On Metric Space for Discrimination by Using an Artificial Algorithm Imitating the Empirical Rule —As an Example of Support to Clasificate REM Sleep Behavior Disorder

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As an example of "automatic algorithms" imitating human discrimination by persons with specialized knowledge and skills based on their sensory information in accordance with the empirical rule not clearly written, we developed algorithms imitating visual assessments to evaluate REM sleep not accompanied by a decrease in muscle activity.
Key words: REM Sleep Behavior Disorder (RBD), Polysomnography, REM Sleep without Atonia (RWA)

1. Introduction

Discrimination and assessments by persons with specialized knowledge and skills based on their sensory information in accordance with the empirical rule not clearly written forms the basis of the transmission of techniques. Therefore, as an example of "automatic algorithms" imitating discrimination in accordance with the empirical rule not clearly written (Fig. 1), we developed algorithms imitating visual assessments to evaluate REM sleep without atonia (RWA) [1].

Due to changes in lifestyle-related habits and the progression of population aging in recent years, various sleep disorders are becoming more prevalent. Sleep disorders include all abnormalities in the quantity, quality, and timing of sleep and sleep-related behaviors that lead to psychosomatic issues [2, 3].

In 1990, the International Classification of Sleep Disorders (ICSD) was published by a joint group comprising the American Sleep Disorders Association, which played a central role, the European Sleep Research Society, Japanese Society of Sleep Research, and Latin American Sleep Society [4]. This classification covers an extremely wide range of sleep disorders [5]. Among these sleep disorders, we focused on REM sleep behavior disorders (RBD), which have been classified under the category of parasomnias. Patients with RBD act out dreams, which is dangerous for the patients themselves as well as others. Therefore, an early diagnosis is essential. An inhibitory system for skeletal muscle activity is normally active during REM sleep, and surface electromyography (EMG) shows no increase in muscle activity [6]. This inhibitory system is impaired under various pathological conditions represented by RBD, resulting in RWA. Thus, RWA needs to be detected in the diagnosis of RBD.

The presence of RWA is currently assessed based on clinical observations and findings. If it is possible to objectify and automate the evaluation of RWA, the potential for an early diagnosis of RBD will increase. In the present study, we developed automatic algorithms and also compared different visual assessment methods.

2. Polysomnography

PSG is used to observe biological phenomena during sleep. The discovery of human brain waves by the German psychiatrist Beger in 1929 [7], assessments of the depth of sleep by Loomis *et al.* in 1937 [8], and the discovery of REM sleep by Aserinsky and Kleitman (1953) [9] provided an impetus for sleep research. Electrooculography (EOG) and chin EMG in addition to electroencephalography (EEG) were subsequently used as standard methods for the assessment of sleep, and a manual was produced in 1968 [10]. In 1965, Gastaut *et al.* identified apnea in Pickwick syndrome, which is known to be sever type of the obstructive sleep apnea syndrome, by adding the recording of respiration during sleep [11], showing the importance of PSG for the clarification of the pathophysiology of sleep disorders. PSG is a simultaneous recording of physiological phenomena such as EEG, EOG, and chin EMG as basic variables and oxygen saturation (SpO_2), anterior tibialis EMG, snoring, body position, body movements, and body temperature for the comprehensive and objective assessment of physiological phenomena such as the depth of sleep, its course, abnormal behaviors, respiration, and circulation during sleep-

