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Case report

Polysomnographic study of sleeplessness and oneiricisms in the alcohol withdrawal syndrome

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Abstract

We describe a polysomnographic observation of the acute phase of the alcohol withdrawal syndrome, characterized by an alteration of the sleep–wake cycle and by the absence of non-rapid eye movement sleep. An atypical transitional state between rapid eye movement sleep and wake with hallucinations and enacting-dream behaviors represented the sole sleep pattern. Analogies of alcohol withdrawal syndrome with fatal familial insomnia and Morvan's fibrillary chorea suggest a common pathophysiological mechanism in these conditions.

Keywords: Polysomnograpy; Alcohol withdrawal syndrome; Recovery; Rapid eye movement sleep behavior disorder; Oneiricism; Fatal familial insomnia; Morvan's fibrillary chorea; Clonazepam

1. Introduction

Alcohol withdrawal is a complex syndrome that ranges from anxiety to insomnia to delirium tremens [1]. Typically, insomnia is one of the heralding aspects, followed by an agitated sleepless state with hallucinations (oneiricism): the patient, especially during the night, can experience fragmentary or global dream-like hallucinations with partial or even absent awareness of reality [1]. A close link between dream activity and hallucinations in delirium tremens was hypothesized in 1881 [2], but the neurophysiological studies of this condition, mostly performed in the 1970s and 1980s [3,4], did not offer a unanimous interpretation. We studied the acute phase and recovery from alcohol withdrawal syndrome on video-polysomnography (PSG). The absence of non-rapid eye movement (NREM) sleep and the presence of an atypical transitional state between rapid eye movement (REM) sleep and wake, associated with hallucinations and enacting-dream behaviors, represented the main findings of the acute phase and this condition promptly responded to clonazepam administration.

2. Case report

A 56-year-old man, an alcohol abuser since the age of 30, spontaneously withdrew from alcohol. He had a normal family and personal history, in particular any premorbid sleep parasomnia and excessive daytime sleepiness (i.e. narcolepsy), were clinically excluded. Within a few days, his wife and daughters reported abnormal motor and verbal activities appearing during the night: jerks, fragmented movements, violent fighting behavior, talking and mimicking daytime actions such as shaving or hair combing. Whenever awakened from these episodes, the patient reported a vivid dream content. Episodes became more intense and prolonged day by day, with a cluster in the early morning hours. In 2 weeks, when the patient was admitted to a General Hospital, the enacting dreams spread throughout the night and appeared also during the daytime, as soon as the patient lapsed into drowsiness. During the rest of the day, the patient was lucid and oriented. Hyperthermia and profuse sweating completed the picture. The patient underwent thiamine, glucose, and electrolyte treatment.

One month after alcohol withdrawal, the patient was admitted to our observation for persisting symptoms. Neurological examination showed signs of lower limb polyneuropathy and mild cerebellar ataxia. When awake, the patient was cooperative, well oriented in time and space. Left alone, he lapsed into drowsiness and oneiricisms. Formal neuropsychological evaluation by means of a

