Original article

# The narcoleptic borderland: a multimodal diagnostic approach including cerebrospinal fluid levels of hypocretin-1 (orexin A)

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## Abstract

**Objectives**: Biological markers of narcolepsy with cataplexy (classical narcolepsy) include sleep-onset REM periods (SOREM) on multiple sleep latency tests (MSLT), HLA-DQB1*0602 positivity, low levels of cerebrospinal fluid (CSF) hypocretin-1 (orexin A), increased body mass index (BMI), and high levels of CSF leptin. The clinical borderland of narcolepsy and the diagnostic value of different markers of narcolepsy remain controversial and were assessed in a consecutive series of 27 patients with hypersomnia of (mainly) neurological origin.

**Methods**: Diagnoses included classical narcolepsy ($n = 3$), symptomatic narcolepsy ($n = 1$), narcolepsy without cataplexy ($n = 4$), idiopathic hypersomnia ($n = 5$), hypersomnia associated with psychiatric disorders ($n = 5$), and hypersomnia secondary to neurological disorders or of undetermined origin ($n = 9$). Clinical assessment included BMI, Epworth Sleepiness Scale (ESS), Ullanlinna Narcolepsy Scale (UNS), and history of REM-symptoms (sleep paralysis, hallucinations). HLA-typing, electrophysiological studies (conventional polysomnography, MSLT, 1-week actigraphy), and measurements of CSF levels of hypocretin and leptin were also performed.

**Results**: Hypocretin-1 was undetectable in three patients with classic narcolepsy and detectable in the remaining 24 patients. Other narcoleptic markers also frequently found in patients without narcolepsy included ESS > 14 (78% of 27 patients), UNS > 14 (75%), REM symptoms (30%), sleep latencies on MSLT < 5 min (41%), $\geq 2$ SOREM (30%), DQB1*0602 positivity (52%), BMI > 25 (52%), and increased CSF leptin (48%). Hypersomnia was documented by an increased time 'asleep' in 41% of patients. Overlapping clinical and electrophysiological findings were seen mostly in patients with narcolepsy without cataplexy, idiopathic hypersomnia, and psychiatric hypersomnia.

**Conclusions**: (1) Hypocretin dysfunction is not the 'final common pathway' in the pathophysiology of most hypersomnolent syndromes that fall on the borderline for a diagnosis of narcolepsy. (2) The observed overlap among these hypersomnolent syndromes implies that current diagnostic categories are not entirely unambiguous. (3) A common hypothalamic, hypocretin-independent dysfunction may be present in some of these syndromes.
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*Keywords*: Hypocretin; Leptin; Hypersomnia; Sleep; Narcolepsy; Depression; Idiopathic hypersomnia; Neurological disorder; HLA; Actigraphy; Epworth sleepiness scale; Ullanlinna narcolepsy scale

## 1. Introduction

Human narcolepsy is a neurological disorder characterized by hypersomnia, cataplexy, sleep paralysis and hypnagogic hallucinations [1]. This full tetrad of symptoms is present in only a minority of narcoleptic patients, and cata-plexy is the only pathognomonic symptom of narcolepsy. Biological markers of narcolepsy include sleep-onset REM periods (SOREM) on multiple sleep latency tests (MSLT) and DR2/DQB1*0602 positivity on HLA-typing, which may however be absent in some patients with the disorder [1].

In the absence of a gold standard for the diagnosis of narcolepsy, the definition of its clinical borderland – and in particular the differentiation between such entities as narcolepsy without cataplexy, idiopathic hypersomnia and

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hypersomnia associated with psychiatric disturbances – remains a matter of controversy [2,3].