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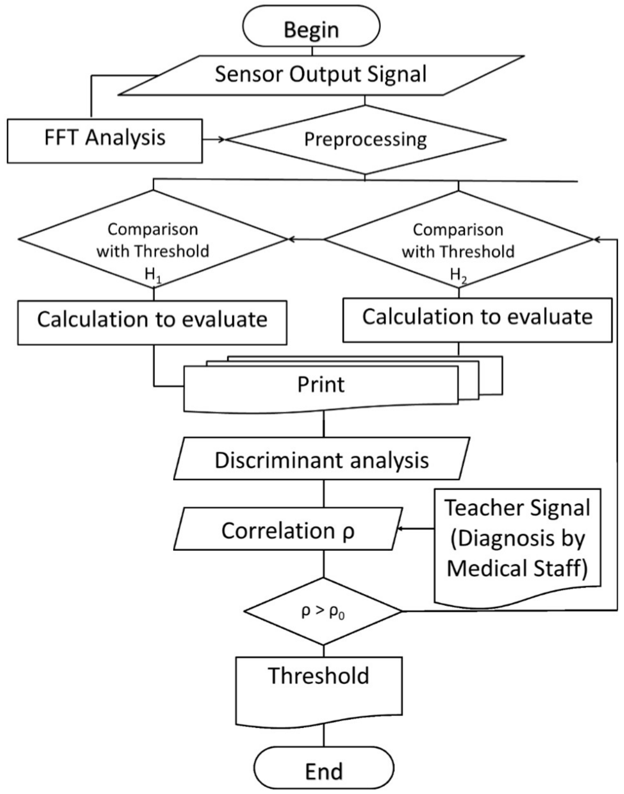

Fig. 1. An example of the flow for an automatic algorithm imitating assessment in accordance of the empirical rule not clearly written.

ing overnight [12–14].

As essential diagnostic criteria of RBD in the ICSD, in addition to abnormal behaviors in daily life or during video monitoring using polysomnography (PSG), the presence of RWA, i.e., increased tonic or phasic EMG activity despite REM sleep suggested by eye movements and brain waves on the PSG records, was adopted [15]. Since single night PSG often shows no abnormal behavior, the confirmation of RWA is an important issue.

3. Materials and Methods

PSG was performed on 12 males aged 60–80 years (mean ± standard deviation: 72.7 ± 1.7 years) with suspected RBD who visited the Good Sleep Center, Nagoya City University Hospital and 13 healthy males aged 20–60 years (40.5 ± 13.2 years). Surface EMG activity of the chin muscles was recorded using Alic 5 (Philips Respironics GK, Tokyo) overnight at a sampling frequency of 200 Hz. PSG recording was initiated after devices such as a sensor were applied at 19:00. The lights out time was 22:00 and the lights on time was 5:30, at which point recording was completed.

In the present study, the EMG activity of the chin muscles that appeared during REM sleep was extracted. Since muscle activity may be classified into tonic and phasic components, RWA was assessed in each component, and the percentage of the RWA duration in the total REM sleep duration was compared between automatic and visual assessments.

4. Assessment Methods and Development of Automatic Algorithms

In the present study, algorithms were developed for 3 visual assessment methods to evaluate RWA: the AASM scoring manual [16], the method described by Montplaisir *et al.* [17], and the SINBAR method [18]. Tonic muscle activity was extracted from EMG records, its duration (T_{tonic}) was calculated, and its ratio to the entire REM sleep time (T_{tonic}/T) was outputted. Phasic muscle activity was also extracted, its duration (T_{phasic}) was calculated, and its ratio (T_{phasic}/T) was outputted. A plane K spanned by these ratios T_{tonic}/T, T_{phasic}/T is herein defined as an evaluation space. According to each visual assessment method, the 2 calculated percentages were plotted on (T_{tonic}/T)-(T_{phasic}/T) plane K. Visual assessment methods to evaluate RWA may also be compared using (T_{tonic}/T) and (T_{phasic}/T) values on this plot.

In the statistical analysis, $p < 0.05$ was regarded as significant.

5. Results and Discussion

Various visual assessment methods are used to assess RWA. Each method is complex, and there is no internationally standardized method. The diagnosis of RWA is based on a physician's visual assessment, and an RWA assessment method that may contribute to an evaluation of the severity of the disorder or treatment is awaited. In this study, algorithms for the automatic assessment of RWA were developed.

