



## CLINICAL REVIEW

## Socio-professional handicap and accidental risk in patients with hypersomnias of central origin

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## S U M M A R Y

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Narcolepsy and idiopathic hypersomnia profoundly affect quality of life, education and work. Young patients are very handicapped by unexpected sleep episodes during lessons. Professionals frequently complain about sleepiness at work. Motor discomfort (i.e., cataplectic attacks) surprisingly is less handicapping in narcoleptics than sleepiness but only a few studies clearly assess the problem. Quality of life is also largely impaired in its physical and emotional dimensions. Sleepiness is the major factor explaining a decrease of quality of life and unexpectedly cataplectic attacks have little impact on patients. Another potential problem for these patients is the risk of accidents at work or when driving. Narcoleptic and hypersomniac patients have a higher risk of accidents than apneic or insomniac subjects. But, confounding factors such as duration of driving, number of cataplectic attacks or even objective level of alertness are not always entered in the analytic models mainly because of small samples of patients. Unlike in apneic patients, the effect of treatment on accidental risk has not been studied in narcoleptics or in hypersomniacs. Epidemiological data are needed to improve knowledge concerning these areas. Clinical trials assessing the impact of treatment on driving and work are also urgently needed. Finally, medical treatment does not seem to be completely efficient and physicians should pay more attention to the education, work, life and social environment of their patients.

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### Introduction

Adequate alertness is necessary for well-being and performance in modern society. Sleepiness predisposes an individual to develop serious performance decrements in multiple areas of function as well as to potentially life-threatening domestic, work-related and driving accidents.<sup>1</sup> Excessive daytime sleepiness (EDS) is defined as the inability to stay awake and alert during the day and is often a chronic symptom even if it may vary in intensity and frequency. The prevalence of EDS varies from 6 to 25% of the general adult population. The high variability of these results is due to the absence of a consensual definition of the symptom in epidemiological studies.<sup>2,3</sup>

Excessive daytime sleepiness (EDS) may reflect poor sleep hygiene and insufficient nocturnal sleep or be a part of several sleep disorders: circadian rhythm disorders, sleep fragmentation caused

by obstructive sleep apneas or periodic limb movements during sleep. Neurologic illnesses such as Parkinson's disease, head trauma, multiple sclerosis, myotonic dystrophy, Prader–Willi syndrome also affect daytime alertness but the most severe cases of daytime somnolence are found in patients affected by narcolepsy or idiopathic hypersomnia.<sup>1</sup>

Narcolepsy was first described by Gelineau in 1880. It is characterized by excessive daytime sleepiness and cataplexy.<sup>4</sup> Sleep paralysis, hypnagogic hallucinations and nocturnal sleep disruption commonly occur in patients with narcolepsy, but they are not specific.<sup>5</sup> Narcolepsy with cataplexy affects from 20 to 50 subjects for 100 000 adults in the general population. Both genders are affected with a slight male preponderance.<sup>6,7</sup> Genetic and non-genetic predisposing factors are suspected.<sup>8</sup> Narcolepsy with cataplexy is tightly associated with the human leukocyte antigen (HLA) subtypes DR2/DRB1\*1501 and DQB1\*0602. DQB1\*0602 is more specifically associated with narcolepsy.<sup>9</sup> Current evidence suggests that most cases of narcolepsy with cataplexy are associated with the loss of hypothalamic neurons containing the neuropeptide hypocretin. The lack of hypocretin can be assessed by measuring CSF levels of hypocretin-1. The main hypothesis is that

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the cause of most cases is an autoimmune destruction of hypocretin cells which generally occurs during adolescence.<sup>10</sup>

The onset of narcolepsy generally occurs after five years of age and most typically between ages of 15 and 25 years. Diagnosis is often delayed by several years. Narcolepsy with cataplexy can be diagnosed on clinical grounds only but additional tests are useful to confirm the diagnosis. Nocturnal polysomnography followed by multiple sleep latency test (MSLT) is recommended. HLA typing DQB1\*0602 and measuring CSF levels of hypocretin-1 may be useful in non-characteristic clinical cases. However, issues concerning the standardization of CSF hypocretin tests remain.

