Automatic Quantification of Muscular Activity in Rapid Eye Movement Sleep

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Abstract  Atonia during rapid eye movement (REM) sleep is absent in patients with REM sleep behavior disorder (RBD), a phenomenon called REM sleep without atonia (RWA). RBD patients have symptoms in common with neurodegenerative diseases, and data from follow-up studies on idiopathic RBD patient indicate that RBD predicts development of neurodegenerative diseases, particularly Parkinson’s disease (PD). Therefore, early diagnosis of RWA can help identify and possibly prevent neurodegenerative diseases. Currently, RWA assessment by visual analysis of polysomnogram (PSG) is only moderately reliable and extremely time-consuming, making it difficult to obtain objective, quantifiable results. We developed an algorithm to automatically quantify tonic and phasic electromyographic (EMG) activities of the musculus mentalis during REM sleep using the scoring manual proposed by the American Academy of Sleep Medicine. Hilbert transform and average rectification were used to calculate the amplitudes of phasic and tonic muscular activities, respectively. Parameter values in the algorithm were optimized by cross-referencing the classification result obtained from the algorithm with the result from epoch-by-epoch visual inspection by a neurologist. A total of 2315 REM epochs from 24 PD patients were analyzed. We calculated the optimal parameter set, at which the sum of sensitivity and specificity was the highest, as well as the area under the receiver operating characteristic (ROC) curve (AUC). Verification tests showed good detection accuracy (phasic: sensitivity = 88%, specificity = 82%, AUC = 0.92; tonic: sensitivity = 88%, specificity = 85%, AUC = 0.93). Thus, this automated RWA detection algorithm is potentially useful for rapid and accurate diagnosis of RBD.

Keywords: REM sleep behavior disorder, electromyography, Parkinson’s disease, automatic detection, REM.


1. Introduction

In healthy subjects, rapid eye movement (REM) sleep is characterized by rapid eye movements combined with suppression of skeletal muscle tension (atonia). However, atonia is absent in patients with REM sleep behavior disorder (RBD) [1–3], a condition called REM sleep without atonia (RWA) [4]. Because of the lack of atonia, RBD patients physically act out their dreams during REM sleep, which can result in injury to themselves or others. RBD patients share common symptoms such as nightmares with patients with neurodegenerative diseases including Parkinson’s disease (PD). In fact, follow-up studies on patients diagnosed with sudden onset idiopathic RBD (iRBD) support the hypothesis that RWA is a non-waking symptom that precedes the waking symptoms of neurodegenerative diseases such as PD [5–7]. Therefore, early diagnosis of RBD is important to identify patients at high risk of neurodegenerative diseases, and to allow initiation of therapy as early as possible.

The second edition of the International Classification of Sleep Disorders (ICSD-2) [8] describes the diagnostic criteria of RBD, which include the presence of RWA on polysomnogram (PSG). There are two types of RWA; REM sleep with intermittent phasic muscular activity, and REM sleep with sustained tonic muscular activity. It is important to discriminate between phasic muscular activity from tonic muscular activity, since only tonic muscle activity in REM sleep predicts the development of neurodegenerative disease [6].

To identify RWA, clinicians monitor the electromyographic (EMG) waveform of the musculus mentalis and/or tibialis anterior during PSG recording, to determine the presence of tonic and/or phasic muscle activity for each 30-second epoch [9–13]. The scoring manual proposed by the American Academy of Sleep Medicine (AASM) [4] is used as criteria for identifying phasic and tonic muscular activities in REM sleep.

Phasic (transient) muscle activity in REM sleep is defined by the AASM [4] as: "In a 30-second epoch of REM sleep divided into 10 sequential 3-second mini-epochs, at least 5 (50%) of the mini-epochs contain bursts of transient muscle activity." In RBD, excessive transient muscle activity bursts are 0.1–5.0 seconds in duration and at least 4 times as high in amplitude as the background EMG activity.

