifestyle-related diseases, and rest-activity rhythms of dementia patients. By understanding the characteristics of the rest-activity rhythms of people who are aging or have lifestyle-related diseases, it will be possible to make suggestions for maintaining health and preventing diseases.

Limitations

This study discerned the differences between the 24-h cyclic regression analysis, the 12-h cyclic regression analysis, and the synthetic periodic regression analysis for one subject who maintained a consistent daily schedule. This analysis found that the synthetic periodic regression analysis may be more suitable for some people to assess the rest-activity rhythm than the 24-h or 12-h periodic regression analyses. In the future, it will be necessary to increase the number of subjects. This study need to focus whether the synthetic periodic regression analysis is more suitable than the 24-h or 12-h periodic regression analyses for people who have inconsistent daily schedules. In addition, interpretation of the analysis results may become more complicated because the synthetic periodic regression analysis covers more parameters than the 24-h or 12-h periodic regression analyses. Next stage will determine a normal range for each parameter in the synthetic periodic regression. This range may be useful in interpreting the results of the synthetic periodic regression analysis easily.

Conclusion

The synthetic periodic regression analysis could capture the rest-activity rhythms of this subject accurately. In the future, it is necessary to examine the reliability and validity of the synthetic periodic regression analysis by increasing the number of subjects.

Acknowledgments and conflicts of interest

The authors are grateful to a statistics teacher.
The authors report no conflicts of interest.

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