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LETTER TO THE EDITOR

SREDA in a transient global amnesia patient: the overlooked link?

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Dear Editor,

Transient global amnesia (TGA) is an acute amnestic syndrome defined by the inability to form new memories for less than 24 h, without other neurological symptoms [1–3]. SREDA (*Subclinical Rhythmic Electroencephalographic Discharges in Adults*) is a very rare benign variant that mimics ictal epileptiform discharges and can lead to misdiagnosis of epilepsy [4, 5]. Here, we present an exceptional case of SREDA in a TGA patient.

A 77-year-old woman presented to the emergency department in December 2020 due to a 1-week not-irradiated acute low back pain after a fall. Her past medical history was remarkable by a 1-year history of a mixed anxiety-depressive disorder controlled with paroxetine 20 mg once daily, with adequate tolerance.

On examination, vital signs were normal, as were blood tests. The pain subsided with intravenous paracetamol 1 g every 8 h. Lumbar spine radiography showed an L2 compression fracture of probable osteoporotic etiology, with no surgical indication as there was no structural instability or other neurological symptoms. Just after performing the test, the patient began a clinical picture consisting of repetitive questions ("what day is it today?" and "where am I?"). Neurological examination was otherwise normal, without significant changes in her vital signs.

An urgent simple cranial CT scan was requested, with no evidence of acute intracranial ischemic or hemorrhagic pathology. An urgent electroencephalogram (EEG) (Figs. 1 and 2) revealed the existence of SREDA, without a clinical correlate, so antiseizure treatment was not started. She was ultimately discharged home.

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The first month's EEG was normal, with a resolution of SREDA, as was the third month's brain MRI (including T2-diffusion sequences). In the third-month follow-up consultation with Neurology, she reported lacunar amnesia of the TGA episode, remaining otherwise asymptomatic at present.

TGA is characterized by anterograde amnesia, although there may be a variable degree of patchy retrograde amnesia in the middle of the crisis [2], generated by long-term, declarative (explicit or conscious) episodic memory involvement, due to hippocampal involvement (*Cornus Ammonis* [CA]-1 or Sommer sector). It makes it impossible to form new memories, thus patients repeat questions about their temporal and/or spatial situation. It generally persists a memory gap of what happened during the TGA period [1–3]. Its incidence is 3.4–10.4/100,000 inhabitants/year, reaching 23.5/100,000 inhabitants/year in patients older than 50 years [1]. There is usually no difference between the sexes, but a series of 28 cases from 2015 reported a higher incidence in women older than 50 years [6].

TGA's exact etiopathogenesis is unknown. The most plausible theories would be (A) propagated cortical depression with hippocampal glutamate release and (B) venous stasis of the hippocampal drainage sinuses favored by the Valsalva maneuver [1–3]. Through multivariate analysis, interrelated clinical and epidemiological factors have been found in women, an anxious and/or depressive personality, together with a stressful emotional event; in patients younger than 56 years, a history of migraine; and in men, a precipitating physical exertion. A series of risk factors have been invoked, such as previous immersion in water (especially cold), sexual intercourse, acute pain and other factors (particularly after radiological tests) [3].

The diagnosis of TGA is an exclusion clinical diagnosis based on the criteria of Hodges et al. [1, 6], all of which must be met: (1) There must be a well-defined witnessed anterograde amnesia, with information from a reliable witness; (2) No altered level of consciousness or loss of personal identity; (3) Cognitive deficit must be limited to amnesia; (4) No other focal neurological symptoms (e.g., aphasia,

