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Review Article

Defining muscle activities for assessment of rapid eye movement sleep behavior disorder: From a qualitative to a quantitative diagnostic level

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ABSTRACT

Rapid eye movement (REM) sleep behavior disorder (RBD) is a parasomnia characterized by dream enacting behavior. Its polysomnographic hallmark is loss of physiological REM muscle atonia. Current diagnostic criteria require both a typical history of RBD or videographic documentation of abnormal REM-sleep related behaviors and the polysomnographic demonstration of REM sleep without atonia with "the electromyographic (EMG) finding of excessive amounts of sustained or intermittent elevation of submental EMG tone or excessive phasic submental or limb EMG twitching".

Until now, there has not been a generally accepted consensus on how muscle activity during REM sleep should be scored. Moreover, current diagnostic criteria do not specify which muscle or muscle combinations are the most suitable for differentiating between RBD and non-RBD. The term "excessive" refers to the scorer's subjective impression and not to objective quantitative cutoff values.

This article reviews published manual and computer-assisted scoring methods of EMG activity that are applied in RBD research. It includes the existing studies on EMG activity assessment in different muscles, available data on night-to-night variability, as well as recently established quantitative EMG cutoff values. The research that has been undertaken in the last years has greatly improved RBD diagnosis, taking it from a qualitative to a quantitative level. This development is of upmost importance, since RBD is often the first non-motor symptom of a neurodegenerative disease.

1. Introduction

Rapid eye movement (REM) sleep behavior disorder (RBD) is a parasomnia characterized by enactment of dreams that are frequently violent [1]. In addition to a characteristic history for RBD or documentation of abnormal REM sleep-related behaviors through nighttime video recording, the polysomnographic demonstration of REM sleep without atonia is mandatory for a definite RBD diagnosis [2]. Correct diagnosis of RBD is extremely important in order to avoid serious injury to the patient or spouse [3], it is a very treatable condition [4], and there is strong evidence that RBD is an early preclinical manifestation neurodegenerative diseases such as, Parkinson's disease, multiple system atrophy or Lewy body dementia [5–8]. However, the differential diagnostic spectrum of RBD is challenging and comprises of other sleep disorders such as, non-REM parasomnias, sleep apnea syndrome and other movement disorders during sleep, nocturnal seizures, and posttraumatic stress disorder and also malingering [2], which can only be differentiated clearly by polysomnographic examination.

The International Classification of Sleep Disorders 2 established that the diagnosis of RBD requires demonstration of REM sleep without atonia (RWA) [2]. RWA is defined as either excessively sustained or intermittent elevation of EMG tone or excessive phasic EMG activity [2]. In addition, patients need to have either a history of sleep-related injurious, potentially injurious, disruptive behaviors, or documentation of abnormal REM sleep behaviors during polysomnographic monitoring [2].

Objective quantification of muscle activity is not performed for routine assessment of RBD and the definition of "excessive", is based on the individual scorer's subjective qualitative impression. Moreover, no common scoring rules for muscle activity in RBD exist. In addition, different recommendations have been made for EMG montages to detect EMG muscle activity related or unrelated to RBD behavioral episodes.

2. Scoring methods for RWA

2.1. Manual scoring methods for RWA

In recent years, different manual scoring methods have been proposed in RBD research (see also book chapter Frauscher and Högl [9]). The first insights to objectively quantify phasic EMG

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activity during REM sleep were gained from healthy normals, and date back to the mid-seventies and early eighties [10–12]. In 1973, Nakazawa et al. were the first to report normative phasic EMG data in the mentalis during REM sleep in 5 subjects [13]. Perhaps, the first attempt to quantify pathological EMG activity during REM sleep was reported in an eight year old boy with a pontine brain tumor in 1975 [14]. However, the applied scoring method was not described. In 1992, the first systematic scoring system to characterize polysomnographic features of RBD was developed [15]. The authors distinguished between phasic and tonic EMG activity in the submental EMG recording. Phasic EMG activity (EMG activity lasting between 0.1 and 5 s and exceeding four-fold the amplitude of background EMG) was rated for each two second mini-epoch. Tonic or atonic EMG activity was rated for each 20 s epoch depending on whether tonic chin EMG activity was present for more or less than 50% of the epoch [15]. Table 1 specifies this and other manual scoring methods in more detail. Various groups in RBD research [16–21] have used this scoring method, changing the duration of mini-epochs, and the definition of the amplitude criterion. In 2007, this scoring system was incorporated into the AASM manual for the scoring of sleep and associated events [22]. Apart from this original classification system, two different manual scoring systems [23–26] have been published. In order to avoid confusion created by the ambiguous use of the terms ''phasic'' and ''tonic'', Eisensehr et al. coined the terms ''short-lasting'' and ''long-lasting'' EMG activity (Table 1). The authors provide a 0.5 s upper limit for short-lasting EMG activity, and therefore, the lower limit of long-lasting EMG activity of 0.5 s seems comparably short. In addition, the selection of 10 s epochs does not represent the generally used time window for sleep scoring.