Idiopathic hypersomnia is characterized by constant and severe excessive sleepiness with prolonged but unrefreshing naps and with or without prolonged total sleep time.<sup>11</sup> These two variants have been separated in the international classification of sleep disorders, 2<sup>nd</sup> version (ICSD-2).<sup>1</sup> Sleep drunkenness is common in idiopathic hypersomnia and the associated symptoms suggesting that a dysfunction of the autonomic nervous system may be present: headaches, orthostatic hypotension and peripheral vascular complaints. A familial predisposition has been reported but, in contrast to narcolepsy, the disorder is not known to be HLA associated. Polysomnography generally demonstrates normal sleep with or without prolonged duration. MSLT usually shows a mean sleep latency of less than 8 min but is typically longer than in narcolepsy.<sup>12,13</sup> The onset of idiopathic hypersomnia usually occurs before 25 years of age.

Narcolepsy and idiopathic hypersomnia may be considered as orphan or rare diseases as they affect less than 0.1% of the population.<sup>2,14</sup> In Europe and in North America there is now a public health concern about helping patients and families affected by these rare diseases. Due to the complexity of the disease, they often experience difficulties to be diagnosed and often face social and professional consequences.<sup>15,16</sup>

Narcolepsy and idiopathic hypersomnia are very symptomatic of the general issue of rare diseases. There are many articles focussing on the genetics and on the pathophysiology of narcolepsy and idiopathic hypersomnia but in the real life the diagnosis is still delayed. There are also few or no specific studies related to the socio-professional handicap or the accidental risk for these patients.

The aim of our review is therefore to focus on the implications of hypersomnias of central origin on education, injuries at work or at the wheel and quality of life, not only to underline the lack of knowledge on the matter, but also to encourage future studies.

### School performance

Narcolepsy usually starts during childhood or early adolescence<sup>17</sup> and, like hypersomnia, may affect school performance. Several studies looked at that potential impact.

- Broughton et al.<sup>18</sup> showed that narcolepsy may have negative effects on student's concentration and ability to learn. They interviewed a group of 180 subjects with narcolepsy. Fifty-one percent of the narcoleptics interviewed believed that their symptoms were the reason for their poor grades and 34% of them thought that narcolepsy explained their interpersonal problems with teachers. The symptoms of the disease caused discomfort for 32% of them and students with narcolepsy often felt socially isolated.
- Stores et al.<sup>19</sup> studied the psychosocial profile of a group of children with narcolepsy ( $n = 42$ ) and compared them with other excessively sleepy children (EDS) ( $n = 18$ ) and controls. The educational assessment which was provided by teachers included days of absence from school during the previous term and their impression about stated key aspects of the child in

the teaching situation. To assess these qualities, items were recoded into a continuous variable by combining values from teacher's ratings of problems with learning, not reaching academic potential, not working hard enough, and being difficult to teach. Each item was scored 0–1 (a score equal to 1 value indicating a problem), providing a composite educational difficulties score ranging from 0 to 4. Due to teachers' time limitation, examination of the children's school records was not considered feasible. Compared to controls, children with narcolepsy and those with excessive daytime sleepiness showed no differences regarding absence rates ( $6.4 \pm 11.9$  days for narcolepsy,  $5.4 \pm 4.8$  days for excessive daytime sleepiness and  $1.4 \pm 2.2$  days for controls). However, the composite educational difficulties score was significantly higher in children with narcolepsy ( $1.98 \pm 1.39$ ) than in controls ( $0.50 \pm 0.68$ ;  $p < 0.001$ ).

These studies were retrospective and limited. We found no additional study on narcoleptics at school.

One important issue is to understand how excessive sleepiness may impact school results. Sleepiness probably affects attention and then memory process. Sleep is useful for memory and several studies have shown that different types of learning have unique sleep-related memory consolidation mechanisms that act in dissociable brain regions at different times throughout the night.<sup>20</sup>

Moreover, sleepiness may also contribute to depression and other psychological problems in narcoleptics, despite treatment for EDS. Narcoleptic patients remain at significant risk for psychiatric and psychosocial disorders<sup>21,22</sup> and their condition may also affect their learning and school performances.

### Absenteeism and performance

It seems that the vast majority of narcoleptics have difficulties facing normal professional activities due to their symptoms. In the Broughton et al.<sup>18</sup> study, a survey of 180 narcoleptic patients with sleep attacks, 95% reported inability to concentrate, 43% memory problems, 31% interpersonal conflicts, 24% personality changes and 18% reported an impact on work performance and professional advancement. Narcoleptics also commonly avoid situations which could be embarrassing or harmful if they have cataplexy or sleep attacks. Besides these objective impairments at work, they also feel uncomfortable to be misperceived as lazy, sleep deprived or drug addicted by colleagues or supervisors at work.

