

# Idiopathic hypersomnia

## A series of 42 patients

Claudio Bassetti and Michael S. Aldrich

Department of Neurology, University of Michigan Medical Center, Ann Arbor, Michigan, USA

Correspondence to: Michael S. Aldrich, MD, Department of Neurology, Sleep Disorders Center, University of Michigan Hospitals, Taubman Center 1920/0316, 1500 E. Medical Center Drive, Ann Arbor, MI 48109–0316, USA

### Summary

*The features of idiopathic hypersomnia are not well defined. We reviewed clinical and laboratory information on 42 subjects with idiopathic hypersomnia and obtained detailed follow-up evaluations on 28 of them. Only 29% of subjects had 'classic' idiopathic hypersomnia with non-imperative sleepiness, long unrefreshing naps, prolonged night-time sleep, difficult awakening with sleep drunkenness and prominent mood disturbances. Thirty-two percent had clinical features similar to narcolepsy, i.e. irresistible sleepiness, short and refreshing naps, few problems with awakening and good response to stimulants, without cataplexy or any indication of abnormal REM (rapid eye movement) sleep.*

*The other 39% had intermediate clinical characteristics. We found no increase in the frequency of the human leucocyte antigens associated with narcolepsy. Overall, response to stimulants was good in three-quarters of the patients and spontaneous improvement of sleepiness occurred in one-quarter. Possible aetiologies identified in 10 patients included viral illness, head trauma and primary mood disorder. Idiopathic hypersomnia is a rare syndrome in which clinical heterogeneity suggests a variable or multifactoral pathogenesis. Only a minority of cases correspond to classical descriptions. Stimulants are often beneficial and spontaneous improvement appears to be more common than in narcolepsy.*

**Keywords:** idiopathic hypersomnia; hypersomnia; sleepiness; narcolepsy; sleep; sleep disorders

**Abbreviations:** HLA = human leucocyte antigen; MSLT = Multiple Sleep Latency Test; REM = rapid eye movement (sleep)

### Introduction

Hypersomnia with excessive propensity to sleep can present as excessive daytime sleepiness or prolonged night-time sleep or both. Diencephalic tumours, encephalitis and stroke were recognized as causes of hypersomnia at the turn of the last century and, following the descriptions by Gélinau (1880) and Adie (1926), narcolepsy was recognized as the principal form of non-structural hypersomnia, with intoxications, endocrinopathies and psychogenic hypersomnias representing its major differential diagnosis. Although Wilson suggested the existence of several 'narcolepsies' (Wilson, 1928) and others used the term narcolepsy synonymously with irresistible sleepiness or considered it to be a psychiatric disorder or a form of epilepsy, reports of several series of patients from the 1930s to the 1960s provided strong evidence in support of the concept of narcolepsy as a distinct and usually idiopathic sleep disorder with excessive sleepiness, cataplexy, sleep paralysis and hypnagogic hallucinations as its cardinal symptoms (Redlich, 1931; Daniels, 1934; Yoss

and Daly, 1960). Shortly after the description of rapid eye movement (REM) sleep in 1953, the phenomenon of periods of REM immediately after sleep onset was discovered in narcoleptics and interpreted as the critical biological marker of the disease (Vogel, 1960; Rechtschaffen *et al.*, 1963). The evidence supporting the view of narcolepsy as a specific clinical entity associated with sleepiness, cataplexy and periods of REM at sleep onset appeared conclusive.

As the syndrome of narcolepsy became more clearly defined, it became apparent that some patients with non-structural hypersomnia had a different clinical picture. Between 1954 and 1980 Bedrich Roth and colleagues characterized such patients and described a syndrome, which they called idiopathic hypersomnia, associated with non-imperative sleepiness, long unrefreshing naps, prolonged night-time sleep, difficulty reaching full wakefulness after sleep and sleep drunkenness (Roth and Bruhová, 1969; Roth *et al.*, 1969, 1972; Roth and Nevšimalova, 1975; Roth,

1976a, b, 1980). Psychiatric and neurovegetative symptoms, a positive family history and a chronic course with poor response to stimulants were other typical features.

Although the two entities, narcolepsy and idiopathic hypersomnia, initially appeared distinct, current evidence suggests that there is some overlap between them. First, some narcoleptics may not have cataplexy or may develop it years or decades after the onset of excessive daytime sleepiness (Parkes *et al.*, 1975; Passouant and Billiard, 1976; Billiard *et al.*, 1983). Secondly, other forms of non-structural hypersomnia including sleep apnoea, periodic limb movements in sleep, delayed sleep phase syndrome and the upper airway resistance syndrome can sometimes be associated with periods of REM at sleep onset (Moscovitch *et al.*, 1993). Thirdly, some patients with narcoleptic symptoms do not have periods of REM at sleep onset (Berti *et al.*, 1967; Roth, 1976b; Roth *et al.*, 1969). Fourthly, a recent study from our centre indicated that there is substantial overlap in the clinical features of narcolepsy and idiopathic hypersomnia (Aldrich, 1996). We, therefore, performed a systematic study of patients with idiopathic hypersomnia with two specific aims: (i) to define clinical and paraclinical features of idiopathic hypersomnia according to current diagnostic standards and (ii) to assess the relationship between idiopathic hypersomnia and narcolepsy.

## Patients and methods

We reviewed a database of >4000 patients evaluated over 10 years (1986–1995) at the Sleep Disorders Center of the University of Michigan and identified 63 patients (1.5%) who were diagnosed with idiopathic hypersomnia. Over the same interval, 258 patients (6%) were diagnosed with narcolepsy with or without cataplexy. In order to minimize the risk of misdiagnosing idiopathic hypersomnia, 135 other patients with excessive daytime sleepiness, in whom clinical data were insufficient to determine definitively its cause, were 'diagnosed' with excessive-daytime-sleepiness-not-otherwise-specified and were not included in this study. We also excluded patients initially diagnosed with idiopathic hypersomnia or excessive-daytime-sleepiness-not-otherwise-specified who later were found to have upper airway resistance syndrome and responded favourably to treatment with continuous positive airway pressure.

We then reviewed clinical and paraclinical information available for the 63 patients diagnosed with idiopathic hypersomnia to identify those who met the following criteria: (i) excessive daytime sleepiness for >1 year; (ii) absence of definite cataplexy; (iii) mean sleep latency on Multiple Sleep Latency Tests (MSLT) of <10 min; (iv)  $\leq 1$  sleep-onset REM period on MSLT; (v) apnoea + hypopnea index (number of apnoeas plus hypopneas per hour of sleep) of <10; (vi) periodic limb-movement index of <20; (vii) no improvement after a trial of increased night-time sleep and; (viii) no other apparent cause for sleepiness. These criteria closely resemble the diagnostic criteria for idiopathic hypersomnia used by

the International Classification of Sleep Disorders (1990). We used the term 'definite cataplexy' to refer to brief episodes of definite bilateral weakness that were brought on by emotion. We cannot exclude the possibility that some patients included in this study had very mild forms of cataplexy that did not meet this stringent definition. To determine the apnoea + hypopnea index, we defined an apnoea as a period of airflow cessation for at least 10 s. A hypopnea was defined as a period of at least 10 s associated with a definite decrease in either airflow or respiratory effort that was either accompanied by a decrease in oxyhaemoglobin saturation of at least 4% or followed by an arousal.

After reviewing the clinical and polygraphic information, the diagnosis of idiopathic hypersomnia was not retained in 21 patients because of an apnoea + hypopnea index of >10 ( $n = 9$ ), the presence of the insufficient sleep syndrome ( $n = 3$ ) (International Classification of Sleep Disorders, 1990), a mean sleep latency on MSLT of >10 min ( $n = 3$ ), hypersomnia secondary to a structural brain disorder ( $n = 2$ ), a primary complaint of insomnia ( $n = 2$ ) and subsequent appearance of definite cataplexy ( $n = 2$ ). The remaining 42 subjects constituted the study group. The 42 subjects included most of the 26 subjects with idiopathic hypersomnia reported by Aldrich (1996). The two groups were not identical because the earlier report had somewhat different inclusion criteria and did not include subjects who were evaluated after 1993.