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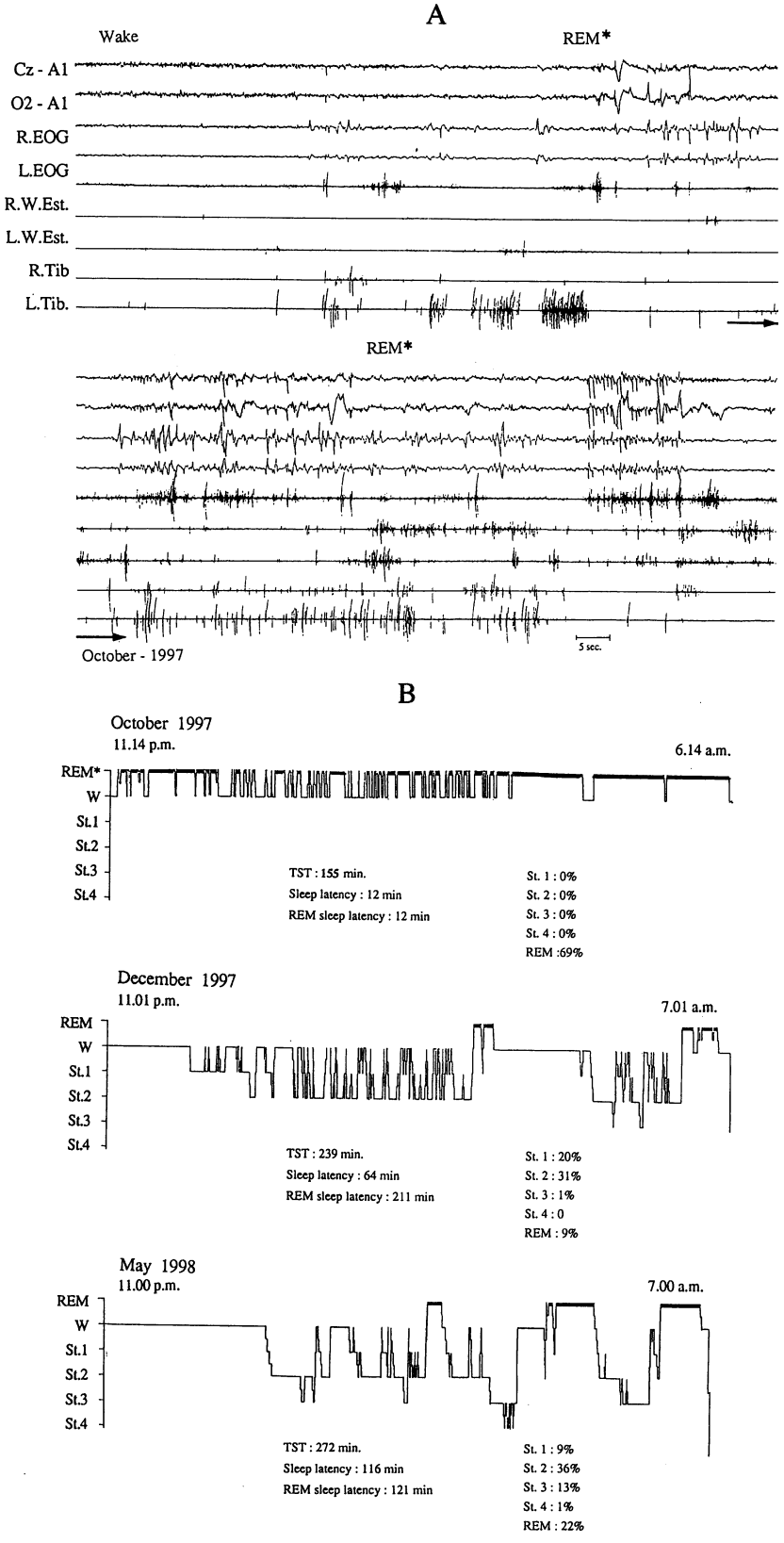
battery of tests aimed at detecting cognitive impairment [5] was normal. The patient underwent 24-h video-PSG, performed with an extended montage [6]. PSG, scored following standard criteria [7] and with allowance for REM sleep without atonia [6], demonstrated that the abnormal hallucinatory behavior appeared during abnormal REM



sleep without atonia. The latter was characterized by the persistence or even increase in electromyographic (EMG) axial muscle tone and marked limb myoclonic activity, intermingled with increased axial and limb motor activity in the presence of REM sleep atonia, and emerging directly from wakefulness (Fig. 1A). Non-REM sleep was absent. Total nocturnal sleep time was restricted to 155 min and characterized by reduced sleep efficiency (37%) and shortened sleep latency (12 min) (Fig. 1B). MSLT was not performed, but the 24-h PSG confirmed that the patient also experienced daytime sleepiness, with a prolonged nap (102 min) in the post-prandial period. At that time, we added clonazepam 4 mg per day. Within 3 days, the hallucinatory-like behavior, as well as the fever and the abnormal sweating, progressively disappeared and the patient could sleep quietly during the night.

Three months after alcohol withdrawal with clonazepam reduced to 2 mg at bedtime because of improving conditions, the patient reported a progressive recovery of sleep and a dramatic improvement in daytime sleepiness. PSG showed the reappearance of stage 2 NREM sleep and physiological REM sleep with muscle atonia (Fig. 1B). Total sleep time, as well as sleep architecture were partially restored, daytime sleepiness disappeared and clonazepam was then withdrawn.

Seven months after alcohol withdrawal, the patient reported a complete normalization of the sleep–wake schedule. PSG demonstrated the normalization of sleep architecture (Fig. 1B).

3. Discussion

Our observation documented that hallucinations and enacting dreams, typical of the acute alcohol withdrawal syndrome, correspond to an abnormal transitional state between wakefulness and REM sleep, clinically characterized by oneiricism, and polygraphically by a typical REM sleep electroencephalographic (EEG) tracing, rapid eye movements, in the presence of a lack of physiological muscle atonia and increased myoclonic activity. Polygraphically, this picture fits the established criteria for REM sleep behavior disorder (RBD). RBD represents an abnormal behavioral condition, characterized by motor or verbal activity arising during REM sleep without chin muscle atonia, eventually associated with increased limb and chin twitching. RBD is confined to night, characterized by normal overall sleep architecture and absence of excessive daytime sleepiness. RBD mostly appears as a chronic disease, either idiopathic or associated with neurodegenerative conditions affecting the brainstem, and with brain tumors, multiple sclerosis, stroke and narcolepsy [6].