Memory disorders and lack of concentration have also been reported by 40–50% of the patients, who have a tendency to attribute their career difficulties to their memory impairments.<sup>18</sup> Naumann et al.<sup>23</sup> have recently explored the nature and the severity of cognitive deficits in narcoleptics. In two studies, narcoleptic patients were compared to matched controls on a range of attention, memory and executive control tasks. These studies have shown that there were deficits in narcoleptic patients regarding their attention and all executive function tests whereas memory and relatively routine alertness tasks were largely unaffected or mildly impaired.

To our knowledge there are no studies that investigated specifically the absenteeism of narcoleptics. However excessive daytime sleepiness (but not narcolepsy by itself) seems to be linked with increased daytime absenteeism.<sup>24</sup>

Despite the fact that narcolepsy seems to strongly limit job performance, no consensus has been found to quantify the severity of the disease at work or the job handicap. Until now, there was only one German publication<sup>25</sup> which suggested that this disease may benefit from disability process for severe patients. Recently, Ingravallo et al.<sup>26</sup> explored the interobserver reliability of the Italian

Medical Commissions. These committees decide to grant disability and handicap benefits for patients affected by narcolepsy. Fifteen narcoleptic patients were examined by four Medical Commissions in simulated sessions. Levels of judgement differed between the four commissions on the percentage of disability ( $p < 0.001$ ), the severity of handicap ( $p = 0.0007$ ) and the need to inform driving license authority ( $p = 0.032$ ). The authors found a low interobserver reliability among Medical Commissions in their decisions to grant or not disability and handicap benefits. Even if the different Medical Commissions shared common clinical indicators for narcolepsy's severity such as EDS, numbers of daytime naps, cataplexy severity and quality of life impairment; they failed to evaluate patient's handicap evenly. Commissions only agreed on identifying the most severe and the mildest patients. There was no consensus on the minimum benefit a patient with narcolepsy should gain, essentially due to the inability to quantify the patient's handicap. This result illustrates the need of a better quantitative and qualitative evaluation of patients with narcolepsy in professional settings in order to perform a consensual procedure for handicap evaluation.

Narcolepsy may indeed result in unemployment. Different studies have shown an important rate of unemployment among patients with narcolepsy, varying from 30%<sup>21</sup> to 59%.<sup>27</sup> In most cases, patients blamed narcolepsy for their unemployment.<sup>17,27</sup>

### Quality of life

Undeniably, narcolepsy has an impact on quality of life. Quality of life is a general concept that combines different areas. Domains of life considered to be affected by illnesses are called health-related quality of life (HRQoL). Generic and specific tools have been developed to assess HRQoL but most of these measures do not include sleep as a specific dimension.<sup>28</sup> Among the available questionnaires, the Medical Outcomes Study 36-items Short Form (SF-36) is the most frequently used.<sup>29</sup> This questionnaire includes 36 questions divided in eight dimensions of health: physical functioning, role limitation due to physical problems, role limitation due to emotional problems, social functioning, mental health, energy/vitality, pain and general health perception. The higher the score, the better the quality of life. The SF-36 includes the dimension "vitality" but does not ask any direct question about sleep. Beside these generic measures, the Functional Outcomes of Sleep Questionnaire (FOSQ) specifically assesses the impact of excessive sleepiness on physical, mental and social functioning in everyday activities.<sup>30</sup>

Sleep is recognized to play an important role in our life and its quality. Several studies have shown that patients suffering from sleep disorders such as sleep apnea, narcolepsy, restless legs syndrome and insomnia have a poorer quality of life than the general population, particularly when related to energy and fatigue.<sup>28,31</sup>

Regarding sleepiness, Briones et al.<sup>32</sup> first showed its major impact on HRQoL. Using the SF-36 scale, they studied 129 subjects from 25 to 65 years old and without severe chronic medical or psychiatric diseases. They demonstrated that 3 dimensions of the SF-36 ("general health perception", "energy/fatigue" and "role limitations due to emotional problems") had a score significantly correlated with the score of the Epworth Sleepiness Scale (ESS) ( $r = -0.30$ ,  $-0.41$ , and  $-0.30$  respectively;  $p$  values were all  $< 0.001$ ). Sleepiness, as assessed by ESS score, explained 8% of the variance in general health perceptions, 17% of the variance in energy/fatigue, 6% of the variance in the summary well-being, and 3% of the variance in the summary measure of functional status. Interestingly, the multiple sleep latency test (MSLT), an objective measure of sleepiness, was also correlated with "energy/fatigue" ( $r = -0.19$ ;  $p < 0.05$ ).

