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⊗ Sleep and Wakefulness Evaluation in Critically Ill Patients One Step Forward

Over the last two decades, there has been a growing interest in sleep abnormalities of critically ill patients. Early studies using standard EEG criteria (1) have shown that these patients exhibit a reduction in REM and N3 stages of sleep and excessive sleep fragmentation, whereas the normal circadian rhythm is lost (2, 3). Thus, although the total sleep time may be normal, the quality of sleep is poor, and these patients could be considered as sleep deprived (4, 5). Sleep disturbances remain mostly undiagnosed, mainly owing to a lack of easily applicable diagnostic tools.

Recent studies have shown that in critically ill patients, the conventional EEG criteria for evaluation of sleep and wakefulness are difficult to apply (6, 7). In these patients, the K complexes and sleep spindles, used to identify N2 stage, are often absent (atypical sleep), whereas EEG during behaviorally confirmed wakefulness may be abnormal, characterized by an increase in slow-wave activity and a decrease in high-frequency activity (pathological wakefulness). These EEG patterns have been observed in 30–50% of critically ill patients and usually coexist (6, 8). It is important to realize that EEG during pathological wakefulness may be similar to non-REM sleep, and therefore the diagnosis necessitates behavioral criteria. It follows that sleep assessment offline is unable to distinguish pathological wakefulness from sleep.

Recently, Younes and colleagues described and validated a continuous index, the odds ratio product (ORP), for the evaluation of sleep depth in ambulatory patients, using EEG power spectrum analysis (9). The ORP is an index of sleep depth derived from the relationship of powers of different EEG frequencies in 3-second

epochs, and it ranges between 0 (very deep sleep) and 2.5 (full wakefulness). An ORP value less than 1.0 predicts sleep, and an ORP value greater than 2.0 wakefulness with 95% accuracy, whereas the range between 1.0 and 2.0 represents unstable sleep. An ORP value greater than 2.2 predicts wakefulness with almost 100% accuracy (9).

In this issue of the *Journal*, Dres and colleagues (pp. 1106–1115) report, for the first time, ORP in mechanically ventilated critically ill patients during a 15-hour period preceding a spontaneous breathing trial (SBT) (10). The aim was to investigate if ORP and polysomnographic indices indicating atypical sleep and pathological wakefulness are associated with SBT outcome. Among 44 eligible patients, 37 had an acceptable quality of EEG recordings and were included in the study. ORP analysis was possible in 31 of them (84%). During the total recording period, the average ORP, the percentages of total recording time with ORP greater than 1.5, greater than 2.0, and greater than 2.2, and intraclass correlation coefficient between ORP in the right and left hemispheres (R/L ORP) were calculated. In the general population, the latter index averages 0.87 (0.76–0.95; 10th–90th percentile range) and is rarely less than 0.7 during the night (M. Younes, M.D., Ph.D., written communication, February 3, 2019), indicating that sleep depth changes in parallel in both hemispheres. Nineteen patients (51%) successfully passed the SBT, whereas 18 (49%) failed. Among the success group, 11 were extubated, and 8 were considered unready for extubation for various reasons. Pathological wakefulness or atypical sleep was highly prevalent, occurring in 14 (38%) and 17 (46%) patients, respectively, whereas conventional scoring of sleep was feasible only in 19 patients (51%). Neither atypical sleep/pathological wakefulness nor sleep architecture was associated with SBT outcome.

These results contrast with those of Thille and colleagues (8), who observed that in difficult-to-wean patients, atypical sleep was associated with longer weaning time. The difference is likely due to the patients studied because Thille and colleagues studied

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patients who had already failed SBT (8). Interestingly, Dres and colleagues (10) showed that the average ORP, the proportion of time with ORP greater than 2.2, and R/L ORP were significantly higher in patients who were extubated. Furthermore, low R/L ORP (<0.7), indicating different sleep depth between hemispheres, was strongly associated with SBT failure. Notwithstanding the small number of patients included, these results indicate that continuous sleep depth assessment and hemispheric EEG correlation in critically ill patients is feasible and may identify patients not ready to be weaned from the ventilator. Provided that EEG is acceptable for ORP analysis, this index may overcome the limitation of applying conventional sleep scoring criteria and the obstacles in pathological wakefulness diagnosis. Furthermore, ORP measurement is less demanding than full polysomnography (use of only frontal or central electrodes may be adequate) (9), whereas the results can be presented in real time. Therefore, the state of vigilance could be continuously monitored. The extent to which this approach can be applied in critically ill patients should be prospectively studied. Importantly, Dres and colleagues reported that the analysis of ORP was feasible in 70% of eligible patients (31 of 44) (10), showing again that the technical issues of EEG data acquisition in critically ill patients remain a challenge.

Dres and colleagues (10) found that the vast majority of studied patients exhibited some degree of obtundation or pathological or incomplete wakefulness (ORP, >1 to <2) and assumed that this pattern is likely due to sleep deprivation (2, 11). However, brain dysfunction linked to critical illness could be a possibility, despite the fact that the patients were deemed ready for termination of ventilation. Critical illness (particularly sepsis) may cause long-term central nervous system dysfunction (12). Impaired memory and executive function are common findings in ICU survivors, whereas sleep abnormalities have been observed even 6 months after hospital discharge (13, 14). Could ORP-derived indices be used as a monitoring tool during the acute and long-term recovery phases of critical illness? Studies are urgently needed to better clarify the pathophysiology of abnormal EEG patterns in the critically ill.

The incidental finding of different sleep depth between hemispheres in patients failing the SBT (R/L ORP, 0.54 ± 0.26 [mean \pm SD]) is very interesting, although its clinical significance is unknown. This pattern presents many similarities to unihemispheric sleep, which is widely used by birds and cetacean mammals for the purpose of avoiding predators or allowing the simultaneous sleeping and surfacing to breathe (15). Dres and colleagues (10) have postulated that the observed regional difference in sleep might be due to the reactivation of a primitive adaptive mechanism during conditions in which natural sleep is considered unsafe. However, regional brain damage, similar to regional damage observed in other organs (i.e., inhomogeneous lung damage in patients with acute respiratory distress syndrome) (16) could also be possible. Follow-up of R/L ORP may shed light on the pathophysiology and clinical significance of this regional difference in brain activity. Research in this fascinating area has just begun! ■

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