Based on the 3 visual assessment methods described above, respective automatic algorithms for the assessment of RWA were constructed. PSG was performed on 12 subjects with suspected RBD and 13 healthy subjects. In the former group, chin EMG records were analyzed using our automatic algorithms. The percentage of the RWA duration in the total REM sleep duration was assessed separately for the tonic and phasic components, and compared with that calculated using each visual assessment method by physicians and medical technologists. As a result, we identified a method that provided results that did not significantly differ from those obtained by visual assessments.

In addition, chin EMG records in 12 subjects with suspected RBD and 13 healthy subjects were analyzed using the automatic algorithms developed in this study. In each evaluation method, a scatter plot on plane K was produced (Fig. 2). The group with suspected RBD was discriminated from the healthy group in accordance with the linear discriminant analysis (LDA). At first, F-test was conducted as a statistical test to examine whether the centers of gravity (CoG) overlap for each group where the significant level was set to be 0.05. F-value was estimated from the Wilks' Lambda Λ and compared with the critical value $F_0(2, 22) = 3.4434$ because the number of the explanation variable equals to 2 and the sum of the samples equals to 25. In the LDA, Wilk's lambda tests how well each level of independent variable contributes to the model. The scale ranges from 0 to 1, where 0 means total discrimination, and 1 means no discrimination. Significant difference of the CoG could be observed from the F-test if the F-value is greater than the critical value. Based on this statistical evidence, it

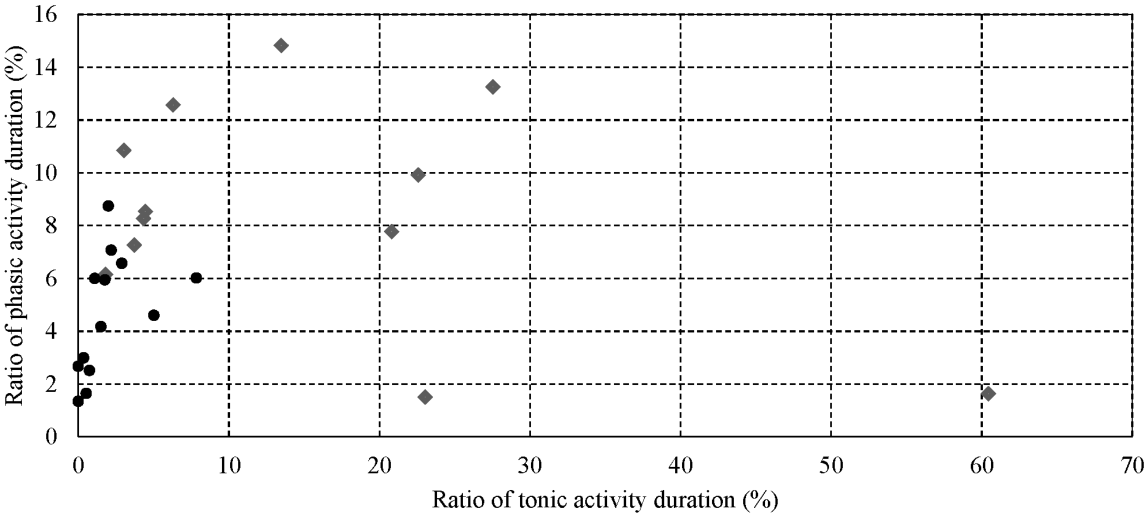

Fig. 2. An example of a scatter plot on plane K for the assessment method described by Montplaisir *et al.* [17] (black circle, healthy subjects; gray diamond, patients).

Table 1. Results of the LDA for each visual assessment method.

	AASM	Montplaisir *et al.*	SINBAR
Λ	0.435	0.467	0.331
F	14.3	12.6	22.2
b_{tonic}	2.53	2.01	1.51
b_{phasic}	1.68	2.00	3.84
MGD	2.19	2.05	2.73
ϵ	0.14	0.15	0.086
r_i	0.84	0.84	0.92

is possible to discriminate the two groups or more.