In 2001, a British study<sup>33</sup> described the health status and psychosocial aspects of people with narcolepsy. They used the SF-36, the Beck depression inventory (BDI), and the Ullanlinna narcolepsy scale (UNS), which is an epidemiological tool designed to diagnose narcolepsy. A total of 305 questionnaires were included in the final analysis. The results showed that the subjects had significantly lower median scores on all eight domains of the SF-36 than normative data, and scored particularly poorly for the domains of role physical, energy/vitality, and social functioning. The BDI indicated that 56.9% of subjects had some degree of depression and the BDI was found as influencing significantly the SF-36 scores of narcoleptics. However, a high prevalence of depression is common in narcoleptic patients compared to the general population.<sup>34</sup> The SF-36 scores of treated patients were not significantly different to the ones of untreated patients, indicating that the treatment seemed insufficient to adequately restore the quality of life of patients. More sophisticated studies are however needed to clarify that point.

An Italian study<sup>35</sup> also used the SF-36 in EDS patients affected by narcolepsy or other sleep disorders. One hundred and eight adults with narcolepsy, 115 with obstructive sleep apnea syndrome (OSAS) and 42 with idiopathic hypersomnia (IH) were enrolled for a multicentric cross-section study employing self-administered questionnaires investigating the HRQoL (SF-36), EDS and cataplexy. A psychometric analysis and the standardized scoring of the 8 scales of the SF-36 were performed. The correlation between SF-36 scales and clinical features of narcolepsy was measured by a multiple linear regression analysis. Narcoleptic patients presented lower scores in all domains of the SF-36 scale (except for the dimension "Bodily Pain") compared to the reference for the Italian population. Some of the variance of physical functioning ( $R^2$  0.07), role functioning-Physical ( $R^2$  0.31), general health ( $R^2$  0.15), vitality ( $R^2$  0.10), social functioning ( $R^2$  0.21) and role functioning-Emotional ( $R^2$  0.15) was explained both by EDS (inverse correlation) and disease duration (direct correlation). The more severe the sleepiness, the lower the SF-36 score; and the longer the duration of the disease, the lower the SF-36 score. Namely, the narcoleptic group was not homogeneous including patients with and without treatment. The duration of the disease had more impact on SF-36 in non-treated patients than in treated ones. Narcolepsy seriously impacts patients' health-related quality of life in terms of physical and emotional functions, and restricting social life. EDS is obviously the main symptom determining this impairment and surprisingly cataplexy did not show any correlation with SF-36 scales.

The effect of narcolepsy on HRQoL was also investigated by Dodel et al.<sup>36</sup> by using the SF-36 and the EQ-5D Health Utility Index in 75 narcoleptic patients. The EQ-5D is an instrument with five questions on mobility, self-care, pain, usual activities and psychological status. It includes visual analogic scales on quality of life. Other sociological factors (employment status, living with a partner, professional advancement), which may influence HRQoL in narcoleptics, were also examined. In this study, narcoleptic patients also presented considerably lower scores in all 8 dimensions of the SF-36 than the reference of the general German population. It was also demonstrated narcolepsy had a significant impact on the EQ-5D score. The patients specifically complained about the impact of narcolepsy on "usual activity" (63.8%), "pain/discomfort" (61.7%), and "anxiety/depression" (41.1%). However, apart from irresistible sleep episodes ( $p < 0.03$ ), signs and symptoms of narcolepsy had non-significant independent impact on HRQoL. The analysis showed a strong influence of employment status, living with a partner, and professional advancement in most of the SF-36 subdimensions and on the EQ-5D.

