Fluids and Barriers of the CNS

LETTER TO THE EDITOR

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Commentary on "Transient intracranial pressure elevations (B waves) associated with sleep apnea": the neglected role of cyclic alternating pattern

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Riedel et al. recently published an interesting paper on the association between intracranial pressure (ICP) elevation, measured through the Lundberg B waves, and sleep apnea in a group of patients with idiopathic intracranial hypertension (IIH) and hydrocephalus [1].

ICP B waves are defined as short, repetitive elevation of intracranial pressure of up to 50 mmHg with a frequency of 0.5-2 waves/min, which are typically observed in patients with IIH, but can also be measured in subjects with normal intracranial pressure [2].

Obstructive sleep apnea (OSA) is a multi-systemic syndrome characterized by phasic interruptions of airflow during sleep, leading to severe sleep fragmentation and cardiovascular consequences, presenting a typical 20-40 s periodicity (Panel A, Fig. 1).

According to Riedel et al. [1], there is an interesting association between ICP B waves and sleep apnea. The overlap of B waves with repetitive respiratory events induces a further increase in the ICP elevation (See Panel B in Fig. 1). The synusoidal pattern becomes particularly relevant during obstructive respiratory events (compared to central-type events), whereas the introduction of CPAP leads to overall reduction of phasic ICP elevations.

Riedel et al. [1] show the temporal coupling between ICP fluctuations, nasal airflow flattening, thorax and abdomen activity changes, SatO2% oscillations and sleep stage dynamics.

In Panel B (Fig. 1) severe sleep fragmentation characterized by numerous brief awakening lasting < 2 min is recognizable in a patient with idiopathic normal pressure hydrocephalus and OSA during stage N2 of NREM sleep.

It is known that OSA is closely associated cyclic alternating pattern (CAP) oscillations, including not only fast but also slow-wave arousals [3], tightly linked to the severity of the ongoing sleep-disordered breathing [4]. CAP is the electrophysiological biomarker of sleep instability, periodically interrupting the EEG background during NREM sleep (Panel C). It is interesting to notice that CAP shares exactly the same time domain of Lundberg B waves, ranging from 2 to 60 s, and overcomes the rigid boundaries of 30 s for sleep scoring. The remaining stationary EEG activity during NREM sleep is described as non-CAP sleep (Panel D, Fig. 1).

Instead of speaking of brief awakenings or arousals, we suggest that the association between Lundberg B waves and the OSA-dependent sleep-fragmentation is more

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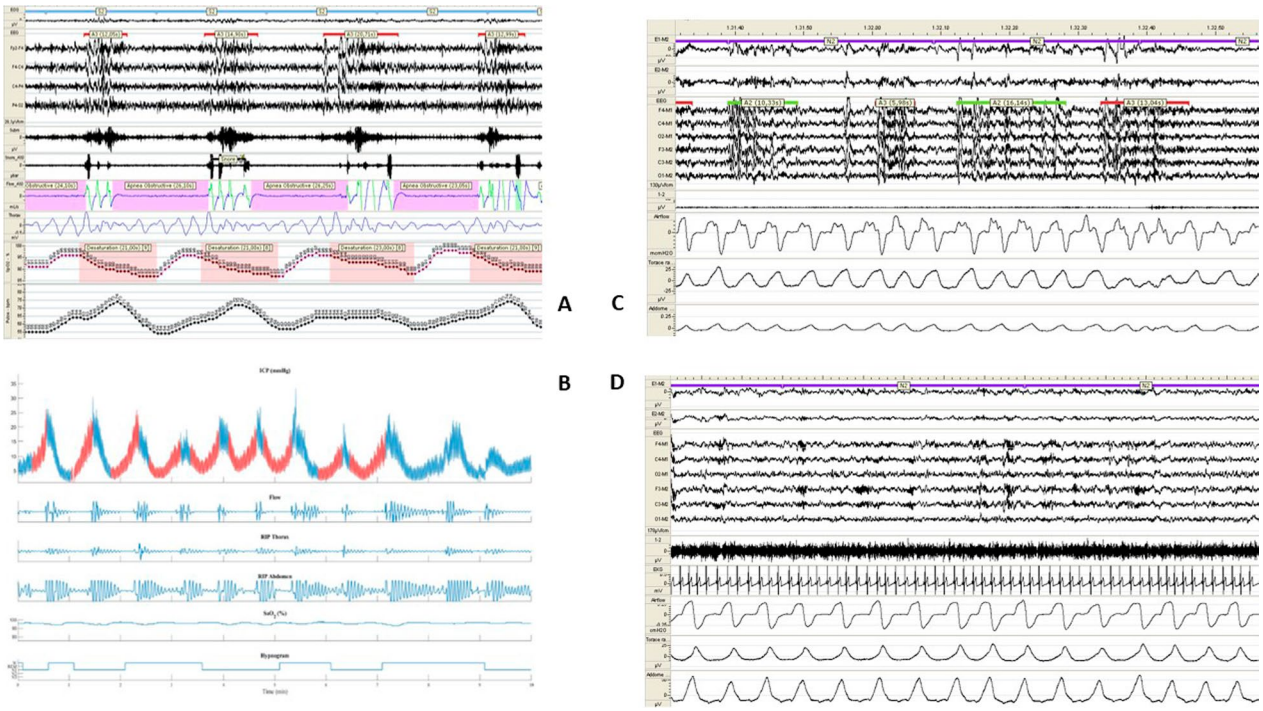

Fig. 1 **A** Vertical integration between CAP fluctuations during NREM sleep, respiratory events, oxygen desaturation and pulse rate dynamic in a patient affected by OSA. **B** figure published in Riedel et al., 2023 showing the vertical integration between ICP oscillations, obstructive apnea events and sleep fragmentation. **C** example of physiological CAP fluctuations during NREM sleep in a healthy subject. **D** example of stable NREM with no CAP intrusion

adequately mirrored by CAP metrics. The relationship between CAP and ICP B waves was already anticipated in a previous study on sleep in a comatose patient [5].

Riedel et al. [1] demonstrated that Lundberg B waves are significantly modified by CPAP in the explored OSA cohort. CAP undergoes the same evolution, reducing its fluctuations under non-invasive ventilation [6].

These findings may explain the partial loss of a clear-cut oscillatory pattern of ICP fluctuations during REM sleep, as it is know that CAP physiologically occurs only in NREM sleep [7].

Regardless of the sleep stage, NREM sleep can been described as a bimodal brain state with the alternation of stable (non-CAP) and unstable (CAP) regimens (respectively see Panel C and Panel D in Fig. 1). A "vertically integrated" approach, inclusive of extra-encephalographic features (e.g. cardiopulmonary coupling, behavioural changes and perhaps, also the intracranial B waves), is probably the most adequate methodology to investigate all the oscillations during NREM sleep [8]

To the best of our knowledge, studies exploring the link between ICP elevations and CAP had never been performed. We foster the exploration of the potentially entangled relationship between these two periodic events with further investigations.

Author contributions
C.M. and L.P. wrote the main manuscript text and prepared figures. All authors reviewed and approved the manuscript in its final form.

Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Competing interests
The authors declare no competing interests.

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