We then performed a retrospective clinical assessment. Clinical notes were available for all 42 subjects and 29 had completed a standard 66-item sleep questionnaire. This questionnaire includes questions about general patient characteristics, sleep habits, sleep-wake complaints, past and current medical history and social history. Most questions are answered with a five-point scale as follows: 1 = never or almost never; 2 = rarely, not more than once per month; 3 = occasionally, one to three times per month; 4 = often, more than one to two times per week; 5 = always or almost every day. Data on patients with idiopathic hypersomnia were compared with those of 67 narcoleptics from a previously reported study (Aldrich, 1996) who (i) had completed the same questionnaire, (ii) had an apnoea + hypopnea index of <10, and (iii) had a periodic limb-movement index of <20. Thirty-nine of the narcoleptics had definite cataplexy while the remaining 28 did not and were diagnosed with monosymptomatic narcolepsy.

We also reviewed sleep studies. Polysomnography performed with standard techniques was usually obtained between 22.00 and 06.00 hours. Sleep-stage scoring was done visually according to standard criteria (Rechtschaffen and Kales, 1968). An apnoea was defined as >90% reduction in nasal/oral airflow lasting  $\geq 10$  s. A hypopnea was scored if a reduction in airflow lasting  $\geq 10$  s was accompanied by an arousal, or by a fall in oxyhaemoglobin saturation of  $\geq 4\%$ . MSLTs were usually recorded the day after the polysomnogram and scored according to standard guidelines (Carskadon *et al.*, 1986). Sleep onset with periods of REM

**Table 1** Idiopathic hypersomnia-type excessive-daytime-sleepiness score

- 
- (1) Sleep attacks are usually not irresistible
  - (2) Duration of involuntary naps is usually >1 h
  - (3) Naps/sleep are usually difficult to be terminated by external stimuli
  - (4) Naps are usually unrefreshing or there is confusion after naps
  - (5) Stimulants are not effective (<50% subjective improvement)
- 

Yes = 1; no = 0; total score = sum of subscores, i.e. number of 'yes' answers given.

was defined as sleep onset which was followed by periods of REM sleep within 15 min.

To assess for the presence of upper airway resistance syndrome, monitoring of endo-oesophageal pressure with the use of a water-filled catheter was performed in 12 patients. Mean and peak negative inspiratory pressures were recorded during wakefulness, non-REM and REM sleep. Typing of Class II human leucocyte antigen (HLA) haplotypes was available in 18 of the 42 patients.

We also performed a prospective clinical assessment and one of us (C.B.) attempted to contact all 42 subjects. Four had died and 10 were not available; the remaining 28 were interviewed in person or by telephone and completed a detailed questionnaire covering the following points: past and present history of sleep-wake complaints; onset, evolution, character, severity and factors that improved or aggravated excessive daytime sleepiness; Epworth Sleepiness Score (Johns, 1994); frequency, duration and refreshing character of daytime naps; the maximal amount of night-time sleep; the frequency of night-time sleep >12 h; awakening difficulties; sleep drunkenness defined as confusional behaviour on awakening with nonsense speech, slurred speech, gait ataxia or amnesia; automatic behaviour defined as daytime episodes of nonsense speech or behaviour with partial or complete amnesia; neurovegetative disturbances (frequent headaches, frequent orthostatic dizziness or Raynaud-like phenomena); symptoms of anxiety or depression; history of serious infections or head trauma with loss of consciousness preceding the onset of excessive daytime sleepiness; family history of excessive daytime sleepiness; and response to treatment. Combining the answers to five questions each we also created an 'idiopathic hypersomnia-like' excessive-daytime-sleepiness score based on data and criteria from Honda and Roth (Roth, 1976a; Honda, 1988) (Table 1).

Statistical analysis was performed using the Mann-Whitney *U* test, contingency tables and the  $\chi^2$  test for non parametric variables; and the Student's *t* test and a one-way ANOVA (analysis of variance) for parametric variables. Statistical significance was set at  $P < 0.05$ .

## Results

Hypersomnia began at a mean age of  $19 \pm 8$  years (range 6-43) and often worsened over several years. The onset of hypersomnia was preceded or accompanied by transient insomnia ( $n = 5$ ), weight gain ( $n = 2$ ), viral illness ( $n = 4$ ) or minor head trauma ( $n = 3$ ). Although some subjects noted

increased hypersomnia with alcohol, heavy meals, winter, increased physical activity, psychological stress and menses, most did not identify any aggravating factors and appeared to tolerate brief periods of reduced sleep fairly well. A few subjects described fluctuations in the severity of hypersomnia of uncertain cause.

Almost all subjects had problems with driving due to sleepiness and most described problems at work or in their social life. About 60% took one or more involuntary naps per day. Naps usually lasted for >30 min in 51% and were usually unrefreshing in 77%. Dreaming was recalled after most naps by 40%. Neurovegetative symptoms (frequent headaches, orthostatic disturbances, Raynaud-like symptoms) were reported by 50% of subjects and 27% had a combination of two or more of these symptoms. None was disabled by these symptoms or reported syncope.

Almost half described restless sleep with frequent arousals. Although 82% had slept for  $\geq 12$  h on at least one occasion, only 25% had prolonged night-time sleep episodes two or more times per month. Habitual dreaming was present in 40%. Habitual problems with awakening occurred in 55% but sleep drunkenness was reported by only 21%. Subjects with or without sleep drunkenness differed significantly in the 'time to get going' in the morning ( $82 \pm 77$  versus  $25 \pm 27$  min) but not with regard to other clinical features. The lifetime prevalence of psychiatric symptoms was 57%. Common associated medical conditions included hypothyroidism (10%), 'recurrent infections' (10%) and obesity (25%). However, treatment of hypothyroidism did not improve the sleep disturbance.

Polysomnographic studies were unremarkable on average apart from short sleep latency ( $6.4 \pm 5.7$  min). Latency to REM sleep, the amount of REM sleep, the mean apnoea + hypopnea index (4.0) and the mean periodic limb-movement index (2.6) were normal. The mean sleep latency during MSLT was in the pathological range but was higher than in the comparison groups of narcoleptics (Table 2).

We compared clinical and paraclinical characteristics of the subjects with idiopathic hypersomnia with those of a group of previously reported patients with narcolepsy (Aldrich, 1996) (Table 2). Only 7% of subjects with idiopathic hypersomnia were African-American compared with 27% of narcoleptics ( $P < 0.02$ ). Habitual snoring was common (45%) but was not more frequent than in narcoleptics. There were no significant differences between the three groups in the hours of sleep per weekday and the time to get going in the morning. Hypnagogic hallucinations and sleep paralysis

**Table 2** Clinical, polygraphic and genetic findings in idiopathic hypersomnia and narcolepsy

Parameter	Idiopathic hypersomnia	Mono-symptomatic narcolepsy <sup>†</sup>	Narcolepsy with cataplexy <sup>†</sup>
Subjects ( <i>n</i> )	42	28	39
Mean age at diagnosis (years)	35	34	46
Female : male	27 : 15	13 : 15	25 : 14
Caucasian : African-American : Asian	39 : 3 : 0	20 : 7 : 1	27 : 11 : 1
Automatic behaviour	61%*	25–35% <sup>‡</sup>	31–38% <sup>‡</sup>
Sleep paralysis <sup>§</sup>	40%	27–36% <sup>‡</sup>	49–58% <sup>‡</sup>
Hypnagogic hallucinations <sup>§</sup>	43%	14–30% <sup>‡</sup>	74–75% <sup>‡,***</sup>
Hours of sleep per weekday	8.4 ± 1.9	7.7 ± 0.4	7.8 ± 0.3
Time to get going in the morning (min)	42	48	36
Sleep efficiency	93 ± 5%	93 ± 5%	86 ± 12%**
Total sleep time (min)	464 ± 50	468 ± 47	432 ± 75
Number of awakenings (>1 min)	20 ± 11	9 ± 7***	17 ± 10
Slow wave sleep (% of total sleep)	8 ± 5	8 ± 4	5 ± 4
REM sleep (% of total sleep)	18 ± 7	19 ± 4	16 ± 6
Mean sleep latency on MSLT	4.3 ± 2.1*	2.8 ± 1.1	2.2 ± 1.2
Periods of sleep onset with REM/ chances on polysomnogram + MSLT	12/303 (4%)*	93/188 (49%)	106/210 (50%)
DR2 (number of positives/total tested)	6/18 (33%)*	4/7 (57%)	9/11 (82%)
DQ1 (number of positives/total tested)	13/18 (72%)	7/7 (100%)	9/10 (90%)