Hypocretins are peptides, synthesized by neurons in the posterior and lateral hypothalamus, which have widespread projections within the brain and have been implicated in sleep-wake functions, feeding and metabolic control [4]. Recent studies suggest a dysfunction of the newly described hypocretin (orexin) neurotransmitter system in narcolepsy. First, positional cloning has identified hypocretin-receptor-2 gene mutations as the cause of narcolepsy in dogs and orexin knockout mice have a narcolepsy-like phenotype [5,6]. Second, a mutation was found in one of 74 tested human patients and a polymorphism in the prehypocretin gene in six of 178 patients [7,8]. Third, hypocretin-1 was found to be low or absent in the CSF of > 90% of patients with classical narcolepsy (narcolepsy with cataplexy) [9]. In a recent study Ripley et al. confirmed these results, reporting levels of CSF hypocretin-1 < 100 pg/ml in 37 of 42 patients with narcolepsy [11]. Fourth, an 85–95% reduction of hypocretin neuronal expression was demonstrated post mortem in the brains of patients with narcolepsy with cataplexy [7,12]. Finally, an increased body mass index (BMI) and CSF leptin levels were described in narcoleptics, suggesting an altered regulation of food intake and/or metabolism [10,13].

The aim of the study was twofold. First, we wanted to test the hypothesis that CSF hypocretin-1 is reduced also in narcoleptic patients without cataplexy (so-called monosymptomatic narcolepsy) and in patients with other forms of (mainly) neurological hypersomnia, which belong to the borderland of narcolepsy. Second, we wanted to assess the diagnostic value of a multimodal approach including clinical, electrophysiological, genetic, BMI and CSF leptin data in this same patient group.

Preliminary results of this work have been presented before [14]. A few patients reported here were included in a multicenter study [15].

## 2. Subjects and methods

We studied 27 consecutive Caucasian patients (12 women and 15 men; mean age 38 years, range 16–53) with hypersomnia of variable etiology. The main diagnoses (see also Table 1) included narcolepsy with cataplexy (classical narcolepsy, $n = 3$), symptomatic narcolepsy following Bickerstaff's encephalitis ($n = 1$), narcolepsy without cataplexy ($n = 4$), idiopathic hypersomnia ($n = 5$), hypersomnia associated with psychiatric disorders ($n = 6$), HIV-encephalopathy ($n = 1$), brainstem stroke ($n = 2$), periodic hypersomnia ($n = 1$), post-viral illness ($n = 1$), and head trauma ($n = 1$). In two patients, hypersomnia remained of undetermined origin despite extensive work-up.

All patients complained of excessive daytime sleepiness and had an abnormal score ($>10$) on the Epworth Sleepiness Scale (ESS). Sleepiness secondary to insufficient sleep was excluded in all patients where this diagnosis was considered by the absence of a clear-cut improvement of hypersomnia following sleep extension. Pharmacological treatments were discontinued 7–10 days before hospital admission. Assessment included clinical examination, standard sleep questionnaire, Ullanlinna Narcolepsy Scale (UNS [16]), conventional polysomnography, multiple sleep latency test (MSLT), 1-week actigraphy (light sensor data included, Motion-Logger device, Ambulatory Monitoring Inc., Ardsley, NY), HLA-typing, clinical and psychometric evaluations.

An ESS cut-off point of > 14 had given in a previous study a 97% sensitivity and 100% specificity in distinguishing narcoleptics from normal controls [16]. A UNS cut-off point of > 14 was found to have 100% sensitivity and 99% specificity in distinguishing narcoleptics from a mixed group of patients with obstructive sleep apnea, epilepsy, depression, multiple sclerosis, and other conditions [16]. Sleep drunkenness was defined by the presence of a protracted transition from sleep to wakefulness with gait instability, slurred speech, and prolonged time 'to get going' (usually > 30 min) [17].

Lumbar punctures were performed between 13:00 and 16:00 h with the patient lying down; the CSF was frozen at −80 °C. Measurement of hypocretin-1 levels and leptin were performed by radio-immunoassay in crude CSF as previously described [9,11]. Intra-assay variability was 4.3% and the detection limit was 40 pg/ml. The mean hypocretin-1 levels in the CSF of 48 healthy controls was $344 \pm 107$ pg/ml (range: 224–653) and levels < 194 pg/ml were considered as abnormal [11]. The mean leptin levels in the CSF of 34 controls were recently found to be $0.27 \pm 0.10$ ng/ml (range: 0.10–0.35) [10].