Tonic (sustained) muscle activity in REM sleep is defined by the AASM [4] as: "An epoch of REM sleep with at least 50% of the duration of the epoch having chin EMG amplitude greater than the minimum amplitude in non-rapid eye movement (NREM) sleep."

However, the AASM definitions have some drawbacks [4]. One problem with the AASM criteria is that they do not clearly explain how to define the background level and amplitude of muscular activity. In addition, parameter values are not optimized by cross-referencing with the results of visual observation by clini-

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cians. The criteria can be impractical, as visual assessment of PSG data sets that can last for 8 hours per patient require prohibitive amounts of time, and thus would not be suitable for busy clinicians. Finally, there exists a possibility that the criteria may be judged differently not only between clinicians, but even within the same clinician (i.e., potentially low intra-rater reliability).

Several previous studies have proposed methods for automatic quantification of RWA [14–16]. Ferri et al. [14, 15] proposed an automatic quantitative method (the atonia index) to evaluate RWA. However, the atonia index is not based on the AASM scoring manual criteria [4], and does not discriminate between phasic and tonic muscle activities. Although they compared the results of RBD diagnosis obtained using the atonia index with those from visual analyses, they did not compare the two methods on an epoch-by-epoch basis [15]. Another method proposed by Mayer et al. [16] was also not based on the AASM scoring manual criteria [4], and the accuracy of the method was not assessed by cross-referencing with the results of visual observation by clinicians.

This study reports an algorithm for automatic quantification of phasic and tonic muscular activities in REM sleep, which is based on the AASM scoring manual criteria [4]. We also report the results of parameter optimization and accuracy assessment achieved by cross-referencing the output of the algorithm with the results of epoch-by-epoch visual observation by a neurologist. Part of this study was presented orally at the 53rd annual conference of the Japanese Society for Medical and Biological Engineering in June, 2014 [17].

2. Method

2.1 Algorithm

We developed algorithms to automatically detect epoch-by-epoch phasic and tonic muscular activities of the mentalis muscle in REM sleep, which are described in detail in sections 2.1.1 and 2.1.2 below. Figures 1 and 2 show examples of phasic and tonic muscular activities, respectively, of the muscle in REM sleep. The muscle was selected for EMG measurement because a study showed that it has the highest rate of phasic EMG activity out of a set of 13 simultaneously recorded muscles [10]. The muscle is also recommended for both phasic and tonic muscular activity evaluation by the AASM [4] and ICSD-2 [8].

2.1.1 Algorithm to detect phasic muscular activity in REM sleep

The following is the automatic quantification algorithm to detect phasic mentalis muscle activity epoch by epoch in REM sleep:

Step 1. Transform the differential EMG data of the muscle in each REM sleep epoch to instantaneous amplitude time series \( A_k \) \((k = 1, 2, ..., 6000 \text{ Hz} \times 30 \text{ s points})\) by Hilbert transform (Fig. 3).

Step 2. Calculate the mean values of \( A_k \) for each 30-second REM sleep epoch. We define this series as \( B_m \) \((m = 1, 2, ..., \# \text{ of REM sleep epoch})\). The minimum value in \( B_m \) is defined as the background level.

Step 3. Divide each REM sleep epoch into 10 mini-epochs (3-second) (Fig. 3). A mini-epoch contains a burst if \( A_k \) is continuously higher than \( C \times \) background level, and lower than \( 50 \times \) background level, for 0.1–5.0 second. The parameter \( C \) is a threshold parameter, and the value of \( C \) is optimized in this paper.

Step 4. If five (50%) or more mini-epochs out of 10 contain bursts, then the corresponding REM sleep epoch contains phasic muscular activity.

2.1.2 Algorithm to detect tonic muscular activity in REM sleep

The following is the automatic quantification algorithm to detect tonic mentalis muscle activity epoch by epoch in REM sleep:

Step 1. Divide each 30-second REM sleep epoch into 30...