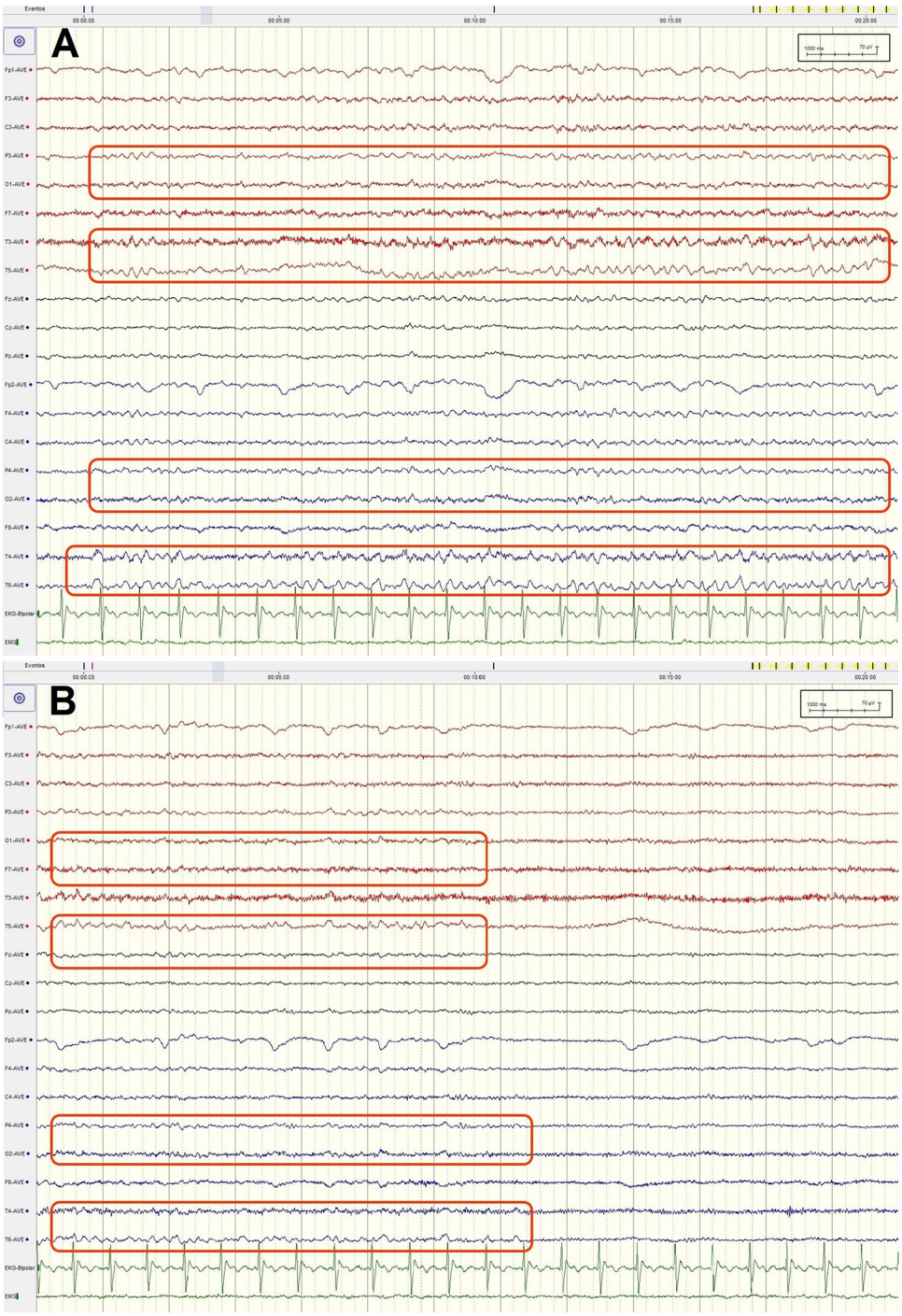

Fig. 1 EEG during wakefulness at baseline. It shows an intermittent activity formed by rhythmic θ waves (4–6 Hz) of acute morphology and up to 100 µV of amplitude, which presents a diffuse distribution, although with a clear predominance over middle-posterior temporal regions and to a lesser extent occipital and parietal regions (red rectangles). With a certain right temporal predominance. Up to 1 min long (**A**). It shows that although there is a small variability in frequency, the activity appears and disappears abruptly, without a clear temporal or spatial evolution, with no subsequent slowing down nor changes in the background activity. It is not accompanied by any obvious clinical manifestation (**B**). Montage type: referential; Recording speed: 30 mm/s; Sensitivity: 10 µV/mm; High frequency filter: 70 Hz; Low frequency filter: 0.5 Hz; Notch filter: with a cutoff frequency of 50 Hz. The space between two continuous vertical lines is equal to 1 s. *EEG:* electroencephalogram.

apraxia, homonymous hemianopia, etc.) or seizure deficits (e.g., Todd's palsy, etc.); (5) Absence of a recent history of traumatic brain injury or active epilepsy (e.g., antiseizure medication or epileptic seizures in the last 2 years). (6) Resolution of symptoms in less than 24 h; (7) Mild vegetative symptoms (headache, nausea and/or dizziness) may occur during the acute phase.