Finally, Teixeira et al.<sup>17</sup> compared the impact of treated narcolepsy on HRQoL with the impact of obstructive sleep apnea/hypopnea

syndrome (OSAHS) treated or not by continuous positive airway pressure (CPAP). The SF-36 and the Functional Outcomes of Sleep Questionnaire (FOSQ) were used. The FOSQ is designed to assess the impact of sleep disorders on multiple activities of everyday living.<sup>30</sup> It includes 30 items exploring five domains: general productivity, social outcome, activity level, vigilance and intimate relationships. Forty-nine treated narcolepsy patients, 56 untreated OSAHS and 48 CPAP treated OSAHS patients were recruited for this study. It showed that treated narcoleptics had lower SF-36 scores than treated OSAHS patients and similar SF-36 results than untreated OSAHS patients. Narcoleptics had also lower FOSQ scores than both treated and untreated OSAHS patients. Moreover, they were sleepier than OSAHS patients on ESS scores ( $p < 0.001$ ).

These results are in favour of a persistent impact of narcolepsy on HRQoL even in treated patients. However, several limitations of this study have to be taken into consideration: the small number of patients and the lack of data about compliance of patients.

Conversely, one study demonstrated the improvement of HRQoL in narcoleptics treated with modafinil.<sup>37</sup> Subjects with narcolepsy enrolled in a nine-week, placebo-controlled, double-blind study and were randomized to placebo, modafinil 200 mg, or modafinil 400 mg. After the study, consenting subjects received modafinil in a 40-week open-label extension. The SF-36 was given to subjects at baseline, study endpoint, and several open-label time points. 481 subjects completed a baseline and double-blind endpoint HQL assessment. Compared to population norms, baseline HQL scores reflected substantial burden in vitality, social functioning, and performing usual activities. At study endpoint, subjects in the 400 mg modafinil group had significantly higher scores than placebo for 10 of the 17 HQL scales. The 400 mg modafinil group had more energy, fewer difficulties performing usual activities, fewer interferences with social activities, improved psychological well-being and higher productivity, attention and self-esteem compared to placebo subjects ( $p < 0.05$ ). The positive treatment effects were sustained over the open-label extension.

Another study evaluated the effects of modafinil on sustained attention performance and quality of life in patients with sleep apnea syndrome presenting residual sleepiness while being treated with nasal continuous positive airway pressure (nCPAP).<sup>38</sup> This randomized, double-blind, placebo-controlled, parallel-group

study demonstrated that modafinil used adjunctively improved performance on the psychomotor vigilance task (PVT) and reduced functional impairments measured by the FOSQ. After 1 week and 4 weeks of treatment, nCPAP plus modafinil improved FOSQ total scores compared with treatment of nCPAP plus placebo ( $p < 0.05$ ). The FOSQ vigilance subscale score showed improvement at week 1 for patients receiving nCPAP plus modafinil relative to those receiving nCPAP plus placebo treatment ( $p = 0.032$ ). After 4 weeks, activity level and vigilance subscales of the FOSQ also demonstrated significant improvement ( $p < 0.05$ ).

The efficacy of sodium oxybate versus placebo to improve quality of life in patients with narcolepsy was evaluated in a multicenter, double-blind, placebo-controlled trial.<sup>39</sup> The change of quality of life was measured by the FOSQ in 285 participants, aged between 16 and 75 years old with a median Epworth sleepiness scale score of 18 and a maintenance of wakefulness test sleep latency of 9.56 min. Results showed that the administration of sodium oxybate produced significant dose-related improvements in the total FOSQ and particularly in the activity level, general productivity, vigilance and social outcomes subscales.

The main results concerning relationships between narcolepsy and quality of life evaluated by the SF-36 scale are summarised in Table 1.

### Driving and professional accidental risk

Elevated risks of motor vehicle crashes due to sleepiness and cataplexy in patients with untreated narcolepsy have been reported very early in the literature.<sup>40</sup> Sleep disorders are a significant contributing factor in motor vehicle accidents.<sup>41</sup> The proportion of individuals with sleep-related accidents is 1.5- to fourfold higher in the hypersomnolent patients group than in the control group. Apneics and narcoleptics account for 71% of all sleep-related accidents. 49% of male narcoleptics and 30% of female narcoleptics reported a sleep-related accident when only 13% of male apneics and 9% of female apneics did. These results show a higher risk for narcoleptics compared to apneic patients.

Interestingly in the Aldrich study,<sup>41</sup> the patients presented more sleep-related accidents than controls, but they did not present a higher risk for total accidents.