MSLT = Multiple Sleep Latency Tests. <sup>†</sup>Data from Aldrich (1996). Monosymptomatic narcolepsy was defined as narcolepsy by ICSD criteria (International classification of sleep disorders, 1990) with >2 periods of sleep onset with REM on MSLT but with no definite cataplexy. <sup>‡</sup>Range of percentage obtained from questionnaire or clinical assessment. <sup>§</sup>Occasionally, often or always. \**P* < 0.05 versus monosymptomatic narcolepsy and narcolepsy with cataplexy. \*\**P* < 0.05 versus idiopathic hypersomnia and monosymptomatic narcolepsy. \*\*\**P* < 0.05 versus idiopathic hypersomnia and narcolepsy with cataplexy.

occurred in similar proportions in idiopathic hypersomnia and monosymptomatic narcolepsy. There were no statistically significant differences in clinical or paraclinical measures between idiopathic hypersomnia subjects with and without sleep paralysis or hypnagogic hallucinations. Apart from latency to REM sleep, other polysomnographic findings were similar in the three groups. Human leucocyte antigens DR2 (33%) and DQ1 (72%) were less common in idiopathic hypersomnia than in monosymptomatic narcolepsy and narcolepsy with cataplexy, and were similar to prevalences in normal controls (Schenck *et al.*, 1996), but subjects with idiopathic hypersomnia who were positive for the DR2 haplotype (*n* = 5) had younger mean age of onset of symptoms (mean 12 versus 21 years) than subjects who were negative for DR2.

A possible cause of hypersomnia was identified in 10 of 42 (24%) subjects. Four subjects reported that excessive daytime sleepiness began in association with a viral illness (for example, *see* patient report for Subject 3b), three had onset of excessive daytime sleepiness that was temporally related to head trauma (for example, *see* patient report for Subject 3a), and three had prominent psychiatric complaints with parallel fluctuations of mood and excessive daytime sleepiness, poor response to stimulants and improvement with antidepressants (for example, *see* patient report for Subject 1b). Two patients had one relative with narcolepsy-cataplexy and 14 had at least one family member with unexplained excessive daytime sleepiness. A positive family history for diabetes was present in 52%.

Endoesophageal pressure monitoring, performed in 12 subjects, suggested increased upper airway resistance in three men and two women of whom four were habitual snorers but only one was obese. The mean peak negative oesophageal pressure in these five subjects was 38 cm of water (range 21–56 cm) but only two had frequent short arousals or a crescendo pattern of increasingly negative pressures preceding arousals. Treatment with continuous positive airway pressure did not improve excessive daytime sleepiness in any of the five. Two subjects had uvulo-palato-pharyngoplasty without significant improvement of excessive daytime sleepiness.

The mean follow-up time in our clinic was 3 years. A satisfactory response to treatment with stimulants, defined as greater than 50% subjective improvement of sleepiness or a normalization of the Epworth Sleepiness Score, was obtained in 18 of 25 (72%) while the mean sleep latency on MSLT usually remained abnormal. There was spontaneous improvement of excessive daytime sleepiness in nine out of 35 (26%) subjects followed for >1 year, including all four subjects with hypersomnia that developed after viral illness. No statistically significant differences were found between subjects with and without a possible aetiology for the other main clinical and paraclinical characteristics.

### Prospective clinical assessment

We identified three clinical syndromes according to the character of hypersomnia and the idiopathic hypersomnia

**Table 3** Subgroups of idiopathic hypersomnia patients

	'Narcoleptic' idiopathic hypersomnia	'Mixed' idiopathic hypersomnia	'Classic' idiopathic hypersomnia
Subjects ( <i>n</i> )	9	11	8
Idiopathic hypersomnia-like EDS-score	0.14	0.56	0.80
Female : male	4:5	8:3	5:3
Clinical features			
Age of onset of EDS	22	17	24
Duration of EDS (years)	22	20	13
Epworth Sleepiness Score	18 ± 4	17 ± 4	16 ± 4
Sleep attacks of >1 h <sup>†</sup>	1/9*	4/11	7/8
Frequent sleep attacks <sup>‡</sup>	5/9	4/11	6/8
Sleep attacks refreshing <sup>‡</sup>	5/9**	1/11	0/8
Sleep paralysis	4/9	5/11	2/8
Hypnagogic hallucinations	5/9	4/11	3/8
Automatic behaviours	6/9	7/11	3/8
Awakening problems <sup>‡</sup>	1/9	5/11	6/8***
Sleep drunkenness	1/9	2/11	3/8
Psychiatric complaints	2/9**	7/11	6/8
Sleep per day >12 h <sup>§</sup>	0/7	1/10	5/7***
Time to 'get going' in the morning (min)	7 ± 6*	39 ± 40	72 ± 62
Response to stimulants	7/7	5/9	3/5
Possible aetiology	1/9****	6/11	3/8
Spontaneous improvement	1/9	2/11	3/8
Sleep laboratory			
Total sleep time on polysomnogram (min)	441 ± 23*	458 ± 48	490 ± 50
Sleep efficiency	89 ± 5%*	94 ± 3%	96 ± 2%
Number of awakenings (>1 min)	28 ± 15	21 ± 11	17 ± 12
Slow wave sleep (% total sleep)	6 ± 6	9 ± 8	9 ± 6
REM sleep (% total sleep)	14 ± 7**	19 ± 8	22 ± 4
Mean sleep latency on MSLT (min)	4.3 ± 1.1	4.4 ± 2.2	3.9 ± 2.4
Periods of sleep onset with REM/ chances on polysomnogram + MSLT	4/63 (6%)	2/75 (3%)	1/52 (2%)
HLA findings			
DR2 (number of positives/total tested)	0/4	5/8***	0/3
DQ1 (number of positives/total tested)	1/4	5/11	3/3

EDS = excessive daytime sleepiness; MSLT = Multiple Sleep Latency Tests; HLA = human leukocyte antigen. <sup>†</sup>Often or always. <sup>‡</sup>More than once a day. <sup>§</sup>At least twice a month. \**P* < 0.05 versus 'classical'; \*\**P* < 0.05 versus 'mixed' and 'classical'; \*\*\**P* < 0.05 versus 'narcoleptic' and 'mixed'; \*\*\*\**P* < 0.05 versus 'mixed'.

excessive-daytime-sleepiness score in the 28 subjects available for a detailed clinical assessment (Table 3).

### (1) 'Classic' idiopathic hypersomnia

Eight subjects had an idiopathic hypersomnia excessive-daytime-sleepiness score of  $\geq 0.75$ . They tended to have sleepiness that was not overwhelming, to take long unrefreshing naps of up to 4 h, to have prolonged night-time sleep and to have difficult awakening. Three had sleep drunkenness, five reported a total amount of night-time sleep of at least 12 h more than twice per month, one patient occasionally slept for up to 20 h/day, and one reported that difficult awakening was his most distressing problem. Most patients had psychiatric symptoms and seven of the eight had a positive family history for diabetes mellitus. Two patients had obesity and eating disorders; in one case eating occurred also at night. Satisfactory improvement of excessive

daytime sleepiness was reported by three out of five patients in whom stimulants were attempted.

**Subject 1a.** A 27-year-old carpenter presented with a complaint that he 'was always hard to wake up'. At the age of 10 years he had an episode of sleep of  $\geq 24$  h following a tooth extraction with local anaesthesia. Persistent excessive daytime sleepiness began at the age of 15–16 years, when he had to 'sleep for the rest of the day' after school, and worsened over the next several years. He usually was able to resist sleepiness in important situations but he had a few car accidents related to sleepiness and reported occasional automatic behaviours while driving. Involuntary naps lasted 15 min to 2 h, were always unrefreshing, were never associated with dreaming and were not easily terminated by external stimuli. He often felt disoriented after naps with slurred speech and difficulties walking for ~20 min. He had sleep paralysis rarely. He slept an average of 8–9 h per night

during the week and up to 18 h per day on weekends, had problems awakening every day and required several hours to 'get going' in the morning. He snored loudly but his sleep was otherwise quiet without awakenings.

Physical examination was normal. The Epworth Sleepiness Score was 18/24 and he was negative for HLA-DR2 and positive for HLA-DQ1. Psychiatric evaluation revealed no psychopathology. Four polysomnograms performed over a 9-year span, including one with endoesophageal pressure monitoring, were unremarkable apart from short sleep latencies. The mean sleep latency on four MSLTs was between 2.4 and 5.1 min with no periods of REM at sleep onset. Uvulo-palato-pharyngo-plasty improved his snoring but not his sleepiness. Treatment trials with pemoline, fluoxetine and protriptyline were unsuccessful. Best results were obtained with methylphenidate (40–60 mg/day) but it produced subjective improvement of <50% and the Epworth Sleepiness Score remained abnormal at 16/24.

