SHORT REPORT

Bilateral paramedian thalamic syndrome: abnormal circadian wake-sleep and autonomic functions

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Objectives: To describe wake-sleep and body core temperature (t°) rhythm abnormalities in two patients with bilateral paramedian thalamic calcifications.

Methods: Patients underwent (18F)FDG PET scans and 24 hour polygraphic recordings of wake-sleep and t°.

Results: PET showed bilateral thalamic hypometabolism in both patients with additional basal ganglia or mesiolateral frontal and cingular hypometabolism. Wake-sleep studies showed abnormal sleep organisation and in the case with frontal and limbic PET hypometabolism, pre-sleep behaviour associated with “subwakefulness” EEG activities, lack of EEG spindles and K complexes, and features of status dissociatus. The t° rhythms showed increased mesor in both (37.4°C and 37.75°C) and inverted rhythm in one patient.

Conclusions: Paramedian thalamic structures and interconnected, especially frontal and cingular, areas play a part in the organisation of the wake-sleep cycle and attendant autonomic functions.

Chronic bilateral vascular paramedian thalamic lesions cause “subwakefulness” behaviour associated with slowing of EEG background activity with intermixed alpha/theta activities, and a lack of both deep sleep and alert wakefulness EEG activities. Similar behavioural and EEG patterns are seen in fatal familial insomnia (FFI), a prion disease with prominent involvement of the medial and anterior thalamic nuclei and limbic cortex. Circadian autonomic functions have not been explored in paramedian thalamic syndromes other than FFI. We recorded EEG and t° in two patients with non vascular bilateral paramedian thalamic lesions, exploring the relation between thalamic structures and circadian wake-sleep and vegetative functions.

METHODS

Two patients with bilateral paramedian thalamic calcifications underwent (18-FDG) PET scans on a GE-Advance PET tomoscan. Regional cerebral glucose metabolism was measured and images reconstructed and analysed with statistical parametric mapping. Regional cerebral activity of individual patients was compared with the regional activity of a group of 19 controls.

Cognitive functions were assessed by Mini Mental Status Examination, the Brief Battery for Mental Deterioration, computerised tests exploring psychomotor performance.

Patients underwent recording of EEG, ECG, eye movements, and chin and tibial anterior EMG by means of Vitaport. The 24 hour t° was analysed by means of a Mini-Logger 2000 rectal probe. Plasma growth hormone, melatonin, prolactin and cortisol were analysed in patient 2 during 24 hour polysomnography.

RESULTS

Patient 1
A 63 year old woman with ataxia and dysarthria since she was 58 years old, had calcifications of the medial thalami and quadrigeminal tubercles extending into the right lenticular nucleus. PET revealed hypometabolism in the thalamus and caudate bilaterally, and the right putamen and insula (fig 1A). Neuropsychological tests demonstrated only deficits of attention in acoustic and visual tasks and motor slowing in manual
Dexterity. The 48 hour polygraphic recordings showed normal wake/sleep EEG activities. During the daytime, the patient napped repeatedly, reaching stage 2 twice and REM sleep once. Night sleep showed prevalent light sleep stages, and protracted awakenings (fig 2A). All sleep stages were however evident, with normal EEG sleep figures and physiological REM sleep atonia. Total sleep time was reduced (3 h 26 min), and sleep efficiency decreased (52%–55%, normal >85%).

The 24 hour t° oscillation was present but with a mesor at 37.4°C, significantly higher than 15 normal controls (mean (SD) 37.05 (0.17)°C); rhythm amplitude, 0.47°C, was normal; the rhythm was however inverted, as the nadir was in the afternoon, whereas acrophase was at 05:52 during sleep (acrophase in 15 normal controls, mean (SD) 16:16 (1:20) h:m) and the physiological decrease in t° during sleep was absent (fig 2A).

**Patient 2**

A 57 year old woman developed depression, memory loss, and hypersomnia at 46 year of age and, at 52 years, visual hallucinations. At 55 years of age there began episodes of screaming and terrifying dreams during sleep, sometimes associated with jumping out of bed. At age 56 years, she became voracious and developed compulsive behaviours, urgency, and faecal incontinence. Sleep episodes would occur throughout the daytime, during which the patient did not respond to callings. Examination disclosed snout and brisk deep reflexes, and slow gait with retropulsion. Computed tomography demonstrated calcifications in the medial thalami and in the mesencephalon. Low blood calcium with normal parathormone and the brain changes led to the diagnosis of pseudo-hypoparathyroidism. PET showed a bilateral hypometabolism in the thalamus, the hippocampal structures, the orbitofrontal, the mesial frontal, and the cingulate cortices; the dorsolateral, especially left frontal cortex was also involved (fig 1B). Neuropsychological tests showed impaired long term and short term verbal memory, increased false alarms during visual attention tests, reduced verbal fluency, inadequate vigilance with difficulties in maintaining concentration and attention, and psychomotor slowing. Four days of continuous Vitaport showed daytime periods of reduced motor activity associated with EEG alpha/theta activity; this occupied 17%–63% of day and 7%–17% of night time. Non-REM sleep was characterised by a continuous theta/delta activity, and by the complete absence of sleep spindles and K complexes. REM sleep was slightly reduced (15%–22%, normal 25%) (fig 2B). There were significant (p<0.001) circadian oscillations of t°, but mesor was significantly increased (37.75 (0.06)°C); rhythm amplitude was normal (0.45 (0.06)°C). The t° decreased

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**Figure 2** The 24 hour t° rhythm (upper panels) and concomitant wake-sleep histograms (lower panels) in patient 1 (A, second day) and patient 2 (B). The x axis bar denotes the dark period. NW-NS =non-wake–non-sleep activity; A-NREM = atypical NREM sleep.
normally during the night and acrophase occurred normally at 15:00±00:02 h:m (fig 2B). Melatonin secretion and the circadian rhythmicity of cortisol, GH, and prolactin were normal.

DISCUSSION

In our patients, (18-FDG) PET demonstrated bilateral hypometabolism of the thalamus and caudate, extending to the right putamen and insula in patient 1. Patient 2 had additional involvement of the hippocampus, the orbitofrontal and mesial and lateral frontal cortices. Circadian studies exploring concomitant alterations of sleep and autonomic functions demonstrated milder disturbances in patient 1, with daytime sleep episodes, nocturnal awakenings, decreased total sleep time on the second night, and reduced sleep efficiency; T° patterns were characterised by increased mesor at 37.4°C and inversion of the rhythm without the physiological decrease during sleep. Patient 2 displayed impaired alertness with sub-wakefulness daytime EEG activities, and prominent sleep abnormalities, with lack of EEG spindles and K complexes, and alpha/theta activities intermingled with continuous theta/delta activity during NREM. These abnormalities fulfilled the description of “status dissociatus”. The wake-sleep changes were more prominent in patient 2 probably because of the additional involvement of the limbic areas, shown by PET. Our observations confirm previous reports of daytime drowsiness and “subwakefulness” patterns, sometimes reaching “status dissociatus”, in chronic paramedian thalamic lesions, and emphasise that changes may extend to autonomic functions such as T°. Abnormalities seem particularly evident when the frontal and limbic areas are involved in addition to the thalamus. In such cases, the clinical features mimic those of FFI and “Agrypnia Excitata”, a syndrome related to dysfunction of the thalamolimbic system.

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