**Table 1**  
Narcolepsy and quality of life.

Study	Groups	SF-36 (mean $\pm$ SD or 95% CI)							
		Physical function	Role physical	Bodily pain	General health	Vitality	Social functioning	Role emotional	Mental health
Briones et al. <sup>32</sup>	ESS < 12	82 $\pm$ 21	81 $\pm$ 33	75 $\pm$ 26	73 $\pm$ 18	64 $\pm$ 17	88 $\pm$ 18	85 $\pm$ 29	78 $\pm$ 13
	ESS > 12	75 $\pm$ 4	74 $\pm$ 33	72 $\pm$ 27	63 $\pm$ 21	50 $\pm$ 20	83 $\pm$ 21	79 $\pm$ 33	75 $\pm$ 15
	<i>p</i> value	>0.100	>0.100	>0.100	0.008	0.001	>0.100	>0.100	>0.100
Beusterien et al. <sup>37</sup>	Narcolepsy untreated (placebo)	79 (76,81)	45 (39,50)	73 (69,76)	67 (65,69)	35 (32,38)	62 (58,65)	59 (53,64)	66 (64,69)
	Narcolepsy + Modafinil 200 mg	82 (80,84)*	53 (48,59)*	73 (69,76)	69 (67,72)	43 (40,46)*	66 (62,69)	66 (60,71)	69 (67,71)
	Narcolepsy + Modafinil 400 mg	80 (78,83)	59 (53,64)*	72 (69,75)	68 (66,70)	45 (42,48)*	71 (67,74)*	69 (64,75)*	70 (67,72)
Vignatelli et al. <sup>35</sup>	Narcolepsy	82 $\pm$ 19	49 $\pm$ 38	72 $\pm$ 28	57 $\pm$ 22	50 $\pm$ 20	59 $\pm$ 26	51 $\pm$ 42	61 $\pm$ 19
	OSAS	78 $\pm$ 22	57 $\pm$ 42	75 $\pm$ 25	57 $\pm$ 19	54 $\pm$ 19	69 $\pm$ 23	61 $\pm$ 42	65 $\pm$ 20
	Idiopathic hypersomnia	84 $\pm$ 21	48 $\pm$ 42	77 $\pm$ 23	60 $\pm$ 17	50 $\pm$ 20	61 $\pm$ 28	47 $\pm$ 44	62 $\pm$ 20
Teixeira et al. <sup>17</sup>	Narcolepsy	68 (53,70)	25 (24,51)	68 (59,77)	49 (42,57)**	40 (30,43)	50 (44,63)	33 (42,68)	60 (50,64)**
	Untreated OSAHS	75 (54,73)	50 (33,58)	61.5 (49,66)	47 (42,57)**	35 (28,40)	50 (47,65)	67 (37,64)	60 (54,66)**
	Treated OSAHS	80 (67,82)	50 (42,64)	67 (57,74)	71 (54,69)	30 (27,40)	63 (53,71)	67 (50,73)	76 (65,77)
Dodel et al. <sup>36</sup>	Narcolepsy	77 $\pm$ 23	45 $\pm$ 40	72 $\pm$ 30	54 $\pm$ 18	40 $\pm$ 20	62 $\pm$ 31	70 $\pm$ 40	66 $\pm$ 19

\* $p < 0.05$  for difference between treatment group and placebo.

\*\* $p < 0.001$  for difference between treated OSAHS patients and narcoleptics.

SD: standard deviation.

95% CI: 95 percent confidence intervals.

ESS: Epworth sleepiness scale.

OSAS: obstructive sleep apnea syndrome.

OSAHS: obstructive sleep apnea/hypopnea syndrome.

Other studies in larger samples have shown that apneic patients present a higher risk than controls for traffic accidents,<sup>42</sup> which contradict the Aldrich study findings. But, the very small samples (228 apneics and 56 narcoleptics) can explain the absence of significant results.

Kotterba et al.<sup>43</sup> studied a population of 43 men and 41 women affected by narcolepsy and compared them with a control group of 48 men and 47 women. Narcoleptic patients reported a higher accidental rate than controls but this difference was present only in narcoleptics under the age of 40. Above the age of 40, patients did not differ in terms of accidental risk. These results could mean that older narcoleptics tend to cope better with their disease and adapt their driving behaviour to their handicap unlike younger drivers.

