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LETTER TO THE EDITOR

Hypersomnia due to bilateral thalamic lesions: unexpected response to Modafinil

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Introduction

Hypersomnia, together with apathy and cognitive/behavioural dysfunction, is a prominent symptom in bilateral thalamic lesions (BTL), usually resulting from occlusion of the artery of Pecheron, a solitary trunk arising from the posterior cerebral artery and supplying the paramedian thalami [1–3]. In the acute phase, hypersomnia may fluctuate and alternate with insomnia or sleep/wake cycle disruptions; in the long term, both recovery and persistence of hypersomnia have been described [2,3].

There is no standardized treatment for this disorder. Improvement of BTL-related hypersomnia has been reported with bromocriptine, amphetamines [2] and with the non-amphetamine wakefulness-promoting modafinil [1,2]. However, the long-term response of BTL to modafinil has never been assessed with objective methods.

Case report

A 44-year-old man with MRI-ascertained bilateral paramedian thalamic lesions secondary to vasculitis in the course of streptococcus pneumoniae meningoencephalitis came to our attention because of irregular sleep/wake pattern with prolonged daytime naps (Fig. 1a, actigraphy). Two months after stroke, he developed a regular hypersomnic pattern with an average assumed sleep time of 14 h/day (Fig. 1b), including daytime episodes during which arousal could not be provoked by auditory or tactile stimuli, together with neurological signs of frontal lobe impairment: abulia, grasping, impaired attention, marked reduction in verbal fluency, hypophonia, motor

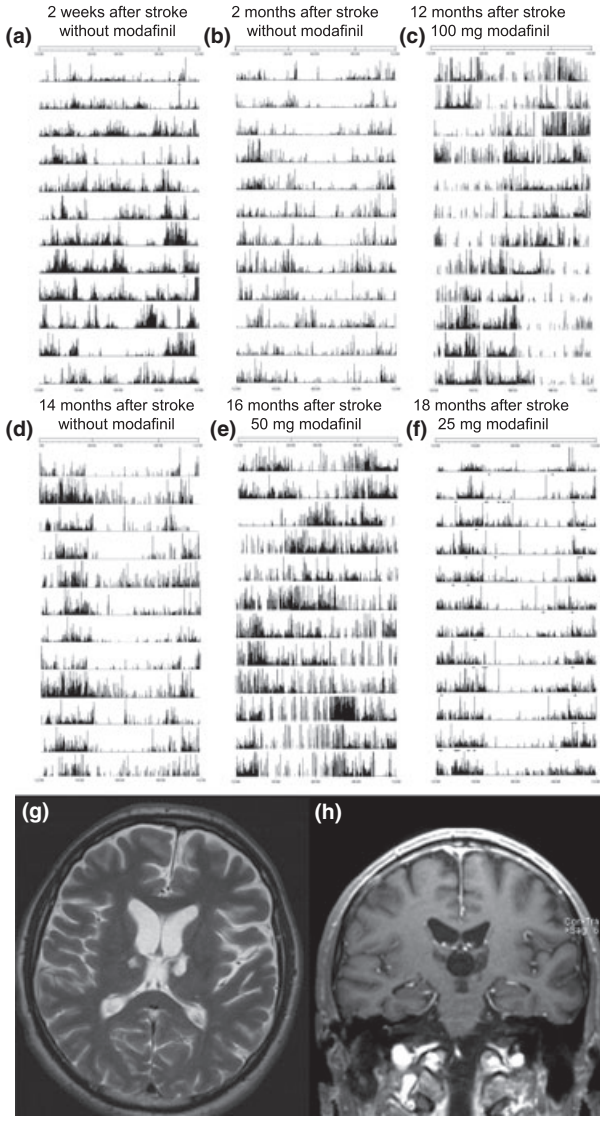

Figure 1 Actigraphic recordings and Brain MRI. Panels (a–f) show 12-days whilst actigraphic recordings. Panels (a–f) show 12-day continuous actigraphic recordings. Vertical bars present number of movements per unit of time. Higher black bars signify more movements and suggesting that the patient is awake, whilst low or missing black bars suggest sleep. Panels (g–h) present brain MRI 20 months after the onset of the symptoms. Axial FSE T2-weighted (g) and coronal-enhanced T1-weighted (h) images show bilateral mesial thalamic non-enhancing chronic encephalomalacic lesions. The lesions appeared to involve the expected location of the anterior, the medial–dorsal and the medial–ventral nuclei. On the left side, the lesion was larger and involved the subthalamic area, at the junction with the cerebral peduncle of the midbrain. The third ventricle appears passively enlarged because of focal and bilateral thalamic volume loss.

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impersistence, imitation and utilization behaviour, absence of finalistic gestures and reduced capacity for interaction. Attempts to improve the patient's wakefulness by a morning dose of 100 mg of modafinil led to an unexpected prominent circadian rhythm disruption (Fig. 1c), which returned to the regular hypersomnic pattern after modafinil withdrawal (Fig. 1d). A second attempt with 50 mg modafinil produced the same abnormal circadian response (Fig. 1e). A trial with a very low dose of modafinil (25 mg) was effective in reducing total assumed sleep and daytime sleep, without impairment of the circadian pattern (Fig. 1f). According to clinical observation with this medication, the patient had become more active during daytime. A new MRI scan confirmed BTL (Fig. 1g and h), and efficacy of 25 mg/day of modafinil persisted so far up to 18 months.

Discussion

Herein, we reported a dose-dependent unexpected sleep/wake cycle disruption with modafinil in a rare case of BTL, documented with repeated actigraphy over a period of more than 1.5 years. Actigraphy is a small watch-like instrument, worn on the wrist, which monitors movement and is used to assess the sleep–wake cycle over several consecutive days. On the basis of movement activity, actigraphy identifies periods of sleep with an accuracy above 80% with respect to polysomnography.

Different thalamic nuclei play an important role in sleep regulation [2], and an impairment of the ascending brainstem arousal system to the median thalamus has been postulated as the cause of the hypersomnia in BTL [2]. In addition, the paraventricular nucleus and the intergenicular leaflet are thalamic regions directly connected with the suprachiasmatic nucleus of the hypothalamus and involved in the regulation of circadian rhythms [4].

Modafinil is a stimulant with unknown mechanism of action which, in the herein described case, induced an abnormal circadian response, maybe because of its action on an impaired thalamic circuit. This is the first long-term documentation of an abormal dose-dependent response to modafinil in BTL, which confirms modafinil as a possible effective treatment but suggests to start from very low dosages to avoid abnormal circadian disruption and recommends repeated actighrapic monitoring to assess response in these patients.

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Disclosure of conflict of interest

The authors declare no financial or other conflict of interests.

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