*Subject 1b.* This machine operator presented at the age of 23 years with a 1-year history of sleep-wake disturbances that began during rotating shift work. She first noted a decrease in sleep needs while working night shifts and required only 4–5 h of sleep per day as compared with her usual 8–9 h. She lost ~10 kg and felt alert and energetic. Two months later, after a sleepless period of 61 h, she became sleepy and sleep needs progressively increased over the next several months to 11 to 15 h per day. On one occasion, she slept 22 h. She felt depressed and exhausted, had problems driving and stopped working. Although drowsiness could usually be overcome in important situations, she fell asleep involuntarily in relaxed settings. Afternoon naps of 1–3-h duration were usually unrefreshing and were often accompanied by dreaming. Sleepiness was worse with alcohol use, during menses and in winter months. She reported mood swings and depressive phases since late childhood. Her mood often fluctuated in parallel with sleepiness. It took her ~60 min to 'get going' each morning but she had no sleep drunkenness. She had occasional hypnagogic hallucinations, no sleep paralysis, frequent Raynaud-like phenomena and occasional orthostatic symptoms.

Physical examination was notable for mild obesity. Two polysomnograms were unremarkable apart from short latencies to sleep and high sleep efficiencies. Endoesophageal pressure monitoring was normal. The mean sleep latency on two MSLT was 3.0 and 4.0 min, with a SOREMP in one of nine naps. HLA testing was negative for DR2 and positive for DQ1. Treatment with pemoline was effective but not tolerated due to anxiety. Methylphenidate was ineffective. With protriptyline (30 mg/day), she took naps only on weekends and had subjective improvement of excessive daytime sleepiness by 50–60%, but she remained unable to work at her most recent follow-up visit at age 28 years.

## (2) 'Narcoleptic'-like idiopathic hypersomnia

Nine subjects had an idiopathic hypersomnia excessive-daytime-sleepiness score of <0.25. They tended to have overwhelming excessive daytime sleepiness, to take short refreshing naps and to awaken without difficulties. Sleep attacks occurred in one subject even while standing. In a second subject, sleep attacks were almost instantaneous and were initially misdiagnosed as seizures. Sleep drunkenness was reported by only one subject (Subject 2b below). Satisfactory improvement of excessive daytime sleepiness was noted by all seven subjects in whom stimulants were attempted and two considered the improvement to be 'miraculous'. In one subject excessive daytime sleepiness had persisted for >60 years.

*Subject 2a.* This computer center manager presented at the age of 42 years. She first noted excessive daytime sleepiness in high school when she dozed off repeatedly in school and in church. Over the following years, excessive daytime sleepiness worsened and she had irresistible sleep attacks of <10-min duration occurring up to several times a week even while talking or standing. Sleep episodes were easily terminated by external stimuli, were usually unrefreshing and were almost always accompanied by dreaming. Sleepiness fluctuated in irregular cycles of several weeks duration without apparent exacerbating factors. She often dozed at work and frequently had to let someone else drive her car because of drowsiness.

She slept 7 h per night and had hallucinations at sleep onset almost every night. She described her sleep as otherwise quiet. She did not snore and had no problem getting up in the morning. There was a history of Raynaud-like phenomena and frequent tension-type headaches but no psychiatric symptoms. She reported that both parents and five of seven siblings had excessive daytime sleepiness but not cataplexy.

Physical examination was normal. The Epworth Sleepiness Score was 17. The patient was negative for HLA-DR2 and positive for HLA-DQ1. Two polysomnograms were unremarkable apart from short latencies to stage 1 sleep. Endoesophageal pressure monitoring during the second polysomnogram was normal. The mean sleep latencies on two MSLTs were 3.0 and 4.0 min with a period of REM at sleep onset in one out of nine naps. A trial of increased sleep at night was ineffective. With dextroamphetamine (10–15 mg/day), she reported a subjective improvement of excessive daytime sleepiness by 50–60%, was able to drive without problems and did not fall asleep at work. The Epworth Sleepiness Score decreased to 9/24.

*Subject 2b.* This housewife presented at the age of 29 years. She first experienced symptoms during teenage years when she always felt tired and slept for 12 to 15 h on weekends. Over the following years, she developed problems with drowsiness while driving and had irresistible sleep attacks of <30 min duration that occurred two or more times

per day even while talking or eating dinner. Naps were not easily terminated by external stimuli, were often refreshing and were always accompanied by 'thinking' experiences. Sleepiness was worse with sleep deprivation and during winter months. She had sleep paralysis at sleep onset every night, usually lasting for 1–5 min. She slept 8.5 h/night with three or more awakenings per night, sometimes snored, had problems getting up almost every morning and occasionally felt 'drunk' on awakening with an unstable gait and slurred speech that lasted for a few minutes. There was a history of sleepiness in her mother and brother and possible sleep drunkenness in her mother.

Physical examination was notable only for moderate obesity. The Epworth Sleepiness Score was 16/24. She was negative for HLA-DR2 and HLA-DQ1. Two polysomnograms were unremarkable apart from short latencies to sleep and an increased number of awakenings. Endoesophageal pressure monitoring was unremarkable. The mean sleep latencies on two MSLTs were 2.7 and 4.5 min with no periods of REM at sleep onset. Treatment with pemoline (112.5 mg/day) and methylphenidate (20 mg/day) eliminated daytime sleep episodes and produced subjective improvement of sleepiness of >90%.

### (3) 'Mixed' idiopathic hypersomnia

Eleven subjects had idiopathic hypersomnia with excessive daytime-sleepiness scores and clinical features intermediate between the other two groups. Naps were usually brief and not refreshing. Only one subject reported night-time sleep of >12 h at least three nights per month and only two had sleep drunkenness. Satisfactory improvement of excessive daytime sleepiness was reported by five out of nine subjects in whom stimulants were attempted.

**Subject 3a.** This 30-year-old factory worker developed mild sleepiness at age 26 years, while working night shifts. On one occasion, returning home from a 12-h night shift, he fell asleep while driving and was involved in a motor vehicle accident. At age 29, he had a second car accident associated with brief loss of consciousness and amnesia for several hours. Brain MRI was normal. Sleepiness became progressively worse, although not irresistible and he began taking two or three naps per day of 1–2 h duration that were easily terminated by external stimuli, were usually unrefreshing and were not accompanied by dreaming. He had automatic behaviours during which he misplaced things: once he put clothes in the refrigerator. He slept an average of 8.5 h/night, often had more than three awakenings per night, often snored and took one or two naps to make a total of 10–12 h of sleep per day.

Physical examination was normal. The Epworth Sleepiness Score was 14. He was negative for HLA-DR2 and DQ1. Two polysomnograms were unremarkable apart from short latencies to sleep. The mean sleep latencies on two MSLTs were 4.5 and 2.7 min with no periods of REM at sleep

onset. Dextroamphetamine (10 mg/day) produced subjective improvement estimated at 75%. His Epworth Sleepiness Score normalized (7/24) and he no longer required naps.

**Subject 3b.** At age 20 years, after an episode of mycoplasma pneumonia, this college student developed problems staying awake in classes and her sleep needs increased from 7–8 h to >10 h per day. She had to take naps of several hours almost daily and on weekends she slept up to 14 h per day. She had irresistible sleep attacks of >1 h duration occurring almost daily even while talking and she avoided driving for >20 min because of sleepiness. Naps were easily terminated by external stimuli, were rarely refreshing and were sometimes accompanied by dreaming experiences. She had almost daily hypnagogic hallucinations. Night-time sleep was quiet but unrefreshing.

The Epworth Sleepiness Score was 21/24. Two polysomnograms were unremarkable except for short sleep latencies. The mean sleep latency on the MSLT was 7.6 min with no periods of REM at sleep onset. With pemoline (18.75 mg/day), she had a subjective improvement of ~50% and the Epworth Sleepiness Score improved to 14. Sleepiness gradually improved and 2 years later she reported that excessive daytime sleepiness had essentially resolved.