All patients were investigated either in Bern ($n = 21$) or in Zurich ($n = 6$), were seen by the principal investigator (C.B.) at least once and gave informed consent for the study. Diagnoses were made according to standard criteria (International Classification of Sleep Disorders). We required, for the purpose of this study, normal psychometric testings for the diagnosis of idiopathic hypersomnia.

## 3. Results

The main results of the study are summarized in Table 1.

### 3.1. Hypocretin levels

Hypocretin-1 was detectable in the CSF of 24 of 27 patients. One of the 24 patients, with a diagnosis of idiopathic hypersomnia, had hypocretin-1 levels above published norms. Hypocretin-1 concentrations were below the detection limit of the assay (<40 pg/ml) in three patients with classical narcolepsy. One patient with hypersomnia after severe head injury and a second patient with post-viral hypersomnia had hypocretin-1 levels below published norms of 176 and 140 pg/ml, respectively. Conversely,

Table 1
Main results of the study[a]

| Gender, date of birth, BMI | ESS/UNS | SP/HH/SD | PSG AHI; PLMI | MSLT SL; SOREM | Actigraphy time 'asleep' | Psychiatric evaluation | CSF-HCT; CSF-Leptin (pg/ml; ng/ml) | HLA/ DR2/DQB1*0602 | Remarks |
|---|---|---|---|---|---|---|---|---|---|
| *Narcolepsy with cataplexy* | | | | | | | | | |
| 1. W.B., male, 1955, 32 | 20/16 | + /+/− | 38; 0 | 2 min; 4/5 | 28% | Normal | < 40; 0.43 | + /+ | |
| 2. N.W., female, 1938, 36 | 20/26 | + /+/+ | 2; 0 | 7 min; 4/4 | NA | Normal | < 40; | + /+ | |
| 3. J.G., female, 1983, 20 | 17/NA | + /−/− | 0; 9 | 2.5 min; 5/5 | NA | Normal | < 40 | + /+ | |
| 4. G.C., male, 1967, 32 | 15/11 | + /+/− | 0; 10 | 2 min; 1/5 | 30% | Normal | 266; 0.22 | − /− | Sympt. narcolepsy |
| *Narcolepsy without cataplexy* | | | | | | | | | |
| 5. M.P., male, 1955, 27 | 21/18 | − /−/− | 7; 0 | 2 min; 2/5 | 28% | Normal | 301; 0.30 | + /+ | |
| 6. D.T., female, 1953, 29 | 19/17 | − /+/+ | 1; 0 | 3 min; 3/5 | 43% | Normal | 262; 0.38 | + /+ | Depression in the past |
| 7. A.G., male, 1956, 24 | 18/17 | − /−/+ | 6; 0 | 1 min; 3/5 | NA | Neurotic disord. | 292; 0.38 | − /− | |
| 8. M.S., male, 1969, 25 | 16/15 | + /+/+ | 0; 0 | 5 min; 2/5 | 29% | Affective disord. | 254; 0.34 | − /− | |
| *Idiopathic hypersomnia (IH)* | | | | | | | | | |
| 9. L.V., female, 1974, 23 | 14/17 | − /−/− | 1; 0 | 12 min; 0/5 | 37% | Normal | 314; 0.29 | − /− | |
| 10. S.S., female, 1970, 30 | 18/19 | − /−/+ | 4; 0 | 4 min; 0/5 | 36% | Normal | 287; 0.47 | + /+ | |
| 11. M.V., female, 1963, 23 | 21/20 | − /−/+ | 2; 0 | 6 min; 0/5 | 36% | Normal | 294; 0.43 | + /+ | |
| 12. S.S., male, 1947, 27 | 17/NA | − /−/+ | 1; 0 | 6 min; 0/5 | 31% | Normal | 266; 0.26 | − /− | Son also with IH |
| 13. H.T., male, 1936, 27 | 17/19 | − /−/− | 8; 0 | 2 min/0/5 | 33% | Normal | 1160 | − /− | Mother with EDS |
