Abnormal circadian rhythms of plasma melatonin and body temperature in the delayed sleep phase syndrome

In a study published in this Journal in 1992 Alvarez et al described normal profiles of plasma melatonin in a group of 12 patients with the delayed sleep phase syndrome, an idiopathic sleep disorder manifested by an inability to fall asleep and wake spontaneously at desired clock times and a phase delay of the major sleep-promoting hormone in relation to the desired time for sleep.1 Because of animal data indicating a central role of melatonin in circadian regulation, they obtained 24 hour plasma melatonin profiles of patients with delayed sleep phase syndrome in a fixed light-dark environment (dark period 2300–0800). On average, plasma melatonin concentrations peaked about 0400 and reflected a normal adult pattern of melatonin secretion. Intrinsic patterns of human melatonin secretion, however, may be masked by patterns of sleep and light exposure.2 Evaluation of circadian oscillators in patients with circadian sleep–wake disorders is complicated by the presence of sleep–wake-onset and sleep–waking-related symptoms.

Over a six week period, an inpatient unit the patient was tapered off benzodiazepines over four weeks and then remained medication free for another two weeks. She showed occasional irritability that was attributed to benzodiazepine withdrawal. During this period the patient was allowed to regulate her circadian exposure to light and dark and to sleep when she wished. Although she was unable to sleep from 0000 to 0500, she would go to sleep between 0400 and 0830 each morning and sleep until 1000 to 1300. At the conclusion of this interval, a 24 hour constant routine procedure was undertaken whereby the patient was awake, in virtual darkness (<1 lux), and ate small isocaloric meals every two hours. She was kept awake by engaging her in conversation and sedentary games. Blood samples were obtained via an indwelling intravenous catheter every 30 minutes (1700–1700). Plasma melatonin was measured by StockGrand Ltd (Department of Biochemistry, University of Surrey, UK) using a radioimmunoassay. Rectal temperature was monitored continuously throughout the procedure.

The patient's plasma melatonin rhythm (figure), peaking at 0830, was remarkable particularly for its delayed phase position compared with that typically seen in normal subjects, which peaks in the middle of the night. Rectal temperature exhibited a similarly delayed profile with the nocturnal temperature minimum occurring between about 0500 and 1230. The delayed timing of the plasma melatonin peak and the rectal temperature minimum provide preliminary evidence that a biological abnormality may be present in the delayed sleep phase syndrome and that the biological dysregulation matches the clinical features of the syndrome. Although it is theoretically possible that our plasma melatonin results differed from those of Alvarez et al because their sample consisted mostly of men and our patient was a woman, we have no reason to think that the sex difference might have accounted for the different melatonin profiles. Rather, we suspect that we were able to identify a phase shift in the melatonin profile because its underlying rhythm was unmasked by the 24 hour dim light conditions. Our finding of a similar delay in the circadian temperature rhythm confirms a previous report by Guillemainault et al.3 It is noteworthy that phase advancement of the circadian rhythm of body temperature has been associated with successful treatment of the delayed sleep phase syndrome.4

If this report of delayed plasma melatonin and body temperature rhythms in the delayed sleep phase syndrome is replicated in a large sample of patients, it will provide further evidence that plasma melatonin and body temperature rhythms can serve as reliable markers of phase setting of the human body clock that regulates sleep. The establishment of a biological abnormality in this disorder might also provide some salience to those with the disorder, who until now, might have been told that their sleep–wake disorder was psychological in origin. It will also provide biological markers for the diagnosis and progress of treatment of the syndrome.

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REM sleep behaviour disorder as the presenting symptom of multiple system atrophy

REM sleep disturbances are often encountered during the course of multiple system atrophy.1 The most common features are upper airway dysfunction with snoring and laryngeal stridor and disordered central ventilation with apnoea.2 Other types of sleep disturbance such as rapid eye movement (REM) sleep behaviour disorder (RBD) have also been occasionally reported,3 preceding other signs of the condition in one case.4 REM sleep behaviour disorder is characterised by the occurrence of intense dream-like motor and verbal behavioural activity during REM sleep, the first often violent and potentially injurious.5 We report two new cases in whom REM sleep behaviour disorder preceded other symptoms or signs of the disease, to draw attention to

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