## Discussion

The results of this study provide an opportunity to reassess clinical and paraclinical features of idiopathic hypersomnia. Although early investigations reported ratios of idiopathic hypersomnia to narcolepsy of between 29 : 100 and 58 : 100 (Roth, 1980; van den Hoed *et al.*, 1981; Coleman *et al.*, 1982; Baker *et al.*, 1986), advances in diagnostic evaluation over the past 20–30 years have led to the recognition of several previously unknown or under-appreciated causes of sleepiness and, as a consequence, a reduction in the number of patients diagnosed with idiopathic hypersomnia. The diagnostic criteria we used were derived from the International Classification of Sleep Disorders (1990) and we included only patients in whom well-recognized causes of sleepiness had been excluded with reasonable clinical certainty. A definite diagnosis of idiopathic hypersomnia was made in only ~1% of patients seen at our sleep centre and the ratio of idiopathic hypersomnia to narcolepsy was 16 : 100. If we had excluded the 10 subjects with possible symptomatic hypersomnia, the diagnosis would have applied to only 0.8% of patients and the ratio of idiopathic hypersomnia to narcolepsy would have been 12 : 100. Others have had similar findings. Matsunaga found idiopathic hypersomnia in only seven of 500 consecutive patients (1.4%) and Billiard reported a ratio of idiopathic hypersomnia to narcolepsy of 11 : 100 (Matsunaga, 1987; Billiard, 1996). As the prevalence of narcolepsy is ~20–50 per 100 000 in Caucasians, the prevalence of idiopathic hypersomnia appears to be ~2–5 per 100 000, a figure much lower than the 30–60/100 000 predicted by Roth (1980). Our data suggest

that the prevalence of idiopathic hypersomnia in African-Americans is even lower than it is in Caucasians. We found a female : male ratio of 1.8 : 1 and a frequent positive family history for excessive daytime sleepiness but only rare occurrences of narcolepsy with cataplexy among family members of subjects with idiopathic hypersomnia.

We decided to include in our series the 10 subjects in whom a possible aetiology of idiopathic hypersomnia was identified because a causal relationship with excessive daytime sleepiness was considered unlikely or unproved. Mild head injury and viral illness have been suggested as causes of excessive daytime sleepiness (Guilleminault *et al.*, 1983; Guilleminault and Mondini, 1986). All four subjects in our series with hypersomnia following viral illness spontaneously improved, compared with only five out of 31 others with follow-up information. Thus, in some patients post-viral hypersomnia appears to be a time-limited illness that resembles idiopathic hypersomnia but that can be distinguished, based on its course.

The presence of anxiety or depressive symptoms was not considered diagnostic of an underlying primary psychiatric condition as the cause of hypersomnia unless treatment of anxiety or depression was associated with an improvement of excessive daytime sleepiness. Although anxiety and depressive symptoms were reported in more than half of our subjects, a parallel evolution of excessive daytime sleepiness and psychiatric complaints and an improvement of both with antidepressants, stimulants or both occurred in only three patients. If we had excluded the 10 subjects with possible aetiologies of idiopathic hypersomnia, the only substantial differences in our findings would have been a lower prevalence, a lower proportion of subjects with the 'mixed' form of idiopathic hypersomnia and a lower rate of spontaneous improvement.

We found, like others, that idiopathic hypersomnia usually starts gradually in the first two decades of life similar to narcolepsy (Roth, 1980; Bruck and Parkes, 1996). Prolonged night-time sleep and awakening difficulties often precede the onset of excessive daytime sleepiness. As with narcolepsy, excessive daytime sleepiness is occasionally first experienced following transient insomnia, abrupt changes in sleep-wake schedule, overexertion, general anaesthesia, viral illness or minor head trauma. It is uncertain whether these factors act as a trigger in predisposed individuals, cause idiopathic hypersomnia by themselves, or are coincidental. In our experience, apart from viral illness, these factors more often appear to aggravate preexisting excessive daytime sleepiness than to cause it *de novo*.

Our results confirm findings of others that there is substantial clinical overlap between narcolepsy and idiopathic hypersomnia (Nevimalova-Bruhova and Roth, 1972; Roth *et al.*, 1972; Roth, 1976b; Parkes, 1981; Harada *et al.*, 1988; Broughton, 1989; Aldrich, 1996; Bruck and Parkes, 1996). As with narcolepsy, excessive daytime sleepiness in idiopathic hypersomnia can be exaggerated after alcohol use, intense exercise or heavy meals and in warm environments. It is

often disabling with automatic behaviour and problems at school, at work and while driving. In the descriptions by Roth and colleagues, idiopathic hypersomnia was usually associated with continuous non-imperative sleepiness, prolonged unrefreshing naps without dreaming and difficult arousal (Roth and Bruhovà, 1969; Roth *et al.*, 1969; Roth *et al.*, 1972; Roth and Nevšimalova, 1975; Roth, 1976a, b; Roth, 1980). We found, however, that the character of excessive daytime sleepiness is more variable and can occasionally correspond to that of narcolepsy with irresistible sleep episodes as well as short refreshing naps associated with dreams from which the patients can be aroused easily. Conversely, a few patients with monosymptomatic narcolepsy and narcolepsy with cataplexy have characteristics of sleepiness and sleep duration at night and during naps that correspond to those of classical idiopathic hypersomnia (Nevimalova-Bruhova and Roth, 1972; Roth *et al.*, 1972; Broughton, 1989; Aldrich, 1996; Bruck and Parkes, 1996).

Although Roth and colleagues described the rapid onset of prolonged, deep and undisturbed night-time sleep in idiopathic hypersomnia (Roth and Bruhovà, 1969; Roth *et al.*, 1972), restless sleep with frequent arousals was described by almost half of our subjects and prolonged night-time sleep episodes were frequent in only 25%. Habitual sleep times of >12 h also can occur in a minority of narcoleptics; thus, prolonged night-time sleep is neither specific nor necessary for the diagnosis of idiopathic hypersomnia (Bruck and Parkes, 1996). Hypnagogic hallucinations, sleep paralysis and habitual dreaming were reported by ~40% of the subjects, a proportion similar to that found in monosymptomatic narcolepsy (Harada *et al.*, 1988). However, the hallucinations and dreams tended to be less bizarre, less vivid and less often associated with affect than in narcoleptics.

Roth and colleagues emphasized the importance of awakening problems and sleep drunkenness in idiopathic hypersomnia and suggested that they may be the most disturbing features of the illness (Roth *et al.*, 1972). Sleep drunkenness [also called 'Schlaftrunkenheit' in German, 'ivresse du sommeil' in French, or 'syndrome of Elpénor' after the youngest of Ulysses' comrades who killed himself during an incomplete arousal in the middle of the night (Carrot, 1947)] was present in 50–60% of patients reported by Roth (1980). Although habitual problems with awakening were common in our subjects, particularly in those with prolonged night-time sleep, sleep drunkenness occurred in only 21%. This difference may be, in part, related to the criteria used to define the symptom, as a continuum probably exists between difficult or prolonged awakening and sleep drunkenness. In any case, the symptom is not specific for idiopathic hypersomnia; it can occur in up to 10–30% of narcoleptics and in patients with other disorders associated with sleepiness (Gudden, 1905; Broughton, 1968; Roth, 1980).

Neurovegetative symptoms such as migraine or tension-type headaches, orthostatic disturbances and Raynaud-like symptoms were common in our subjects and in previously



reported patients with idiopathic hypersomnia (Roth *et al.*, 1972; Matsunaga, 1987), but they rarely required specific medical care. Although other vegetative dysfunctions reported in idiopathic hypersomnia include syncope, altered nocturnal cardiovascular responses to arousals, and elevated heart and respiratory rates in sleep (Roth *et al.*, 1972; Schneider-Helmert *et al.*, 1980; Baker *et al.*, 1986), neurovegetative symptoms were equally common in a recent comparison of idiopathic hypersomnia and narcolepsy with cataplexy (Bruck and Parkes, 1996). Thus, these symptoms also appear to be nonspecific.

Roth and colleagues reported a prevalence for psychiatric symptoms of ~50% and for depression of 14–26% in idiopathic hypersomnia (Roth *et al.*, 1972; Roth and Nevsimalová, 1975; Roth, 1976*a, b*). Similar prevalences of psychopathological disturbances have been reported in narcoleptics (Roth and Nevsimalová, 1975; Baker *et al.*, 1986). It seems likely that most of the psychiatric symptoms in these patients are nonspecific responses to chronic illness rather than essential elements of idiopathic hypersomnia.