| *Hypersomnia associated with psychiatric disorders* | | | | | | | | | |
| 14. H.S., female, 1962, 22 | 17/17 | − /−/− | 0; 0 | 5 min; 0/5 | 50% | Affective disord. | 327 | − /− | |
| 15. E.S., female, 1979, 21 | 14/NA | + /+/+ | 1; 0 | 10 min; 0/5 | 46% | Depression | 243; 0.30 | + /+ | |
| 16. N.F., male, 1956, 28 | 12/24 | + /+/+ | 3; 0 | 6 min; 0/5 | 30% | Depression | 257; 0.30 | − /− | |
| 17. I.B., female, 1975, 32 | 21/13 | − /−/+ | 0; 0 | 6 min; 0/5 | 46% | Depression | 240; 0.49 | NA | |
| 18. E.I., female, 1952, 39 | 24/18 | − /−/+ | 5; 0 | 15 min; 0/5 | 56% | Affective disord. | 316; 0.38 | − /− | Following viral illness |
| 19. M.S., female, 1952, 41 | 18/14 | − /+/+ | 4; 0 | 5 min; 0/5 | 37% | Affective disord. | 290; 0.56 | − /− | Father with IH |
| *Other hypersomnias* | | | | | | | | | |
| 20. G.B., male, 1955, NA | 13/NA | − /−/− | 20; 36 | 5 min; 0/5 | 26% | NA | 214; 0.24 | − /− | HIV encephalopathy |
| 21. M.G., male, 1968, 25 | 19/24 | − /−/− | 0; 0 | 9 min; 0/5 | NA | Normal | 265; 0.21 | NA | Thalamic stroke |
| 22. U.M, male, 1962, 22 | 20/20 | − /−/− | 7; 8 | 1 min; 0/5 | 43% | Normal | 316; 0.38 | NA | Ponto-medullary stroke |
| 23. B.H., male, 1953, 28 | 22/4 | − /−/− | 28; 11 | 10 min; 0/5 | 46% | Normal | 272; 0.39 | − /+ | Periodic hypersomnia |
| 24. S.M., female, 1984, NA | 16/NA | + /−/NA | 1; 0 | 8 min; 2/5 | 39% | NA | 140; 0.43 | + /+ | Following viral illness |
| 25. R.A., male, 1962, 22 | 20/13 | − /−/− | 2; 0 | 3 min; 1/5 | 29% | Normal | 273; 0.27 | + /+ | Unclear |
| 26. F.V., male, 1971, 24 | 12/NA | − /−/− | 0; 0 | 0.3 min; 0/5 | 39% | Normal | 400 | + /+ | Unclear |
| 27. B.S., male, 1973, 21 | 12/NA | − /−/− | 0; 0 | 5 min; 0/5 | 45% | Normal | 176 | NA | Severe head trauma |

[a] BMI, body mass index; ESS, Epworth Sleepiness Score; UNS, Ullanlinna Narcolepsy Scale; SP, sleep paralysis; HH, hypnagogic/hypnopompic hallucinations; SD, sleep drunkenness; AHI, Apnea–hypopnea index; PLMI, periodic limb movements in sleep index; MSLT, multiple sleep latency test; SL, sleep latency; SOREM, sleep-onset REM periods; HCT, hypocretin; NA, not available.
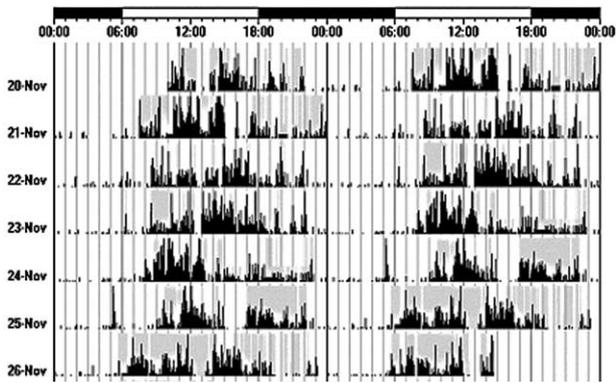
Fig. 1. A 40-year-old woman with hypersomnia associated with psychiatric disorder (H.S., patient no. 14, see Table 1). Actigraphy was performed over 7 days and without any stimulant treatment. This study demonstrates a mean 'time asleep'/day of 12 h (8 h during nighttime, 4 h during daytime). During this week the patient worked only 50% of her time. In this patient the Epworth Sleepiness Score was 17/24 and the mean sleep latency on the MSLT was 5 min (no SOREM). Conventional polysomnography showed a sleep efficiency of 96% and slow-wave sleep (stage 3–4 NREM sleep) during 16% of total sleep time.