In our case, REM sleep without atonia and/or excessive myoclonic activity associated with oneiricisms represented the only sleep pattern in the acute phase, and emerged directly from wakefulness, during the daytime as well as at night. Daytime sleepiness also seemed worse in the acute phase: even if a circadian rhythm of sleep and wake was partially preserved, total sleep time and sleep efficiency were markedly reduced, and the patient complained of drowsiness and sleep loss, rather than of insomnia.

Recovery was characterized by progressive wake–sleep cycle reconstruction, disappearance of daytime sleepiness, hallucinations and oneiricisms and polygraphically by the reappearance of non-REM sleep and the normalization of REM sleep.

Notably, daytime drowsiness associated with a loss of the ability to sleep, intermingled with confusional oneiric status, and the emergence of atypical REM sleep from wakefulness, are clinical features shared by another two neurological disorders, although very different in origin and course: fatal familial insomnia (FFI) and Morvan's fibrillary chorea (MFC). FFI [8] is a rare hereditary prion disease, pathologically characterized by prominent thalamic degeneration, and clinically by loss of sleep, sympathetic hyperactivity and motor signs (dysarthria, ataxia, myoclonus), progressively worsening until death. MFC is a rare disease often linked to autoantibodies against voltage gated potassium channels [9] and to the presence of limbic encephalitis, characterized by spontaneous remission in 90% of cases and progression to death in 10%. It consists of subacute onset insomnia and sympathetic hyperactivity phenotypically mirroring FFI [10], associated with cramps and fasciculations. The PSG picture of these diseases is comparable and characterized by an inability to generate physiological sleep (key features are the suppression of the hallmarks of stage 2 non-REM sleep: spindles and K complexes), drowsiness and by the emergence of REM sleep without atonia [8–10]. Both FFI and MFC share the involvement of the thalamus and connected limbic structures as their pathological correlates, indicating the prominent role that the limbic thalamus plays in the pathophysiology of sleep [11].

Alcohol withdrawal syndrome mirrors FFI and MFC, in terms of the 24-h sleep–wake disruption, inability to sleep and oneiricisms. Oneiricisms appear during an abnormal

Fig. 1. (A): Acute phase. Atypical REM sleep, emerging directly from wakefulness. Montages included EEG (Cz-A1, O2-A1), right and left electrooculogram (EOG) (R.EOG, L.EOG), surface electromyogram (EMG) from mylohyoideus (Mylo), right and left extensor digitorum communis (R.W. Est., L. W. Est.) and right and left tibialis anterior muscles (R.Tib., L.Tib.). Wake EEG, characterized by physiological 9 Hz alpha activity, gives way to lower voltage theta activity, associated with bursts of rapid eye movements and increased EMG chin and excessive limb phasic motor activity (REM*). (B) Hypnograms during the acute phase, 3 and 7 months after alcohol withdrawal. During the acute phase, polygraphic recordings were dominated by atypical REM sleep (REM*) intermingled with abundant wake activity. Three months after alcohol withdrawal stage 2 non-REM sleep and physiological REM sleep with muscle atonia reappeared and NREM–REM sleep cycles were recognizable. Seven months after alcohol withdrawal slow-wave sleep reappeared and sleep architecture was normal.

transitional state between wake and REM sleep, polygraphically corresponding to the criteria of RBD [6], but irrespective of sleep–wake architecture. Another peculiar feature of delirium tremens, the inability to generate non-REM sleep, is again strikingly reminiscent of FFI [8], and differentiates delirium tremens from chronic RBD, in which slow-wave sleep is instead often increased [6]. These clinical similarities with FFI and MFC suggest that all three disorders share a common pathophysiology, characterized by unbalanced sleep and autonomic functions toward functional hyperactivation. This condition has the thalamolimbic system as a unique pathological correlate [11]. Sudden alcohol withdrawal results in a transient homeostatic imbalance (loss of non-REM sleep and motor and autonomic activation) that may be due to the sudden dramatic changes in the gamma-aminobutyric acid (GABA)ergic inhibitory synapses within the limbic system, downregulated by chronic alcohol abuse [12].

Our case also confirms the efficacy of clonazepam to reverse oneiricisms appearing after alcohol withdrawal [13]. Benzodiazepines are considered the first choice pharmacological agents, with thiamine and glucose addition, to reduce alcohol withdrawal severity and especially the incidence of delirium [14]. The efficacy of clonazepam, the first choice drug in chronic RBD [6], in suppressing oneiricisms in delirium tremens is an interesting finding awaiting confirmation in clinical trials.

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