George and collaborators<sup>44</sup> compared the performance on the divided-attention driving test (DADT) of 21 male obstructive sleep apnea (OSA) patients, 21 sex-matched controls and 16 narcoleptics. Narcoleptic patients were younger and sleepier than OSA patients. Tracking error was worse in patients than controls ( $228 \pm 145$  cm for OSA versus  $196 \pm 146$  for narcolepsy versus  $71 \pm 31$  for controls;  $p < 0.001$ ). These results tend to confirm that narcoleptic patients have a higher driving risk than controls.

Kotterba et al.<sup>45</sup> tested 13 narcoleptics versus 10 healthy adults on a driving simulator during 1 h of various driving conditions.

The authors did not find major differences in terms of driving performance between both groups. However, they noticed that after appropriate treatment the accident rate significantly decreased in 5 of the 13 patients. This shows that alerting treatments could improve driving performance in such patients.

Up to now, no study has differentiated the risk of cataplectic patients versus non-cataplectic patients. It would be worth knowing the respective role of motor impairment versus sleep attacks in the driving risk of narcoleptic patients.

More recently, Powell et al.<sup>46</sup> performed a prospective cross-sectional internet-linked survey on driving behaviours to quantify the prevalence of self-reported near-miss sleepy driving accidents and their association with self-reported actual driving accidents. 35 217 (88% of sample) individuals were included in the study. The mean age was  $37.2 \pm 13$  years; the sample included 54.8% women, and 87% Caucasian. Patients affected by narcolepsy reported a four times higher relative risk of accident due to sleepiness (in the three last years) than patients without narcolepsy (OR 3.99 [2.48–6.42],  $p < 0.0001$ ) and a two times higher relative risk of near-miss accident (OR 1.95 [1.53–2.49],  $p < 0.0001$ ). In comparison, patients affected by sleep apnea reported a 2.5 times higher relative risk of accident (in the same period) than those without sleep apnea (OR 2.48 [1.86–3.31],  $p < 0.0001$ ) and a 1.83 higher relative risk of near-miss accident (OR 1.83 [1.65–2.04],  $p < 0.0001$ ).

Using a very different methodology, this study demonstrates that narcoleptic drivers tend to present a higher driving risk than apneic drivers.

Even if there is strong evidence for the accidental risk of patients affected by narcolepsy, the actual legislation is very different depending on countries or even states.<sup>47,48</sup> This proves how difficult it is to quantify driving impairment in these patients.

Maintenance of wakefulness test has been proposed to evaluate driving skill in apneic patients.<sup>49,50</sup> Narcoleptics could benefit from a similar approach to have a better clinical evaluation.

## Final comments

Similarly to many other rare diseases, narcolepsy and idiopathic hypersomnia have not received enough attention from authorities and researchers. This may explain the small amount of data on the social and professional impact of these diseases. Patients are rare,

researchers and scientists involved in the field are few and research findings are therefore scarce.

However, this review underlines the fact that quality of life of patients with narcolepsy is similar or worse than the one of patients with Parkinson's disease or obstructive sleep apnea. But conversely to these two last diseases, which affect people in the second part of the life, narcolepsy can affect subjects in childhood with an impact on school performance and possibly on professional career. Unfortunately, actual options for physicians to evaluate the impacts of narcolepsy on day life areas are limited. Therefore we recommend to systematically ask patients on their quality of life since the beginning of the disease and to assess the effects of treatment on it.

The development of public health plans for rare diseases in Europe and in the United States would improve the level of knowledge. More data are needed to help students and adults with hypersomnia in their affected daily lives.

## Practice points

- We recommend that physicians take systematically account of school performance, work progression, quality of life and social insertion in the evaluation of treatment in hypersomnias of central origin.
- Quality of life can be assessed routinely by several questionnaires such as SF-36 or FOSQ.
- We recommend the regular use of MWT (Maintenance of wakefulness tests) to help physicians in their decisions regarding driving ability of treated hypersomniacs.
- We recommend that physicians help their patients with hypersomnia in finding jobs adapted to their diseases: partial time jobs, avoiding jobs at risk of accidents, napping facilities, no regular driving.
- Patients' associations may facilitate social and professional insertion.

## Research agenda

- Epidemiological data on social and professional impact of narcolepsy and idiopathic hypersomnia (work accidents, absenteeism...) are needed to improve patient management.
- International consensus and guidelines are an issue to improve safety and to prevent accidents.
- Epidemiological data on school life and education consequences of narcolepsy and idiopathic hypersomnia are urgently needed.
- Clinical trials to evaluate the impact of treatment on patient's risk of accidents are necessary to improve road safety.

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