In Table 1, we listed values of Λ, F, standardized coefficients in the linear discriminant function as

$$\frac{z - \langle z \rangle}{\sigma(z)} = b_{tonic} \frac{\dfrac{T_{tonic}}{T} - \left\langle \dfrac{T_{tonic}}{T} \right\rangle}{\sigma\left(\dfrac{T_{tonic}}{T}\right)} + b_{phasic} \frac{\dfrac{T_{phasic}}{T} - \left\langle \dfrac{T_{phasic}}{T} \right\rangle}{\sigma\left(\dfrac{T_{phasic}}{T}\right)}. \tag{1}$$

Mahalanobis generalized distance (MGD), expected error rate estimation in the LDA; ϵ and the identification rate; r_i for each visual assessment method. Using the algorithm based on the SINBAR assessment method, the error rate was the lowest (0.086).

6. Conclusion

We introduced an example of the development and use of "automatic algorithms" imitating discrimination by persons with specialized knowledge and skills based on sensory information in accordance with the empirical rule not clearly written.

The input signals of the system for development are not specialized for biological signals (EMG), and output signals such as those of robots may also be included. The results of the present study will contribute to studies on the extraction of automatic algorithms used for artificial intelligence.

Appendix A.

The procedure of each assessment method in Section 3 is as follows.

• *AASM scoring manual* [16]

1) Tonic REM: On chin EMG records, each 30-second epoch was scored as tonic when sustained muscle activity with an amplitude greater than the minimum amplitude during non-REM sleep was present in at least 50% of the total epoch duration, and the ratio of the tonic REM sleep duration to the total REM sleep duration was calculated.

2) Phasic REM: On chin or 4-limb EMG records, each 3-second mini-epoch having transient muscle activity (0.1–5.0 seconds) with an amplitude $\geq$ 4-fold that of background activity was scored, and the ratio of the phasic REM sleep duration to the total REM sleep duration was calculated.

• *Assessment method described by Montplaisir et al.* [17]

1) Tonic REM: On chin EMG records, each 20-second epoch was scored as tonic when sustained muscle activity with an amplitude $\geq$ 2-fold that of baseline activity (3–7 μV) or $\geq$ 10 μV was present in at least 50% of the total epoch duration, and the ratio of the tonic REM sleep duration to the total REM sleep duration was calculated.

2) Phasic REM: On chin or 4-limb EMG records, each 2-second mini-epoch having muscle activity with an amplitude $\geq$ 4-fold that of background activity was scored, and the ratio of the phasic REM sleep duration to the total REM sleep duration was calculated.

• *SINBAR assessment method* [18]

1) Tonic REM: On chin EMG records, each 30-second epoch was scored as tonic when sustained muscle activity with an amplitude $\geq$ 2-fold that of background activity or $\geq$ 10 μV was present in at least 50% of the total epoch duration, and the ratio of the tonic REM sleep duration to the total REM sleep duration was calculated.

2) Phasic REM: On chin or 4-limb EMG records, each 3-second mini-epoch having muscle activity with an amplitude $\geq$ 2-fold that of background activity was scored, and the ratio of the phasic REM sleep duration to the total REM sleep duration was calculated.

References

[1] H. Takada, F. Kinoshita, M. Nakayama, M. Takada, Development of Artificial Algorithm Imitating Discrimination in Accordance with the Empirical Rule, Proc. IMEC2016 (2016) 1B1-5 (in Japanese).

[2] S. Miyazaki, M. Okawa, N. Yamada, Somnology II—Overview and management of sleep disorders, Kitaohji Syobo, Kyoto, 2011, pp. 2–9 (in Japanese).

[3] T. Sasai, Y. Inoue, PSG recording for REM sleep behavior disorders and pitfalls of determination, *Jpn J Sleep Med* **6** (2012) 497–502 (in Japanese).

