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Editorial

EDITORIAL

Assessing the performance of quantified rapid eye movement sleep without atonia methods for the diagnosis of rapid eye movement sleep behavior disorder: a dog biting its tail

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Since its first formal description [1], rapid eye movement (REM) sleep behavior disorder (RBD) was associated with "….REM sleep pathology with variable loss of chin atonia, extraordinarily increased limb-twitch activity…." at polysomnography (PSG). Indeed, in agreement with the 3rd Edition of the International Classification of Sleep Disorders (ICSD-3) [2], the demonstration of the presence of REM sleep without atonia (RSWA) at PSG is required for a diagnosis of RBD. Implicitly, this seems to indicate that RSWA is considered to be a reliable and objectively measurable biomarker for RBD [3]. However, the diagnosis of RBD has for long time been based on essentially clinical and subjective assessments of symptoms and RSWA, by nonquantitative visual analysis of PSG recordings and, sometimes with the help of synchronized video recording in the attempt to pick up some behavioral episodes arising during REM sleep [4]. Nevertheless, both the ICSD-3 and the American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events: rules, terminology, and technical specifications [5] do not report any clear cutoff values to distinguish RWSA from REM sleep with normal atonia; even if the latter indicates how to score nonatonic epochs that are needed to define RSWA. This is not trivial especially because RSWA has been reported to be present also in the absence of RBD [6–9] and REM sleep muscle tone varies substantially with age [10].

In order to fill the gap in the existing rules, several visual methods have been developed in the last decades to quantify REM sleep atonia and, thus, to help define and identify RSWA in a more precise way [11]. However, as it can be expected, all visual methods are time-consuming and require additional scoring skills and effort; moreover, some of these methods require the inclusion in the analysis of additional electromyographic (EMG) channels, besides the standard submental EMG, such as tibialis anterior muscle leads [12, 13] or EMG channels from the upper limbs [14, 15]. In the latter case, the complexity and the associated cost of the expanded PSG study is also increased by the need for additional channels that are not usually recorded in a standard PSG routine. In order to simplify the process of the quantification of REM sleep atonia and the detection of RSWA, automated approaches have also been proposed, using different algorithms [11, 16, 17], among which the most widely used and validated is the REM sleep Atonia Index (RAI) [18, 19].

Given this scenario, the current issue of *SLEEP* includes a systematic review and meta-analysis by Byun et al. [20] comparing different methods for the quantification of RSWA with respect to their ability to diagnose RBD. The main conclusion of their study is that both visual and automatic (RAI) methods show overall good performance and high sensitivity, while specificity seems to be higher with visual methods, although still acceptable with RAI, which was indicated as being especially useful for the screening of large groups of subjects. Finally, the authors caution the readers about the high risk of bias from their analyzed studies due to patient selection factors and to the significant heterogeneity among these studies.

First of all, the authors should be commended for their effort and contribution to the field because they have provided important information that both the ICSD-3 and AASM Manual should take into account in the immediate future. There is a gap to be filled and there are data in the literature to support the view that different methods can be used and that they are largely convergent and their results correlated among them [21]. However, in agreement with the prudent caution expressed by Byun et al. [20], another aspect needs to be clarified. When the performance of a method to classify patients based on the presence/absence of a certain feature is the goal, the gold standard population to use for the assessment is crucial. In the case of a diagnosis of RBD, the presence of RSWA is a necessary feature; however, as introduced above, it is not clear how this should be accomplished with the current diagnostic criteria and standard procedures. It is obvious to think that, in the patients included in all studies used for the meta-analysis, the diagnosis was based on a subjective visual and nonquantitative assessment of RSWA (i.e. with a procedure based on the current standards which do not include quantification but, most importantly, are based on a visual assessment). This introduces a bias, especially for studies using a visual quantification of RSWA which aims to quantify an already visually assessed present or absent RSWA. It is a conundrum that is not easy to solve but it certainly represents a bias that affects mostly the assessment of the performance of visual methods and certainly less that of automated quantifications of RSWA. Figorilli et al. [21] already indicated this aspect in a previous study and also Byun et al. [20] mention briefly this problem in their paper.

As a final remark, the results of the meta-analysis, overall, seem to bring some optimism on the usefulness of the quantification of RSWA because they show that all methods have a high sensitivity; this parameter is the most important one when a clinical judgment has already been made and an objective parameter is needed to confirm the suspected clinical diagnosis. In any case, it is important to understand how to deal with patients who, despite their typical clinical history of RBD with dream-enacting behaviors, and who also exhibit typical RBD behaviors during video-PSG, quantified RSWA measurement fails to show a pathological value. In order to deal with this, fortunately not frequent, situation, much more detailed evidence is needed on the night-to-night variability of these measures and on the factors able to modify them, such as drugs and substances [22, 23].

Possibly, different EMG montages might be used for research or clinical purposes and, also, in this case, criteria and consensus should be sought by the scientific community. Finally, clear consensus statements are welcome on the need to only have sleep centers experienced in the clinical and PSG diagnosis and management of RBD conduct the PSG studies. Patients with suspected RBD presenting to other sleep centers should be referred to experienced sleep centers before the PSG. This would allow an optimization of the resources, with the choice of the most appropriate montage and type of analysis for each patient which, therefore, would translate into a better management of this disorder.

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