On the other hand, the clinical picture of 'classic' idiopathic hypersomnia overlaps to some degree with psychiatric hypersomnia. The combination of vegetative disturbances with melancholic features has been recognized for many years in the psychiatric literature as 'atypical depression' (Willey, 1924; Missrieglner, 1941; Pai, 1950; Roth and Nevsimalová, 1975; Roth, 1976*a*; Potter *et al.*, 1991). The following points support a link between 'classic' idiopathic hypersomnia and a mood disorder. First, three of our subjects reported parallel fluctuations of excessive daytime sleepiness and psychiatric complaints, as well as exacerbations of excessive daytime sleepiness during winter or with the menstrual period. They also had a positive family history for depression and a good response to antidepressants. Secondly, hypersomnia related to mood disorders is relatively common in young depressed patients, who may spend as much as 16–20 h per day in bed and may have difficulty in 'getting going' in the morning (Michaelis, 1965; Detre *et al.*, 1972; Claghorn *et al.*, 1981; Gravey *et al.*, 1984). Thirdly, although depressive hypersomnia is usually attributed to lack of initiative, apathy, clinophilia (tendency to maintain a reclining position) and associated with normal or only mildly abnormal sleep latencies on MSLT (Zorick *et al.*, 1982; Nofzinger *et al.*, 1991), a propensity for increased non-REM sleep has occasionally been documented. Billiard *et al.* (1994) described a subgroup of young depressed patients with prolonged nighttime sleep and abnormal MSLTs and van den Hoed *et al.* (1981) found that 10% of patients with excessive daytime sleepiness secondary to mood disorders have a mean sleep latency of <5 min on MSLT. Hawkins *et al.* (1985) showed that depressed patients with hypersomnia extend the duration of their sleep significantly more than control subjects when allowed to sleep *ad libitum*.

In our study, as in others, idiopathic hypersomnia was associated with essentially unremarkable polysomnography (Roth *et al.*, 1972; Baker *et al.*, 1986). We found no

evidence of increased REM-sleep pressure in subjects with 'narcoleptic-like' idiopathic hypersomnia and no polysomnographic differences between subjects with 'narcoleptic-like' idiopathic hypersomnia and those with 'classic' idiopathic hypersomnia. These results suggest that other recording techniques or modalities may be more specific for idiopathic hypersomnia than polysomnogram. Billiard *et al.* (1994) and Billiard (1994) emphasized the diagnostic utility of 24-hour recordings to document the facilitation of non-REM sleep in idiopathic hypersomnia and Broughton and Aguirre (1987) suggested the use of evoked potentials to differentiate non-REM from REM.

The striking contrast between the differentiation of the three idiopathic hypersomnia subgroups based on clinical features and the lack of differentiation based on polysomnogram and MSLT raise questions about the relationship between symptoms and sleep onset with REM in narcolepsy and idiopathic hypersomnia. Although Dement *et al.* (1966) suggested that REM sleep episodes are usually experienced by narcoleptics as imperative 'sleep attacks', sleep attacks can be associated with non-REM sleep as well as REM sleep (Hishikawa *et al.*, 1968; Roth *et al.*, 1969). Similarly, although the association of sleep onset with REM with hypnagogic hallucinations and sleep paralysis was identified in several classic papers on narcolepsy (Hishikawa and Kaneko 1965; Dement *et al.*, 1966), these symptoms can occur in disorders that are not associated with frequent occurrences of sleep onset with REM and can occur with polygraphic features of non-REM sleep, even in narcoleptics (Ribstein, 1976; Harada *et al.*, 1988; Aldrich, 1996). Although the occurrence of micro-episodes of REM sleep or ambiguous sleep combining non-REM and REM sleep features could explain the occurrence of clinical REM sleep-related phenomena in the absence of sustained polygraphic REM sleep, it is also possible that sleep paralysis, hypnagogic hallucinations and periods of REM at sleep onset are pathophysiologically related but distinct phenomena that can appear together or in isolation. This hypothesis is supported by the existence of familial cases of isolated sleep paralysis and by the frequent occurrence of sleep paralysis in persons without narcolepsy (Nevimalova-Bruhova and Roth, 1972; Dahlitz and Parkes, 1993).

Despite previous reports of poor responses to treatment (Roth, 1980; Parkes, 1981; Billiard, 1996), we found that three-quarters of patients with idiopathic hypersomnia benefited from stimulants. The most dramatic improvement of excessive daytime sleepiness was obtained with methylphenidate and dextroamphetamine in subjects with the narcoleptic-type of idiopathic hypersomnia. Occasionally, patients with 'classic' idiopathic hypersomnia responded better to antidepressants than to stimulants. As with narcolepsy, subjective improvement of sleepiness was not necessarily accompanied by an increase of sleep latencies on MSLT (Boivin and Montplaisir, 1991; Hublin *et al.*, 1994). Others have reported successful treatment of idiopathic hypersomnia with modafinil (Bastuji and Jouvet, 1988). Our

patients did not report any improvement of their excessive daytime sleepiness after prolonged sleeping for days, a treatment suggested by Roth (1980).

A 'spontaneous' improvement or even disappearance of excessive daytime sleepiness was reported in one-quarter of the idiopathic hypersomnia patients followed in our centre for >1 year, confirming a recent observation by others (Bruck and Parkes, 1996). This outcome contrasts with the almost invariable persistence of excessive daytime sleepiness in narcolepsy (Parkes *et al.*, 1975; Billiard *et al.*, 1983).

Despite the relatively small numbers of subjects in the three idiopathic hypersomnia sub-groups, we believe that our findings have implications concerning the pathogenesis of narcolepsy and idiopathic hypersomnia and the classification of these disorders. Roth (1976a) and Roth *et al.* (1972) differentiated idiopathic hypersomnia clinically into monosymptomatic and polysymptomatic forms and aetiologically into idiopathic and symptomatic forms. They defined monosymptomatic idiopathic hypersomnia as non-narcoleptic essential hypersomnia, and polysymptomatic idiopathic hypersomnia as the association of this hypersomnia with prolonged night time sleep and awakening difficulties. Idiopathic and symptomatic forms were described as clinically similar. Our experience, however, suggests that current criteria for idiopathic hypersomnia identify a clinically more heterogeneous population. Some have the 'classic' idiopathic syndrome described by Roth, while others have excessive daytime sleepiness similar to narcolepsy with a better response to stimulants. A third group has intermediate clinical characteristics. We recognize that this sub-classification may need to be revised in the future based on assessment of larger numbers of subjects.

Although the biological basis of idiopathic hypersomnia is unknown, the clinical and paraclinical features suggest some hypotheses. First, the biological basis of both 'classic' idiopathic hypersomnia and some cases of atypical depression could be related to diencephalic dysfunction. Facilitation of non-REM sleep may be due to a dysfunction of arousal systems (Roth *et al.*, 1969), as suggested by a report of increased levels of monoamine metabolites in the CSF of patients with idiopathic hypersomnia, and by the findings that hypersomnia with an increase of monoamine metabolites in the CSF can be induced in cats by a lesion of ascending activating noradrenergic pathways (Petitjean and Jouvet, 1970; Faull *et al.*, 1983). Although we found, as did others, that patients with classical idiopathic hypersomnia are usually negative for the HLA-DR2 antigen (Honda *et al.*, 1986b; Harada *et al.*, 1988), Montplaisir and Poirier (1988) suggested a higher prevalence of HLA-DR5 and HLA-Cw2 in idiopathic hypersomnia than in controls. The strong association between 'classic' idiopathic hypersomnia and a family history of diabetes found in this study suggests a possible linkage of the disease to other genes.

Secondly, the hypothesis that the subgroup of 'narcoleptic-type' idiopathic hypersomnia represents a non-REM variant of narcolepsy is suggested by the clinical characteristics of

hypersomnia, its good response to stimulants and the rare occurrence of narcolepsy with cataplexy in relatives. On the other hand, a mean duration of excessive daytime sleepiness of >20 years without definite cataplexy, the absence of periods of REM at sleep onset on repeated MSLTs and polysomnograms, and the negativity for HLA-DR2 and DQ1 differentiate these patients from those with classical narcolepsy. A non-REM variant of narcolepsy without cataplexy or sleep onset with REM could be explained with a multimodal model of inheritance of narcolepsy (Nevimalova-Bruhova and Roth, 1972; Meier-Evert *et al.*, 1975; Honda, 1988). The HLA-DR2 haplotype may be crucial for cataplexy and sleep onset with REM, as suggested by its presence in over 95% of Caucasians with narcolepsy and cataplexy. The development of excessive daytime sleepiness in narcolepsy and in the narcoleptic type of idiopathic hypersomnia could depend, however, on other genes and environmental factors, which could thereby account for the rarity of true familial cases of narcolepsy with cataplexy, the reports of monozygotic twins discordant for the disease and the existence of symptomatic forms of narcolepsy.