hypocretin-1 levels were normal in one patient with symptomatic narcolepsy, in whom catalectic episodes were rare and mild, and in four patients with narcolepsy without cataplexy (monosymptomatic narcolepsy). We also observed normal hypocretin-1 levels in all patients with idiopathic hypersomnia, in all patients with hypersomnia associated with psychiatric disorders, and in the remaining group of patients with hypersomnia of (mainly) neurological origin.

### 3.2. Clinical symptoms and findings

Most patients had a severe subjective daytime sleepiness. The mean ESS was 18 (range 12–24). The ESS was > 14 in 21 (78%) of 27 patients. In all our eight narcoleptics the ESS was > 14. The mean UNS was 17 (range 4–26). The UNS was > 14 in 15 (75%) of 20 patients. In seven of eight narcoleptics the UNS was > 14.

So-called REM symptoms were reported by a significant subgroup of our patients. Sleep paralysis was reported by eight (30%) of 27 patients (in five of eight narcoleptics), hallucinations by eight (30%) of 27 patients (in five of eight narcoleptics), and sleep drunkenness by 12 (46%) of 26 patients (in four of eight narcoleptics). Sleep drunkenness was found also in patients with idiopathic hypersomnia (three of five patients) or hypersomnia associated with psychiatric disorders (five of six patients). Sleep paralysis and hallucinations were uncommon in patients without narcolepsy with the exception of patients with hypersomnia associated with psychiatric disorders. Only four of our ten patients with ≥ 1 SOREM on MSLT reported both sleep paralysis and hallucinations. Conversely, two of six patients reporting both REM symptoms had no SOREM on MSLT.

Psychiatric evaluation was considered abnormal in four of the 14 hypersomnolent patients tested who did not have

hypersomnia associated with psychiatric disorders (in whom psychiatric disturbances were required for inclusion in the study) or idiopathic hypersomnia (in whom the absence of psychiatric disturbances was required for inclusion in the study).

The body mass index (BMI) was elevated (>25) in 13 (52%) of 25 patients, and in six of them the BMI was > 30. Elevated CSF leptin levels (>0.35 ng/ml) were found in 10 of 21 patients. In seven of 11 patients with BMI > 25 CSF leptin levels were also increased.

### 3.3. Electrophysiological studies

Polysomnography documented sleep-disordered breathing (apnea–hypopnea index > 10) in patients with classical narcolepsy (*n* = 1), HIV-encephalopathy (*n* = 1), and periodic hypersomnia (*n* = 1). The latter two patients had also a periodic limb movements in sleep index > 10.

The MSLT documented a mean sleep-latency of < 5 min in 11 of 27 patients, seven of whom had narcolepsy (with or without cataplexy). The presence during MSLT of > 2 SOREM was documented in eight of 27 patients, seven of whom had narcolepsy (with or without cataplexy). Overall, five of our eight narcoleptics had both a mean sleep latency < 5 min and > 2 SOREM. On the other hand, only two of our six patients with hypersomnia associated with psychiatric disorders had a mean sleep latency of > 10 min.