Fig. 1 An example of phasic muscular activity in an epoch of REM sleep. A time series of the differential EMG of the muscle is shown.

Fig. 2 An example of tonic muscular activity in an epoch of REM sleep. A time series of the differential EMG of the muscle is shown.

Fig. 3 An example of Hilbert transform of the differential EMG data of the muscle shown in Fig. 1. A time series of instantaneous amplitude is shown.
mini-epochs (1-second). Calculate the average rectified values \(R_p\) (p = 1, 2, ..., 30) of the differential EMG data of the musculus mentalis (Fig. 4).

Step 2. Calculate the average rectified values of the differential EMG data of the musculus mentalis in non-REM (NREM) sleep epochs. We define this series as \(S_q\) (q = 1, 2, ..., # of NREM sleep epoch). The minimum value in \(S_q\) is defined as the background level.

Step 3. If 15 (50%) or more average rectified values \(R_p\) out of 30 are higher than \(T\) times the background level, and lower than 50 times the background level, then the corresponding REM sleep epoch contains tonic muscular activity. The parameter \(T\) is a threshold parameter, and the value of \(T\) is optimized in this paper.

2.2 Experiment
To validate the accuracy of the algorithm, we cross-referenced the results obtained from the algorithm with those from visual observation by a neurologist.

Twenty-four PD patients (10 men and 14 women, age 72.5 ± 6.4 years, disease duration 8.1 ± 5.0 years, United Parkinson’s Disease Rating Scale (UPDRS) part III score 31 ± 11] with RBD symptoms who required PSG examinations to make a diagnosis were studied. All subjects provided written informed consent. The research ethics committee of the National Hospital Organization Toneyama National Hospital, and the committee for ergonomic experiments at the National Institute of Advanced Industrial Science and Technology (AIST) approved the experiment and the data analysis.

PSG data (Embla N7000, Natus Medical Inc. USA) was collected from each patient over one night at the National Hospital Organization Toneyama National Hospital. Each data set consisted of surface differential EMG of the musculus mentalis, electroencephalography (F3-A2, F4-A1, C3-A2, C4-A1, O1-A2, O2-A1), electrocardiography, left and right electrooculography, nasal air flow, and oxygen saturation by pulse oximetry. The sampling frequency of the EMG signals was 200 Hz. The skin impedance of the EMG electrodes was less than 10,000 ohms in all measurements.

2.3 Data analysis
Each 30-second PSG epoch was classified into one of five sleep stages (awake, REM, NREM1, NREM2, and NREM3&4) by a registered polysomnographic technologist (RPSGT) [4]. From a total of 2422 REM epochs, 107 had artifacts and were excluded from analysis. Thus, 2315 REM epochs were analyzed (mean ± SD: 96 ± 51 epochs, maximum: 236, minimum: 25). The differential EMG waveform of the musculus mentalis for each REM epoch was categorized visually as a phasic epoch or tonic epoch by a neurologist. Figures 1 and 2 show sample epochs that were categorized as phasic and tonic epoch, respectively.

The algorithm was applied to the differential EMG waveforms of the musculus mentalis after the raw signals were high-pass filtered (4th order Butterworth; cutoff frequency, 5.3 Hz). In addition, a 5-point moving average filter was applied prior to phasic muscular activity detection. We changed the values of the parameters \(C\) and \(T\) in the algorithm, and calculated the sensitivity and specificity of detection in each case. Threshold parameter \(C\) was varied from 0.1 to 20.0 in increments of 0.1 for phasic epoch detection, and threshold parameter \(T\) was varied from 0.1 to 15.0 with increments of 0.1 for tonic epoch detection. The optimal parameter point, at which the sum of the sensitivity and specificity is highest, was identified. Finally, the area under the receiver operating characteristic (ROC) curve (AUC) was calculated.