A proposed new classification of functional hypersomnias based on our findings is shown in Table 4. This classification, which we consider preliminary and subject to revision based on future findings, is supported by prior studies. The following sub-classification of narcolepsy into three types is supported by previous studies: (i) narcolepsy with cataplexy; (ii) narcolepsy with frequent periods of sleep onset with REM but without cataplexy; and (iii) narcolepsy without cataplexy or periods of sleep onset with REM. Several investigators reported series of narcoleptics in which 7–25% had two or more periods of sleep onset with REM on an MSLT but did not have cataplexy (Parkes *et al.*, 1975, Rosenthal *et al.*, 1990, Moscovitch *et al.*, 1993). Roth *et al.* (1969) described 18 patients with narcolepsy but without cataplexy, sleep paralysis or periods of sleep onset with REM. Our findings suggest that the third type is rare, accounting for <5% of all narcoleptic cases. Our findings also suggest that the 'mixed form' of functional hypersomnia, with features of narcolepsy and classic idiopathic hypersomnia, is also rare, but its occurrence in some patients suggests that idiopathic hypersomnia and narcolepsy make up a spectrum of disorders with overlapping clinical features in some cases.

In summary, idiopathic hypersomnia is a rare sleep disorder that, in the absence of a diagnostic gold standard, remains a diagnosis of exclusion. It usually presents in adolescence or young adulthood with hypersomnia of variable character, normal or prolonged night time sleep, and sometimes with awakening difficulties and sleep drunkenness. Sleep recordings are usually normal except for decreased sleep latencies. Sleep paralysis and hypnagogic hallucinations are common but are probably not due to abnormal pressure for REM sleep. The variable character and course of hypersomnia suggest that the syndrome has multiple aetiologies. The 'classic' form of idiopathic hypersomnia may be related in some cases to atypical depression. Some cases of the

**Table 4** Proposed classification of narcoleptic and non-narcoleptic functional hypersomnias**(1) Narcolepsy**

Characterized by sleepiness with short sleep latencies on MSLT and sleep episodes that are usually irresistible, short-lasting and refreshing.

(1a) Narcolepsy with cataplexy (narcolepsy-cataplexy syndrome)

(1b) Narcolepsy without cataplexy but with at least two periods of sleep onset with REM (monosymptomatic narcolepsy)

(1c) Narcolepsy without cataplexy and without periods REM at sleep onset (non-REM narcolepsy variant).

**(2) Idiopathic hypersomnia (classic idiopathic hypersomnia)**

Characterized by sleepiness and sleep episodes that are usually resistible, long-lasting, not refreshing and not associated with frequent periods of sleep onset with REM; sometimes associated with increased total sleep, difficult awakening and sleep drunkenness.

**(3) Mixed forms**

'narcoleptic' type of idiopathic hypersomnia could represent a non-REM variant of narcolepsy. A variant of idiopathic hypersomnia that follows viral infection appears to have a good prognosis. A genetic basis of idiopathic hypersomnia, if any, is probably unrelated to the HLA-haplotypes linked to narcolepsy. Although idiopathic hypersomnia is a chronic disorder, fluctuations and spontaneous remissions are possible and treatment with stimulants, and less commonly with antidepressants, is beneficial in three quarters of the patients. This study supports the hypothesis of the existence, postulated by others before, of both a narcoleptic and a non-narcoleptic non-REM hypersomnia and suggests that current classifications of functional hypersomnias require revision.

**Acknowledgements**

This research was supported in part by the Schweizerische Stiftung für medizinisch-biologische Stipendien. It was presented in part at the Annual Meeting of the Association of Professional Sleep Societies, Washington, DC, June 1996.

**References**

Adie WJ. Idiopathic narcolepsy: a disease sui generis; with remarks on the mechanism of sleep. *Brain* 1926; 49: 257–306.

Aldrich MS. The clinical spectrum of narcolepsy and idiopathic hypersomnia. *Neurology* 1996; 46: 393–401.

Baker TL, Guilleminault C, Nino-Murcia G, Dement WC. Comparative polysomnographic study of narcolepsy and idiopathic central nervous system hypersomnia. *Sleep* 1986; 9: 232–42.

Bastuji H, Jouvet M. Successful treatment of idiopathic hypersomnia and narcolepsy with modafinil. *Prog Neuropsychopharmacol Biol Psychiatry* 1988; 12: 695–700.

Berti Ceroni G, Gambi D, Coccagna G, Lugaresi E. Considerazioni clinico-poligrafiche sulla narcolessia essenziale 'a sonno lento'. *Sist Nerv* 1967; 19: 81–9.

Billiard M, Besset A, Cadilhac J. The clinical and polygraphic development of narcolepsy. In: Guilleminault C, Lugaresi E, editors *Sleep/wake disorders: natural history, epidemiology, and long-term evolution*. New York: Raven Press, 1983: 171–85.

Billiard M, Dolenc C, Aldaz C, Ondze B, Besset A. Hypersomnia associated with mood disorders: a new perspective. *J Psychosom Res* 1994; 38: Suppl 1: 41–7.

Billiard M. Idiopathic hypersomnia. *Neurol Clin* 1996; 14: 573–82.

Billiard M. L'hypersomnie idiopathique. In: Billiard M, editor. *Le Sommeil normal et pathologique. Troubles du sommeil et de l'éveil*. Paris: Masson, 1994.

Boivin DB, Montplaisir J. The effects of L-dopa on excessive daytime sleepiness in narcolepsy [see comments]. *Neurology* 1991; 41: 1267–9. Comment in: *Neurology* 1992; 42: 1640–1.

Broughton RJ. Sleep disorders: disorders of arousal? [Review]. *Science* 1968; 159: 1070–8.

Broughton RJ. Sleep attacks, naps, and sleepiness in medical sleep disorders. In: Dinges DF, Broughton RJ, editors. *Sleep and alertness: chronobiological, behavioural, and medical aspects of napping*. New York: Raven Press, 1989.

Broughton RJ, Aguirre M. Differences between REM and NREM sleepiness measured by event-related potentials (P300, CNV), MSLT and subjective estimate in narcolepsy-cataplexy. *Electroencephalogr Clin Neurophysiol* 1987; 67: 317–26.

Bruck D, Parkes JD. A comparison of idiopathic hypersomnia and narcolepsy-cataplexy using self report measures and sleep diary data. *J Neurol Neurosurg Psychiatry* 1996; 60: 576–8.

Carrot E, Velluz J. Syndrome d'Elpénor. *Presse Méd* 1947; 55: 573.

Carskadon MA, Dement WC, Mitler MM, Roth T, Westbrook PR, Keenan S. Guidelines for the multiple sleep latency test (MSLT): a standard measure of sleepiness. *Sleep* 1986; 9: 519–24.

Claghorn JL, Mathew RJ, Weinman ML, Hruska N. Daytime sleepiness in depression. *J Clin Psychiatry* 1981; 42: 342–3.

Coleman RM, Roffwarg HP, Kennedy SJ, Guilleminault C, Cinque J, Cohn MA, et al. Sleep-wake disorders based on a polysomnographic diagnosis. A national cooperative study. *JAMA* 1982; 247: 997–1003.

Dahlitz M, Parkes JD. Sleep paralysis. *Lancet* 1993; 341: 406–7.

Daniels LE. Narcolepsy. *Medicine* 1934; 13: 1–122.

Dement W, Rechtschaffen A, Gulevich G. The nature of the narcoleptic sleep attack. *Neurology* 1966; 16: 18–33.