Actigraphy documented an increased mean time 'asleep' ≥ 37%, i.e. ≥ 9 h/day, in 11 of 27 patients including all but one patient with hypersomnia associated with psychiatric disorders (Figs. 1 and 2).
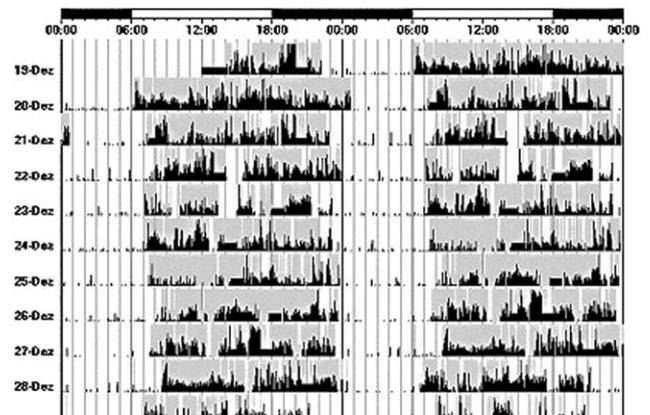


Fig. 2. A 40-year-old man with hypersomnia following ponto-medullary stroke (U.M., patient no. 21, see Table 1). Actigraphy was performed over 15 days and without any stimulant treatment. This study demonstrates a mean 'time asleep'/day of 10.2 h (7.4 h during nighttime, 2.8 h during daytime). During this week the patient worked only 50% of his time. In this patient the Epworth Sleepiness Score was 20/24 and the mean sleep latency on the MSLT was 1 min (no SOREM). Conventional polysomnography showed a sleep efficiency of 97% and slow-wave sleep (stage 3–4 NREM sleep) during 8% of total sleep time.

### 3.4. Genetic studies

In 12 (52%) of 23 patients typing was positive for HLA-DQB1*0602, and in all but one it was also positive for HLA-DR2. A positivity for DR2 and DQB1*0602 in our non-narcoleptic patients was found in 43 and 50%, respectively. It is noteworthy that our single patient with symptomatic narcolepsy was negative for both HLA-markers.

## 4. Discussion

### 4.1. Hypocretin-1 (orexin A) levels in the cerebrospinal fluid

Hypocretin-1 levels in the cerebrospinal fluid, and therefore hypocretin transmission, were not deficient in patients with hypersomnia without cataplexy, including monosymptomatic narcolepsy and idiopathic hypersomnia. In other words, the loss of hypocretin neurons in the lateral hypothalamus may be relevant only for narcoleptics with cataplexy, but not necessarily for narcoleptics without cataplexy and patients with other hypersomnolent syndromes of (presumed) neurological origin. Recent reports of a few patients with hypersomnia, decreased CSF hypocretin levels, and hypothalamic lesions suggest, however, the possibility that in exceptional situations neurological hypersomnia may be associated with (or caused by) a dysfunction of hypocretin transmission.

### 4.2. Multimodal diagnostic approach

The multimodal approach used in this study confirms and expands our knowledge about the clinical overlap of hypersomnolent syndromes without cataplexy. Our findings can be summarized as follows.

*First*, ESS > 12–14 and UNS > 14, previously considered as suggestive of narcolepsy, were confirmed to have a high sensitivity (100 and 88%, respectively) for this diagnosis [18,19]. However, their specificity was low in this series of patients (38 and 40%, respectively). This limits the use, suggested by some, of ESS and UNS in the differentiation of narcoleptic syndromes from other hypersomnias.

*Second*, although this study confirms that so-called REM symptoms (sleep paralysis, hallucinations) are frequent in narcoleptics and often predict the presence of SOREM on MSLT, several exceptions to this rule were observed. Similarly, Aldrich reported a poor correlation between REM sleep propensity – as estimated by the number of SOREM divided by the number of opportunities for SOREM on MSLT and PSG – and sleep paralysis/hallucinations in patients with hypersomnia without cataplexy [20]. These findings suggest, as pointed out before, that sleep paralysis and hallucinations are not invariably related to (detectable) REM sleep abnormalities [2,20,21].