[4] American Psychiatric Association, Diagnostic criteria from DSM-IT, Disk edition, Amer Psychiatric Association Publishing, Washington, D.C., 1994.

[5] Diagnostic Classification Steering Committee, M. J. Thorpy (Chair), International classification of sleep disorders: diagnostic and coding manual, American Sleep Disorders Association, Rochester, 1990.

[6] B. Boeve, M. H. Silber, C. B. Saper, T. J. Ferman, D. W. Dickson, J. E. Parisi, E. E. Benarroch, J. E. Ahlskog, G. E. Smith, R. C. Caselli, M. Tippman-Peikert, E. J. Olson, S. C. Lin, T. Young, Z. Wszolek, C. H. Schenck, M. W. Mahowald, P. R. Castillo, K. Del Tredici, H. Braak, Pathophysiology of REM sleep behavior disorder and relevance to neuro-degenerative disease, *Brain* **130** (2007) 2770–2788.

[7] H. Beger, Uber das Elekrtoenkephalogramm des menschen, *Arch Psychiatr Nervenkr* **87** (1929) 527–570.

[8] A. L. Loomis, E. N. Harvey, G. A. Hobart, Cerebral states during sleep, as studied by human brain potentials, *J Exp. Psyc*. **21** (1937) 127–144.

[9] E. Aserinsky, N. Kleitman, Occurring periods of eye motility concomitant phenomena during sleep, *Science* **118** (1953) 273–274.

[10] A. Rechtschaffen, A. Kales, A manual of standardized terminology, techniques and scoring systems for deep states of human subjects, NIH Publication No. 204, U.S. Government Printing Office, Washington, D.C., 1968.

[11] H. Gastaut, C. A. Tassinari, B. Duron, Polygraphic study of diurnal and nocturnal episodal mainfestations of Pickwick syndrome, *Revue Neurologique* **112**(6) (1965) 568–579.

[12] S. Keenan, Polysomnographic Technique: an overview, In: S. Chokroverty, R. B. Daroff, eds. Sleep Disorders Medicine: basic science, technical considerations, and clinical aspects, 2nd edition, Butterworth-Heinemann, Boston, pp. 151–174, 1999.

[13] M. A. Carskadon, A. Rechtschaffen, Monitoring and staging human sleep, In: M. H. Kryger, T. T. Roth, W. C. Dement, eds. Principles and practice of sleep medicine, 4th edition, Elsevier Saunders, Philadelphia, pp. 1359–1377, 2005.

[14] M. Hirshkowitz, M. H. Kryger, Monitoring techniques for evaluating suspected sleep-disordered breathing, In: M. H. Kryger, T. T. Roth, W. C. Dement, eds. Principles and practice of sleep medicine, 4th edition, Elsevier Saunders, Philadelphia, pp. 1378–1393, 2005.

[15] American Academy of Sleep Medicine. The international classification of sleep disorders: diagnostic and coding manual, 2nd ed., American Academy of Sleep Medicine, Westchester, Illinois, 2005.

[16] C. Iber, S. Ancoli-Israel, A. Chessonn, S. F. Quan, The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications., 1st ed., American Academy of Sleep Medicine, Westchester, Illinois, 2007.

[17] J. Montplaisir, J. Gagnon, M. L. Fantini, R. B. Postuma, Y. Dauvilliers, A. Desautels, S. Rompré, J. Paquet, Polysomnographic diagnosis of idiopathic REM sleep behavior disorder, *Mov. Disord.* **25** (2010) 2044–2051.

[18] B. Frauscher, A. Iranzo, C. Gaig, V. Gschliesser, M. Guaita, V. Raffelseder, L. Ehrmann, N. Sola, M. Salamero, E. Tolosa, W. Poewe, J. Santamaria, B. Högl, Normative EMO values during REM sleep for the diagnosis of REM sleep behavior disorder, *Sleep* **35**(6) (2012) 835–847. doi:10.5665/sleep.1886.