Two-fold cross-validation analysis was used to test the generalization capability of the algorithm. The 24 PD patients were divided into two groups. The total number of REM sleep epochs was 1165 in the first group and 1150 in the second group. The data from a single group was used as the validation data for testing the algorithm, and the data from the other group was used as training data. The values of parameters \(C\) and \(T\) were optimized using the training data set. The cross validation process was performed two times, with the data set from each group used once as the validation data. The average values of sensitivity and specificity were calculated.

3. Results
Figures 5 and 6 show the parameter dependence of sensitivity and specificity for the detection of phasic and tonic epoch, respectively.

The sum of sensitivity and specificity was higher than 160% when \(C = 2.0–4.1\) for phasic epoch detection (Fig. 5). At the optimal parameter point (\(C = 2.7\)), the sensitivity was 88% and the specificity was 82%. AUC at ROC analysis was 0.92 for phasic epoch detection.

The sum of sensitivity and specificity was higher than 170% when \(T = 1.7–2.8\) for tonic epoch detection (Fig. 6). At the opti-
epoch detection. Thus, these results verify that the novel algo-
ثم نبّ الألفام (لمحة: 88% وخصوصية: 85%). AUC في ROC تحليل كان 0.93 للكشف عن منطاق.

두 검증 횟수 validation analysis showed that the average sensitivity and specificity of the validation data were both 84% for phasic epoch detection, and were 92% and 80%, respectively, for tonic epoch detection.

4. Discussion

In this study, we developed an algorithm to quantify automatically the presence of phasic or tonic EMG activity in the musculus mentalis during REM sleep, based on the scoring manual proposed by the AASM [4]. We optimized the parameter values in the algorithm by cross-referencing the results obtained from the algorithm with the results from visual, epoch-by-epoch inspection by a neurologist. Verification test results demonstrated good detection accuracy (phasic: sensitivity = 88%, specificity = 82%, AUC = 0.92; tonic: sensitivity = 88%, specificity = 85%, AUC = 0.93). In ROC analysis, AUC higher than 0.9 can be interpreted as excellent accuracy scores for a given algorithm.

Cross-validation analysis showed that when using validation data not involved in optimizing the algorithm parameter value C, both the average sensitivity and average specificity were at least 84% for phasic epoch detection. High values (average sensitivity = 92%, average specificity = 80%) were also achieved for tonic epoch detection. Thus, these results verify that the novel algorithm has high capability of generalization.

The final algorithm can discriminate phasic and tonic muscular activities in REM sleep, in contrast to the automatic quantification method proposed by Ferri et al. [14, 15], in which the atonia index does not differentiate phasic from tonic muscular activity. This discrimination is important because the mechanisms and treatment efficacies of phasic and tonic muscular activities in REM sleep appear to be different [1]. More importantly, only tonic muscle activity, and not phasic muscle activity, in REM sleep predicts the development of neurodegenerative diseases such as PD in RWA patients [6].

This is the first study that compares the results obtained from an automated quantification method with those from visual inspection by a neurologist on an epoch-by-epoch basis. Moreover, the present algorithm is currently the only automatic quantification method that is qualitatively based on the scoring manual proposed by the AASM [4]. Finally, optimizing the threshold parameter point (T = 2.2), the sensitivity was 88% and the specificity was 85%. AUC at ROC analysis was 0.93 for tonic epoch detection.

Two-fold cross validation analysis showed that the average sensitivity and specificity of the validation data were both 84% for phasic epoch detection, and were 92% and 80%, respectively, for tonic epoch detection.

5. Conclusion

In this study, we developed an algorithm to automatically quantify and differentiate phasic and tonic muscular activities on an epoch-by-epoch basis in REM sleep, which is based on the scoring manual proposed by the AASM [4]. Through parameter optimization and comparison with visual scoring, the sensitivity and specificity were optimized to over 80% for both phasic and tonic muscular activities. Furthermore, ROC analysis verified that the algorithm has excellent accuracy in detecting both types of muscle activity in REM sleep.

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Conflict of Interest

The authors have no conflicts of interest associated with this manuscript.

References


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