- Detre T, Himmelhoch J, Swartzburg M, Anderson CM, Byck R, Kupfer DJ. Hypersomnia and manic-depressive disease. *Am J Psychiatry* 1972; 128: 1303–05.
- Faull KF, Guilleminault C, Berger PA, Barchas JD. Cerebrospinal fluid monoamine metabolites in narcolepsy and hypersomnia. *Ann Neurol* 1983; 13: 258–63.
- Garvey MJ, Mungas D, Tollefson GD. Hypersomnia in major depressive disorders. *J Affect Disord* 1984; 6: 283–6.
- Gélineau JBE. De la narcolepsie. *Gaz Hôp Par* 1880; 53: 626–8, 635–37.
- Gudden H. Die physiologische und pathologische Schlaftrunkenheit. *Arch Psychiat Nervenkrankh* 1905; 40: 989–1015.
- Guilleminault C, Faull KF, Miles L, van den Hoed J. Posttraumatic excessive daytime sleepiness: a review of 20 patients. *Neurology* 1983; 33: 1584–9.
- Guilleminault C, Mondini S. Mononucleosis and chronic daytime sleepiness. A longterm follow-up study. *Arch Intern Med* 1986; 146: 1333–5.
- Harada S, Matsuki K, Honda Y, Someya T. Disorders of excessive daytime sleepiness without cataplexy, and their relationship with HLA in Japan. In: Honda Y, Juji T, editors. *HLA in narcolepsy*. Berlin: Springer-Verlag, 1988: 172–85.
- Hawkins DR, Taub JM, Van de Castle RL. Extended sleep (hypersomnia) in young depressed patients. *Am J Psychiatry* 1985; 142: 905–10.
- Hishikawa Y, Kaneko Z. Electroencephalographic study on narcolepsy. *Electroencephalogr Clin Neurophysiol* 1965; 18: 249–59.
- Hishikawa Y, Nanno H, Tachibana M, Furuya E, Koida H, Kaneko Z. The nature of sleep attack and other symptoms of narcolepsy. *Electroencephalogr Clin Neurophysiol* 1968; 24: 1–10.
- Honda Y. Clinical features of narcolepsy: Japanese experiences. In: Honda Y, Juji T, editors. *HLA in narcolepsy*. Berlin: Springer-Verlag, 1988: 24–57.
- Honda Y, Juji T, Matsuki K, Naohara T, Satake M, Inoko H, et al. HLA-DR2 and Dw2 in narcolepsy and in other disorders of excessive somnolence without cataplexy. *Sleep* 1986b; 9: 133–42.
- Hublin C, Partinen M, Heinonen EH, Puukka P, Salmi T. Selegiline in the treatment of narcolepsy. *Neurology* 1994; 44: 2095–101.
- International classification of sleep disorders: diagnostic and coding manual. Diagnostic Classification Steering Committee. Thorpy MJ, Chairman. Rochester (MN): American Sleep Disorders Association, 1990.
- Johns MW. Sleepiness in different situations measured by the Epworth sleepiness Scale. *Sleep* 1994; 17: 703–10.
- Matsunaga H. Clinical study on idiopathic CNS hypersomnolence. *Jpn J Psychiatry Neurol* 1987; 41: 637–44.
- Meier-Ewert K, Schöpfer B, Rütther E. Drei narkoleptische Syndrome. Katamnestische und polygraphische Ergebnisse. *Nervenarzt* 1975; 46: 624–35.
- Michaelis R. Zur Typologie der Hypersomnien. *Fortschr Neurol Psychiatr Grenzgeb* 1965; 33: 587–99.
- Missriegl A. On the psychogenesis of narcolepsy. *J Nerv Ment Dis* 1941; 93: 141–62.
- Montplaisir J, Poirier G. HLA in disorders of excessive daytime sleepiness without cataplexy in Canada. In: Honda Y, Juji T, editors. *HLA in narcolepsy*. Berlin: Springer-Verlag, 1988: 186–90.
- Moscovitch A, Partinen M, Guilleminault C. The positive diagnosis of narcolepsy and narcolepsy's borderland. *Neurology* 1993; 43: 55–60.
- Nevsimalova-Bruhova S, Roth B. Heredofamilial aspects of narcolepsy and hypersomnia. *Schweiz Arch Neurol Neurochir Psychiatr* 1972; 110: 45–54.
- Nofzinger EA, Thase ME, Reynolds CF 3d, Himmelhoch JM, Mallinger A, Houck P, et al. Hypersomnia in bipolar depression: a comparison with narcolepsy using the multiple sleep latency test. *Am J Psychiatry* 1991; 148: 1177–81.
- Pai MN. Hypersomnia syndromes. *Brit Med J* 1950; 1: 522–4.
- Parkes JD. Day-time drowsiness. *Lancet* 1981; 2: 1213–8.
- Parkes JD, Baraitser M, Marsden CD, Asselman P. Natural history, symptoms and treatment of the narcoleptic syndrome. *Acta Neurol Scand* 1975; 52: 337–53.
- Passouant P, Billiard M. The evolution of narcolepsy with age. In: Guilleminault C, Dement WC, Passouant P, editors. *Narcolepsy*. New York: Spectrum Publications, 1976.
- Petitjean F, Jouvet M. Hypersomnie et augmentation de l'acide 5-hydroxy-indolacétique cérébral par lésion isthmique chez le chat. *C R Seances Soc Biol Fil* 1970; 164: 2288–93.
- Potter WZ, Rudorfer MV, Manji H. The pharmacologic treatment of depression. [Review]. *N Engl J Med* 1991; 325: 633–42.
- Rechtschaffen A, Kales A, editors. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Bethesda (MD): U.S. National Institute of Neurological Diseases and Blindness, Neurological Information Network, 1968.
- Rechtschaffen A, Wolpert EA, Dement WC, Mitchell SA, Fisher C. Nocturnal sleep of narcoleptics. *Electroencephalogr Clin Neurophysiol* 1963; 15: 599–609.
- Redlich E. Epilegomena zur Narkolepsiefrage. *Z ges Neurol Psychiat* 1931; 136: 128–73.
- Ribstein M. Hypnagogic hallucinations. In: Guilleminault C, Dement WC, Passouant P, editors. *Narcolepsy*. Proceedings of the First International Symposium on Narcolepsy. Montpellier: Spectrum Publications, 1976.
- Rosenthal LD, Zorick FJ, Merlotti L, Wittig RM, Roehrs TA, Roth T. Signs and symptoms associated with cataplexy in narcolepsy patients. *Biol Psychiatry* 1990; 27: 1057–60.
- Roth B. Functional hypersomnia. In: Guilleminault C, Dement WC, Passouant P, editors. *Narcolepsy*. Proceedings of the First International Symposium on Narcolepsy. Montpellier: Spectrum Publications, 1976a.
- Roth B. Narcolepsy and hypersomnia: review and classification of 642 personally observed cases. *Schweiz Arch Neurol Neurochir Psychiatr* 1976b; 119: 31–41.

Roth B. Narcolepsy and hypersomnia. Basel: Karger, 1980.

Roth B, Bruhovà S. A clinical and polygraphic study of dreams in narcolepsy and hypersomnia. *Act Nerv Super (Praha)* 1969; 11: 223–8.

Roth B, Nevsimalová S. Depression in narcolepsy and hypersomnia. *Schweiz Arch Neurol Neurochir Psychiatr* 1975; 116: 291–300.

Roth B, Bruhovà S, Lehovský M. REM sleep and NREM sleep in narcolepsy and hypersomnia. *Electroencephalogr Clin Neurophysiol* 1969; 26: 176–82.

Roth B, Nevsimalová S, Rechtschaffen A. Hypersomnia with 'sleep drunkenness'. *Arch Gen Psychiatry* 1972; 26: 456–62.

Schenck CH, Garcia-Rill E, Segall M, Noreen H, Mahowald MW. HLA Class II genes associated with REM sleep behavior disorder. *Ann Neurol* 1996; 39: 261–3.

Schneider-Helmert D, Schenker J, Gnirss F. Deficient blood pressure regulation in a case of hypersomnia with sleep drunkenness. *Electroencephalogr Clin Neurophysiol* 1980; 48: 230–2.

van den Hoed J, Kraemer H, Guilleminault C, Zarcone VP Jr, Miles LE, Dement WC, et al. Disorders of excessive daytime somnolence: polygraphic and clinical data for 100 patients. *Sleep* 1981; 4: 23–37.

Vogel G. Studies in psychophysiology of dreams III. The dream of narcolepsy. *Arch Gen Psychiat* 1960; 3: 421–8.

Wiley MM. Sleep as an escape mechanism. *Psychoanal Rev* 1924; 11: 181–3.

Wilson SAK. The narcolepsies. *Brain* 1928; 51: 63–109.

Yoss RE, Daly DD. Narcolepsy. *Med Clin North Am* 1960; 44: 953–68.

Zorick F, Roehrs T, Koshorek G, Sicklesteel J, Hartse K, Wittig R, et al. Patterns of sleepiness in various disorders of excessive daytime somnolence. *Sleep* 1982; 5 Suppl 2: S165–74.

*Received December 3, 1996. Revised March 1, 1997.*

*Accepted March 17, 1997*