*Third*, we also confirm that sleep drunkenness is not specifically suggestive of idiopathic hypersomnia, as originally proposed by Roth [17], but can occur in a variety of other hypersomnolent syndromes (see Refs. [1,3] for further discussion).

*Fourth*, our MSLT results are in line with the findings of Aldrich et al., showing that the presence of mean sleep latency < 5 min and/or ≥ 2 SOREM is not sensitive/specific enough to be used in isolation for diagnosing narcolepsy [22]. Furthermore, we found that hypersomnia associated with psychiatric disorders may be accompanied by shortened sleep latencies on MSLT. The combination of complaints of excessive daytime sleepiness with altered/depressed mood and increased propensity to lie in bed even when not sleeping (clinophilia), has been recognized for may years and called vegetative/atypical depression [2]. Although many authors have emphasized the normality of MSLT results in these patients [23,24], we show here that 'true hypersomnia'—as defined by a mean sleep latency MSLT < 10 min—can be observed in this clinical context. In fact, hypersomnia associated with psychiatric disorders and idiopathic hypersomnia appeared in this study to be similar in many respects, with the exception of the presence or absence of psychiatric disturbances required for diagnosing both conditions. Female gender, excessive daytime sleepiness with prolonged and deep nighttime sleep, sleep drunkenness, BMI > 25, mean sleep latencies on MSLT > 5 min, absence of SOREM, increased CSF leptin, and increased 'time asleep' on actigraphy appeared to be over-represented in both hypersomnia associated with psychiatric disorders and idiopathic hypersomnia. These findings give further support to the hypothesis that 'atypical depression' and idiopathic hypersomnia may be related, at least in some cases [2]. Further studies are needed to elucidate the nature of this symptom complex, which we suspect may arise from an hypocretin-independent hypothalamic dysfunction. The participation of dopaminergic transmission in promoting wakefulness, regulating eating behavior, and modulating mood and reward mechanisms may turn out to play a central role in these conditions [25–27].

*Fifth*, an increased body mass index (>25) and high levels of CSF leptin, previously reported in human narcolepsy (see above), were found in about 50% of our patients regardless of the etiology of hypersomnia. A few of these patients also had abnormal psychiatric testings and/or increased 'time asleep' on actigraphy. In other words, the association of hypersomnia, increased body mass index/altered energy homeostasis, may be seen in hypersomnolent syndromes other than narcolepsy and may not necessarily be related to a dysfunctional hypocretin transmission.

In summary, our results suggest that normal CSF hypocretin-1 concentrations usually accompany narcolepsy without cataplexy and other (neurological) hypersomnolent syndromes. Thus, hypocretin dysfunction may not necessarily represent the 'final common pathway' in the pathophysiology of hypersomnolent syndromes that fall on the borderline for a diagnosis of narcolepsy. In addition, the observed clinical overlap among these hypersomnolent

syndromes implies that current diagnostic categories are not entirely unambiguous [2,3].

Our observations indicate an unsuspected complexity in the pathophysiology of narcolepsy and related conditions and raise new questions: (1) Do CSF measurements always reflect levels of hypocretin that are present at the active projection areas of the brain? (2) Does the reported destruction of hypocretin neurons occur early or late in narcolepsy, and is such destruction necessary/sufficient to cause cataplexy or the other symptoms of the narcoleptic tetrade? (3) Could a hypothalamic (dopaminergic?) dysfunction be the common underlying cause of such conditions as idiopathic hypersomnia and hypersomnia associated with psychiatric disorders?

## 5. Note

After the submission of this work a paper by Kanbayashi et al. was published reporting normal ($n = 14$) or intermediate (152–198 pg/ml, $n = 3$) levels of CSF hypocretin-1 (orexin A) in a series of Japanese patients with narcolepsy without cataplexy ($n = 5$) and idiopathic hypersomnia ($n = 12$) (J Sleep Res 2002;11:91–3).

## Acknowledgements

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