Neuroimaging, mainly MRI (T2-Diffusion sequences), is useful to confirm the topography and guide the etiology [3]. Diffusion-MRI can support the diagnosis of TGA in 70.6% of patients (69.1% if low diagnostic certainty and 93% if high diagnostic certainty with a reliable witness), as long as it is performed within the first 20 h from clinical onset clinical [7]. EEG usually reveals normal or non-specific findings, and it helps to rule out epileptic seizures, postictal state, and above all, non-convulsive *status epilepticus* [2, 3].

Main differential diagnosis [2, 3, 6] should include: hypoglycemia; transient ischemic attack or posterior circulation

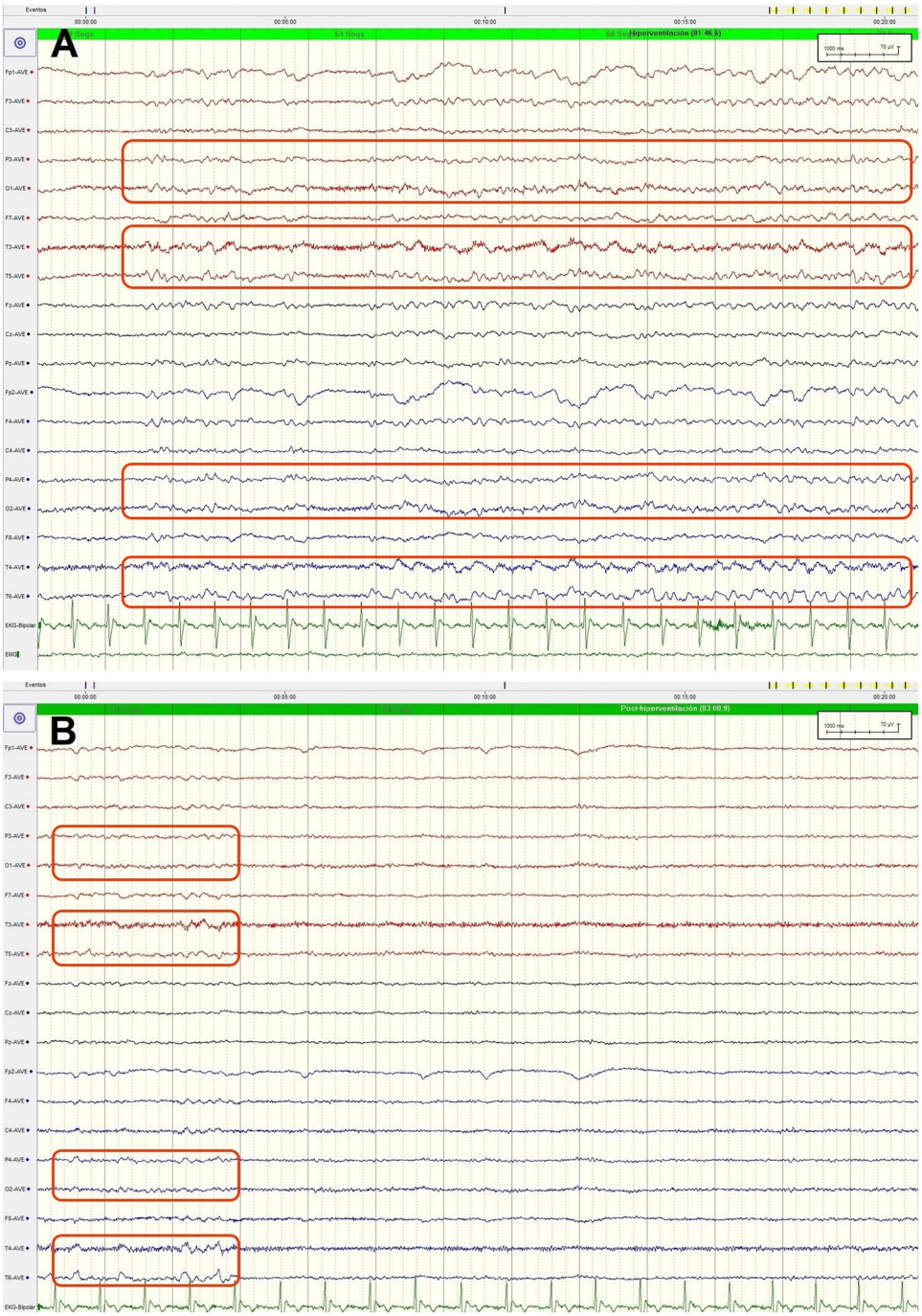

Fig. 2 EEG during wakefulness and hyperventilation. It shows that previously described findings in Figs. 1A and 1B are replicated in (**A**, **B**), respectively (red rectangles). Montage type: referential; Recording speed: 30 mm/s; Sensitivity: 10 µV/mm; High frequency filter: 70 Hz; Low frequency filter: 0.5 Hz; Notch filter: with a cutoff frequency of 50 Hz. The space between two continuous vertical lines is equal to 1 s. *EEG:* electroencephalogram.

stroke; toxic-metabolic causes such as alcohol, sympathomimetics [cocaine], etc.; pharmacological adverse effects (benzodiazepines, tricyclic antidepressants, antipsychotics, etc.); transient epileptic amnesia in the context of focal epileptic seizures with impaired level of consciousness of non-motor cognitive source and/or postictal states; psychogenic amnesia (defined by loss of personal identity); post-traumatic amnesia; Wernicke-Korsakoff syndrome, herpetic and limbic encephalitis, etc.

TGA has no specific treatment but usually has a good prognosis, with recurrence in 2.9–23.8% of cases, with a higher risk in patients with migraine [1–3].

Normal EEG variants of uncertain significance represent rhythms or waves that mimic interictal and ictal disturbances. They are found in about 12% of the EEGs performed, being misinterpreted as epileptiform discharges in up to 30% of patients by the general neurologist [8]. Among them, SREDA is a very infrequent (prevalence of

0.04–0.07%) and enigmatic variant, composed of a delta-theta rhythm at 2–6 Hz (usually theta at 5–6 Hz), with spiky morphology, generalized distribution (maximum in posterior regions), which usually appears among older adults (mean age of 52 years), while awake or in light sleep (stage 1 of NREM sleep) and during hyperventilation, lasting 40–80 s, with a sudden onset and end. It can evolve, resembling epileptic seizures, being a diagnostic challenge. Its pathophysiology is unknown and it has been suggested that could be related to hypoxia in bordering parietooccipital-temporoparietal areas. There may be atypical variants (e.g., frontal SREDA), but there is no posterior slowing nor abolition of the background alpha rhythm [4, 6].