Bliwise et al. examined exclusively phasic EMG activity which they called ''phasic electromyographic metric (PEM)'' (Table 1) [24–26]. This method is another approach focusing on phasic EMG activity, whereas tonic EMG activity is not accounted.

2.2. Computer-assisted scoring methods for RWA

During the previous years, some authors have used computer-assisted algorithms to analyze RWA [27–32]. To date, most of the published information on computer-assisted methods are related to a software solution developed, validated and refined by Ferri et al. focusing on the ''REM atonia index'' [29–31]. The REM atonia index can vary from 0 (complete absence of EMG atonia) to 1 (complete presence of EMG atonia) [29–31]. An atonia index <0.8 is highly suggestive for RBD [30]. Apart from the REM atonia index, three other software programs have been published. In a small pilot study, Burns et al. developed a computer algorithm, which calculated the variance of the chin EMG during three second mini-epochs and compared variances during REM sleep to a threshold defined by variances during non-REM sleep. The authors called this measure the supra-threshold REM EMG activity metric (STREAM) [27]. A STREAM cutoff of 15 identified RBD with 100% sensitivity and 71% specificity. Another software solution by Mayer et al. is based on short-lasting and long-lasting EMG activity, where EMG activity is analyzed for every one second window beyond a threshold curve (based on the difference of the upper and lower envelope of the mentalis muscle recordings) [28]. The authors demonstrated that by applying this method RBD patients could clearly be differentiated from controls. Cutoff values were not provided in this paper [28]. In a small pilot study of six Parkinson's disease patients and six controls, Kempfner et al. [32] applied a semiautomatic analysis of pattern recognition for discriminating between normal and abnormal EMG activity [32]. The authors reported that by using optimal settings it was possible to correctly identify RBD with 100% sensitivity and 100% specificity.

2.3. Advantages and disadvantages of manual and computer-assisted scoring systems

To date, manual scoring methods are the gold standard for scoring of REM-sleep related EMG activity. At least as far as RBD research is concerned, much experience has been gathered with these methods over the last years. The visual scoring approach is the most successful way of detecting artifacts and therefore, avoiding false positive classifications. Moreover, manual scoring methods are easy to apply and reliable in the majority of cases. The potential limitation of manual scoring methods used to be that in some cases, differentiation into phasic and tonic EMG activity could be challenging even for the experienced scorer. This limitation has been overcome following recent work, which simplified this system by applying the novel measure ''any'' to summarize all kinds of EMG activity exceeding 0.1 s irrespective of whether they are phasic, tonic, or in-between EMG activity lasting 5–15 s [18]. The major disadvantage of all manual scoring systems is that they are comparably time consuming and therefore, not feasible in clinical routine practice. Furthermore, they do not account for the absolute number of EMG potentials, but perform arbitrary categorizations into different time windows ranging from 2 to 30 s, which are categorized as positive (they contain a certain amount of EMG activity) or negative (they contain no EMG activity).

Advantages of the published software solutions include: comparably timesaving, rater-independence and ease of application. However, experience gained with the software solutions is still limited since all semiautomatic scoring algorithms have only been used for research purposes. Moreover, introduction of these scoring algorithms for scoring RWA in the limb muscles, which seems to be a necessary further step, has not yet been performed. Another important issue to keep in mind is that in all software programs, detection of artifacts from e.g., snoring, respiratory event related arousals, etc., has to be performed manually by a post-hoc screening of the data sets, since an automatic artifact detection software solution by inter-signal analysis has not yet been integrated.

3. Selection of muscle and muscle combinations for RBD detection

A wide variety of EMG montages ranging from using the chin EMG alone [15,16], over the chin and lower extremity muscles [21,23] to montages containing chin as well as upper and lower extremity muscles [17,18,24–26] has been applied in RBD research. However, only one of these studies was dedicated to investigating thirteen different muscles of the body in order to systematically assess EMG activity rates in different muscles and muscle combinations by an acceptable number of EMG channels [17]. Results demonstrated that the mentalis muscle showed the highest rates of phasic EMG activity followed by the flexor digitorum superficialis muscle on the upper extremity and the extensor digitorum brevis muscle on the lower extremity. In a second study, the authors performed a video EMG correlation analysis and demonstrated that by using the chin alone, 35% of movements would be missed, while adding one muscle of the upper and lower extremities, 95% of motor events would be captured [19]. A very recent study yielding cutoff values for diagnosing RBD has shown that the lower extremities are less appropriate for RBD detection than the upper limbs, which might be explained by the presence of other motor phenomena such as, periodic leg movements during sleep or excessive fragmentary myoclonus [18].

4. Night-to-night variablity

While there are several polysomnographic studies showing that video events vary in their intensity from night-to-night [33–35],