To date, SREDA has been reported occasionally in TGA patients, without a clear pathophysiological correlation [4–6, 9]. However, given the little literature published in this regard, this physiopathological associative possibility cannot be ruled out, as the result of transient cerebral hypoxia involving both temporal lobes, triggering TGA and SREDA as its electroencephalographic expression. The EEG would play a key role in those cases in which neuroimaging findings are normal.

To our knowledge, this is the first described case from Spain, in which SREDA is reported in a TGA patient. It highlights the importance of quickly recognizing the extremely uncommon presentation, but not less important, of a TGA patient with SREDA as its possible electroencephalographic manifestation which is currently under discussion. Taking into account the existence of EEG patterns with no clear association with epilepsy is of utmost importance to prevent misdiagnosis of epilepsy, through a clinical, neuroradiological, and neurophysiological integration, and therefore not initiate useless and deleterious antiseizure therapy, due to overinterpretation of normal EEG patterns consisting of rhythmic sharp contoured nonevolving waves.

The main limitation for a better clinical-neuroradiological-neurophysiological correlation of causality is not having performed cranial MRI (T2-diffusion sequences) in the acute phase. Nonetheless, given the complete resolution of the symptoms in less than 24 h, the conservative management of the L2 compression fracture, and the pandemic situation due to the coronavirus disease 2019 (COVID-19), home discharge was prioritized, with the performance of MRI, and close holistic and interdisciplinary follow-up on an outpatient basis.

Further large-scale, well-designed observational analytical studies with a clinical, neuroradiological and neurophysiological evaluation in the acute phase are needed to demonstrate a causal association between TGA and SREDA, as well as to clarify what type of TGA patients has a higher risk for developing SREDA.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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